
The Plague of Thebes, a Historical Epidemic in Sophocles' Oedipus Rex

Antonis A. Kousoulis,
Konstantinos P. Economopoulos,
Effie Poulakou-Rebelakou, George Androutsos,
and Sotirios Tsiodras

Sophocles, one of the most noted playwrights of the ancient world, wrote the tragedy Oedipus Rex in the first half of the decade 430–420 BC. A lethal plague is described in this drama. We adopted a critical approach to Oedipus Rex in analyzing the literary description of the disease, unraveling its clinical features, and defining a possible underlying cause. Our goals were to clarify whether the plague described in Oedipus Rex reflects an actual historical event; to compare it with the plague of Athens, which was described by Thucydides as occurring around the same time Sophocles wrote; and to propose a likely causative pathogen. A critical reading of Oedipus Rex and a comparison with Thucydides' history, as well as a systematic review of historical data, strongly suggests that this epidemic was an actual event, possibly caused by *Brucella abortus*.

“Wailing on the altar stair, wives and grandams rend the air, long-drawn moans and piercing cries blent with prayers and litanies”—Sophocles, Oedipus Rex, lines 184–186

Sophocles is one of the most noted playwrights of the ancient world and, along with Aeschylus and Euripides, belongs to the trinity of the Attic tragedians who flourished during the golden century of Pericles in Athens (Figure 1). Sophocles lived between 496 and 406 BC; although he seems to have written 123 plays, only 7 have survived in a complete form (1). He lived his entire life in Athens and introduced many innovations in the dramatic arts (1).

The writing of the tragedy Oedipus the King (original Greek title Οιδίππου τύραννος, most commonly known as

Author affiliations: University of Athens Medical School, Athens, Greece (A.A. Kousoulis, K.P. Economopoulos, E. Poulakou-Rebelakou, G. Androutsos, S. Tsiodras); and Society of Junior Doctors, Athens (A.A. Kousoulis, K.P. Economopoulos)

DOI: <http://dx.doi.org/10.3201/eid1801.AD1801>

Oedipus Rex) is placed in the first half of the decade 430–420 BC. The play has been labeled an analytical tragedy, meaning that the crucial events which dominate the play have happened in the past (2,3).

Oedipus Rex, apart from the undeniable literary and historic value, also presents significant medical interest because the play mentions a plague, an epidemic, which was devastating Thebes, the town of Oedipus' hegemony. Several sections, primarily in the first third of the play, refer to the aforementioned plague; the epidemic, however, is not the primary topic of the tragedy. The epidemic, in fact, is mostly a matter that serves the theatrical economy by forming a background for the evolution of the plot.

Given the potential medical interest of Oedipus Rex, we decided to adopt a critical perspective by analyzing the literary descriptions of the plague, unraveling its clinical features, defining the underlying cause, and discussing possible therapeutic options. The ultimate goals of our study were to clarify whether the plague described in Oedipus Rex could reflect an actual historical event, compare it with the plague of Athens, which was described by the historian Thucydides as occurring not long before the time that Sophocles' work appeared (4), and propose the most likely causative pathogen.

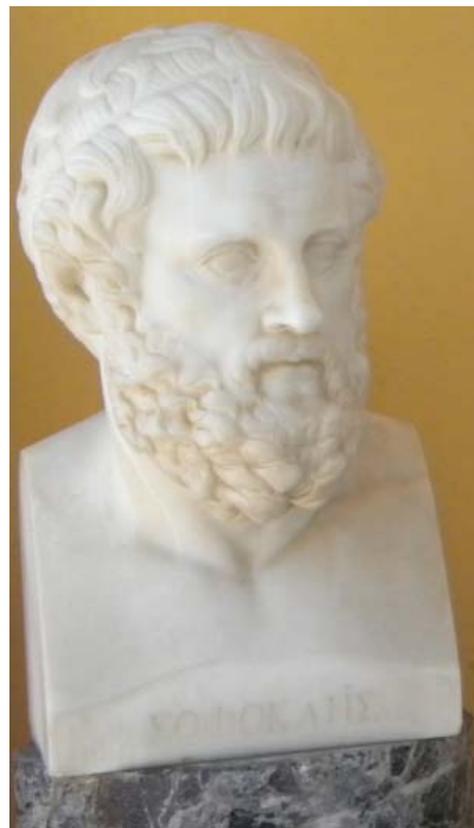


Figure 1. Bust of Sophocles in the Colonnade of the Muses in the Achilleion, Corfu, Greece, July 2011. Photo courtesy Antonis A. Kousoulis.

An Epidemic in Oedipus Rex

In the first scene of the play, Sophocles presents the basic social and historical axes around which he will unfold the plot. The devastating plague that dominates Thebes is presented to the audience through the dialogue between Oedipus and the Priest (lines 1–67) (2,3). The king has already taken some action to deal with this harm by sending his brother-in-law, Creon, to the oracle at Delphi to ask for a salvation plan (lines 68–72). The oracle announces that the plague is a result of religious pollution and that the god Apollo requests that the people of Thebes exile the previously unknown “miasma” (a word of Greek origin with a sense of moral noxious pollution) away from the town (lines 96–98) (2,3). Oedipus asks the citizens to stop praying and focus on finding the cure (lines 142–146) (2,3). In lines 167–215, the Chorus stays on stage to summarize the situation and beg for salvation (2,3).

Searching for the miasma, Oedipus summons the blind prophet Tiresias to reveal who is responsible for this evil (lines 300–313) (2,3). At the moment that Tiresias reveals to Oedipus that the king himself is the cause of the plague (lines 350–353), the epidemic becomes a secondary issue, and, as a result, there are only occasional references to the



Figure 2. Scene from a National Theatre of Greece production of Oedipus Rex at the Odeon of Herodus Atticus, Athens, Greece January 1995. Photo courtesy Effie Poulakou-Rebelakou.

plague during the remainder of the play (lines 665–666, 685–686, 1380–1383, 1424–1428) (2,3).

Therefore, although the first part of the play is rife with references to the plague and its consequences, in the second part there are only sporadic referrals to the epidemic. The fate of Oedipus emerges as a truly tragic one, not so much because he caused the plague, but because of the character’s own personal tragedy (Figure 2).

A Medical Critical Approach to Oedipus Rex

From the start of the drama, the plague in Thebes is a serious matter, as in line 23 where it is referred to as “weltering surge of blood” (φορνίου σάλου). In line 28 the word plague (λοιμός) appears for the first time, with the Greek word for disease (νόσος) being used in lines 150, 217, and 303 (2,3).

Sophocles describes the main characteristics of the epidemic through sporadic sentences. Early in the play it is clarified that the disease is a cattle zoonosis of high mortality rate (“a blight upon the grazing flocks and herds,” line 26, with the herds being cattle,) (2,3). The lethality of this epidemic is particularly terrifying for the protagonists of the play, and the disease’s severity is evinced by the first sentences of the tragedy (“reek of incense everywhere,” line 4). Oedipus fears mass destruction of the city of Thebes (“with the god’s good help success is sure; ‘tis ruin if we fail,” line 146), while the words “weltering surge of blood” (line 24), “fiery plague” (line 166), “the land is sore distressed” (line 685), and “wailing on the altar stair, wives and grandams rend the air, long-drawn moans and piercing cries blent with prayers and litanies” (lines 184–186) (2,3) all illustrate vividly the severity of the situation.

The references to the decline of land and fields could be an example of poetic exaggeration or a suggestion that the fruits or ears may participate in the transmission route of the plague (“a blight is on our harvest in the ear,” line 25) (2,3). Regarding the specific clinical features of the disease, it is clear that the causative pathogen leads to miscarriages or stillbirths (“a blight on wives in travail,” lines 26–27, meaning women give birth to dead babies) (2,3). The plague’s effects are also pointed out by the Chorus: “earth her gracious fruits denies” and “women wail in barren throes” (lines 151, 215) (2,3).

Lines 179–181 turn out to be of high interest: “wasted thus by death on death all our city perishes; corpses spread infection round” (2,3). A word with a meaning of something that brings death is used in the original Greek (θανατοφόρα) to refer to the plague, which suggests that at the time of Sophocles his fellow Greeks were aware of the threat posed by infectious disease. The knowledge of the existence of a highly contagious and fatal disease is phrased clearly in these rhymes, strongly suggesting that Thebans were aware of the oncoming—most possibly from the adjacent city

of Athens—danger (2–4). This hypothesis regarding the source of the disease seems the most reasonable in medical terms, contrary to the philological approach, which declares that the epidemic derived from the gods.

In addition, the Chorus provides us with a major social aspect, as they put the blame on god of war, Ares (“Ares whose hot breath I feel, though without targe or steel he stalks, whose voice is as the battle shout,” lines 190–191) (2,3). It is not quite clear why Ares is being called responsible for this plague, since there is no other such reference in the play. In fact, it is noteworthy that there is no other historic or poetic reference that links Ares to the spreading of a disease (4). However, Thucydides’ correlation of the plague of Athens with the Peloponnesian War (431–404 BC) (5) gives us the opportunity to state that Sophocles connects this epidemic of Thebes with the plague of Athens and attempts to point out the disastrous effects wars always have.

Regarding the play’s approach to treatment of the disease, reading through the drama we once again come across with the theocratic perceptions of ancient Greece. The citizens have become suppliants to the monuments of the gods, asking for mercy (“Why sit ye here as suppliants, in your hands branches of olive filleted with wool?,” lines 2–3; “the common folk, with wreathed boughs crowd our two market-places, or before both shrines of Pallas congregate, or where Ismenus gives his oracles by fire,” lines 19–21) (2,3). Consequently, a solution for the situation is requested from the oracle at Delphi (lines 68–72), while the Chorus plead for Athena, Zeus, Artemis, and Apollo to save the town from the disaster (lines 160–165) (2,3). The aforementioned aspects strongly support the notion that the disease was incurable at this time.

Possible Pathogens Responsible for the Plague in Thebes

The pathogen of the plague described in Oedipus Rex reflects the complexity of every historically emerging zoonosis. Any proposed pathogen should be a highly contagious, zoonotic disease of cattle that causes stillbirth, miscarriages, and infertility, is characterized by high mortality rates, and has the potential to have caused an epidemic in the 5th century BC. The characteristics of pathogens that might be responsible for the plague on the basis of Sophocles’ descriptions in Oedipus Rex are summarized in the online Technical Appendix (wwwnc.cdc.gov/EID/pdfs/11-0449-Techapp.pdf).

After a close inspection of the characteristics, the pathogens that include most (5 of 7) of the features described by Sophocles in Oedipus Rex are *Leishmania* spp., *Leptospira* spp., *Brucella abortus*, *Orthopoxviridae*, and *Francisella tularensis*. Among the diseases caused by these pathogens that can affect humans are the following: 1) tularemia, which

is a disease mainly transmitted through rabbits; 2) smallpox, which is not a cattle zoonosis; 3) leishmaniasis, which is not a highly contagious disease; and 4) leptospirosis, which has been associated with epidemics after rainfall and flooding in relation to rodent infestation. Thus, the most probable cause of the plague in Thebes is *B. abortus*. Brucellosis is a highly contagious zoonosis caused by ingestion of unsterilized milk or meat from infected cows or close contact with their secretions. The mortality rate for untreated brucellosis is difficult to determine from the literature of the preantibiotic era (6); nevertheless, an 80% rate has been reported in situations of comorbidity with endocarditis (7). Epidemics, stillbirths, and miscarriages caused by *B. abortus* have been reported since the time of Hippocrates, which is when this disease was initially described.

However, taking into account that in modern times brucellosis in humans is a severe granulomatous disease characterized by extremely rare direct transmission from person-to-person, insidious onset in sporadic cases (mainly among veterinarians), and low mortality rates, it may be difficult for 21st century physicians and veterinarians to accept *B. abortus* as the causative agent of the plague of Thebes. Alternatively, the plague of Thebes could be a composite of ≥ 2 causative agents, as it has been suggested for the contemporary plague of Athens (6,7). In this case scenario, we could assume that cattle in Thebes may have been having brucellosis, leptospirosis, or listeriosis, while humans could have been affected by a different pathogen such as *Salmonella enterica* serovar Typhi (8,9). It should be noted that exploring the diseases of history requires examining the social, economic, and demographic aspects of each era because this is the only way to better understand how diseases work over centuries (10). Finally, we cannot reject the possibility of dealing with a *Brucella* strain that has evolved to become less deadly than a more lethal ancestor (6).

Thucydides’ Plague of Athens and Sophocles’ Epidemic

The plague that is described in Oedipus Rex could possibly be related to the plague that struck Athens in 430–429 BC (11), the primary source for which is the papers of historian Thucydides (where he refers to an epidemic that has been named the plague of Athens) (5). The following 5 points support this correlation.

Proximate Eras

The first writing of Oedipus Rex most probably took place during the time of the plague of Athens. Sophocles’ epidemic seems to have enough strength to appear as a historical base on which the theatrical economy of the play is evolving (12). The opening of the drama, with the city of Thebes in the midst of plague has often been, historically,

taken as a reference to the plague that devastated Athens in the opening years of the Peloponnesian War and has been used to assist in the dating of this play (13).

Similar Descriptions by Thucydides and Sophocles

Thucydides and Sophocles use similar terms when describing attempts to deal with the epidemic. In the historical case (Athens) and the dramatic case (Thebes), the populace turned to the temples looking for a divine solution to the disaster.

Correlation with Recent Warfare

As mentioned above, in Sophocles' drama, god of war Ares gets the blame for the plague (lines 190–191). The particularity of this reference (4), it seems that Sophocles correlates the epidemic that strikes Thebes with the plague of Athens, which, according to Thucydides, came about as a result of the Peloponnesian War (5).

Similarities Regarding the Nature of the Diseases

It is difficult to compare a historical record to a poetic drama, but, keeping that in mind, both Sophocles and Thucydides refer to animal illness and death (2,8). In addition, the realistic descriptions of the historian and the nightmarish lyrical rhymes of the poet, talk about a disease with a high mortality rate (2,10). As for the clinical features, although Thucydides does not mention the pregnancy or labor pains as described in Sophocles' text, he does refer to abdominal and vulvovaginal symptoms (5).

Common Assumptions about the Possible Causative Pathogen

Historical medical literature has suggested many infectious diseases over time, but few have lasted as the most probable. These diseases mainly include typhoid fever, epidemic typhus, smallpox, plague, measles, and influenza, all of which could be initial candidates for the plague in Oedipus Rex and have been taken into account in this study (online Technical Appendix) (9,10).

Although the above points are of great relevance, they lack the possibility of historical verification and are mainly based on the comparative and critical assessment of Sophocles' and Thucydides' work. Historical certainty can be added by studying the alliances and the warfare involving Thebes during the era of Sophocles (e.g., Boeotian prefecture, Athenian dynasty, Spartan alliance, Persian wars) (14). Bearing in mind the aforementioned observations and the fact no other epidemics were reported in the eastern Mediterranean during the 5th century BC, we posit that the plague described by Sophocles in the tragedy Oedipus Rex has an actual basis in the plague of Athens described by Thucydides in his histories.

Discussion

A severe plague is described in Sophocles' drama Oedipus Rex. According to the World Health Organization, an epidemic is defined as a disease outbreak and, therefore, the occurrence of cases of disease in excess of what would normally be expected in a defined community, geographic area, or season (15). Thus, according to the tragedy's rhymes and with respect to literary talk, this plague should be treated as an epidemic.

It would not be irrational to trust the historical credibility of a literary text. Literature usually reflects the echo of the past. A somewhat similar example is that of archeologist Heinrich Schlieman; before Schlieman, the writings of Homer had been considered a collection of mythological poems. However, with his excavations in Troy, which used the Iliad as a guide, Schlieman provided a perfect example of how literary work can have a factual base (16).

Moreover, we could not overlook that Sophocles is the most realist of the Greek tragedians (1), and ancient tragedies were often placed into a historical frame strongly influenced by major contemporary events (13). Finally, although many of the features of the plot and passages have been interpreted as historical allusions, the plague seems to be recognized as the most critical element that reflects a historical event, with enough strength and clarity to be used even for the dating of the tragedy (12).

Conclusions

The critical reading of Oedipus Rex, its comparison with Thucydides' history, as well as the systematic review of the existing historical data, lead us to strongly suggest that this epidemic, for which the name Plague of Thebes may be used, was an actual historical fact, likely caused by *B. abortus*. With the deadly plague, which struck one of the most historic Greek cities, on the one hand and the tragic fate of a character who has become among the most recognizable in world theater on the other, Sophocles masterminded a dramatic frame and offered a lyrical, literary description of a lethal disease. As the protagonist approached his tragic catharsis, the moral order much desired by the ancient Greeks was restored with the end of the epidemic.

Dr Kousoulis is a research assistant in the History of Medicine Department of the University of Athens and the general secretary of the Society of Junior Doctors. His primary research interests include history of medicine, medical sociology, and epidemiology.

References

1. Sommerstein A. Greek drama and dramatists. New York: Taylor & Francis; 2004.

2. Sophocles. Oedipus the king [in Greek]. Athens: Kaktos; 1993.
3. Sophocles. Storr F, translator. Oedipus the king. London: William Heinemann Ltd; 1912.
4. Rousos T. Comments on Oedipus Rex by the philology group of Kaktos Publications. In: Sophocles. Oedipus the king [in Greek]. Athens: Kaktos; 1993. p. 163–77.
5. Thucydides. Crawley R, translator. The History of the Peloponnesian war. Ware Hertfordshire (UK): Wordsworth Editions Ltd; 1997.
6. Durack DT, Littman RJ, Benitez RM, Mackowiak PA. Hellenic holocaust: a historical clinico-pathologic conference. *Am J Med.* 2000;109:391–7. doi:10.1016/S0002-9343(00)00521-0
7. Langmuir AD, Worthen TD, Solomon J, Ray CG, Petersen E. The Thucydides syndrome. A new hypothesis for the cause of the plague of Athens. *N Engl J Med.* 1985;313:1027–30. doi:10.1056/NEJM198510173131618
8. Papagrigorakis MJ, Synodinos PN, Yapijakis C. Ancient typhoid epidemic reveals possible ancestral strain of *Salmonella enterica* serovar Typhi. *Infect Genet Evol.* 2007;7:126–7. doi:10.1016/j.meegid.2006.04.006
9. Papagrigorakis MJ, Yapijakis C, Synodinos PN, Baziotopoulou-Valavani E. DNA examination of ancient dental pulp incriminates typhoid fever as a probable cause of the Plague of Athens. *Int J Infect Dis.* 2006;10:206–14. doi:10.1016/j.ijid.2005.09.001
10. Littman RJ. The plague of Athens: epidemiology and paleopathology. *Mt Sinai J Med.* 2009;76:456–67. doi:10.1002/msj.20137
11. Wilson GN. Disease. In: Group TF, editor. Encyclopedia of ancient Greece. New York, USA; 2006. p. 233.
12. Knox BM. The date of the Oedipus Tyrannus of Sophocles. *American Journal of Philology.* 1956;77:133–47.
13. Storey IC. Aspects of ancient Greek drama. In: Storey IC, Allan A, editors. A guide to ancient Greek drama. Oxford: Wiley-Blackwell; 2004. p. 1–71.
14. Pedagogical Institute, Hellenic Ministry of Education. Ancient History. Athens: Didactic Books Publishing Organization 2009.
15. World Health Organization. Health Topics. Disease Outbreaks. 2010 [cited 2010 Sep 12]. http://www.who.int/topics/disease_outbreaks/en/
16. Yardley M, Rutka J. Troy, Mycenae, and the otologic demise of Herr Heinrich Schliemann. *J Otolaryngol.* 1998;27:217–21.

Address for correspondence: Antonis A. Kousoulis, History of Medicine Department, School of Medicine, University of Athens, 131 Lambrou Katsoni Str., Athens, 18344 Greece; email: antonis.kousoulis@gmail.com

etymologia

Prion

[pri'on, pre'on]

From *protein* + *infection*. Nobel laureate Stanley B. Prusiner, American neurologist and biochemist, coined the word prion in 1982 to describe the noninfectious agents he proposed as the cause of scrapie. Prusiner noted that, “Because the dominant characteristics of the scrapie agent resemble those of a protein, an acronym is introduced to emphasize this feature... the term ‘prion’ (pronounced *pree-on*) is suggested.” Prions are now recognized as etiologic agents of other transmissible spongiform encephalopathies, including bovine spongiform encephalopathy and Creutzfeldt-Jakob disease.

Sources: Dorland's Illustrated Medical Dictionary. 31st ed. Philadelphia: Saunders; 2007; The Nobel Prize in Physiology or Medicine 1997: Stanley B. Prusiner [cited 2011 Oct 25]; http://nobelprize.org/nobel_prizes/medicine/laureates/1997/prusiner-autobio.html; Prusiner SB. Novel proteinaceous infectious particles cause scrapie. *Science.* 1982;216:136–44. doi:10.1126/science.6801762

The Plague of Thebes, a Historical Epidemic in Sophocles' Oedipus Rex

Technical Appendix

Table. Characteristics of pathogens possibly responsible for the plague of Thebes described by Sophocles in Oedipus Rex*

Pathogen	Disease	Zoonosis in cattle	Stillbirth/miscarriage	Infertility	Highest reported acute mortality rate	Highly contagious (droplets/aerosol transmission)	Epidemics have been described	Described as early as 5 th century BC
<i>Yersinia pestis</i>	Plague	No (reported mainly in rodents, cats, camels) (1,2)	NA	NA	100% (1,2)	Yes (2)	Yes (1,2)	Probably yes (1350 BC) (3)
<i>Leishmania</i> spp.	Leishmaniasis	Yes (4)	Yes (≈10.5% for cutaneous and visceral) (5)	NA	70% (6)	No (sandfly bite) (7)	Yes (7)	Probably yes (7th century or possibly as early as 2500 to 1500 BC) (8)
<i>Leptospira</i> spp.	Leptospirosis	Yes (9)	Yes (in acute infection) (9)	NA (reported in animals)	50–70% (10)	No (rarely reported direct transmission between humans) (9)	Yes, usually in association with rainfalls, flooding and rodent infestation (9)	Probably yes (recognized as an occupational hazard of rice harvesting in ancient China) (9)
<i>Lyssavirus</i> spp.	Rabies	Yes (11)	NA	NA	100% (11)	No (11)	Yes (12)	Yes (Eshuma Code of Babylon circa 2000 BC) (11)
Hepatitis E Virus	Hepatitis E (13)	Yes (13)	Yes (13)	NA	4% (13) (73% in pregnancy) (14)	No (13,14)	Yes (13,14)	No (earliest outbreak attributed to HEV was in Delhi, 1955) (13,15)
Coronaviridae	Common cold, SARS	Yes (16)	NA	NA	15% (55% in persons >60 years of age) (17)	Yes (17)	Yes (16,17)	No (first characterized in the 1960s) (18)
<i>Influenzavirus A</i>	Influenza	Yes (19)	Yes (20)	No (21)	5–10% (22) (may be higher) (23)	Yes (24)	Yes (22,23)	Yes (25)
<i>West Nile virus</i>	West Nile virus infection	No (26,27)	No (26,27)	NA	10% (26)	No (26–28)	Yes (26,27)	Probably not (molecular dating shows low possibility of human infection before 1000 years ago) (29)
DEN 1-4 <i>Flaviviruses</i>	Dengue and dengue hemorrhagic fever	Not the same virus in humans and cattle (30,31)	Not in a high rate (32)	NA	47% (33)	No (30)	Yes (30)	No (earliest record of Dengue symptoms found in China, during Chin dynasty, 265-420 A.D.) (30)

Pathogen	Disease	Zoonosis in cattle	Stillbirth/miscarriage	Infertility	Highest reported acute mortality rate	Highly contagious (droplets/aerosol transmission)	Epidemics have been described	Described as early as 5 th century BC
<i>Brucella abortus</i>	Brucellosis	Yes (34)	Yes (35)	No (34) (only in natural host) (36)	80% in cases in which endocarditis was concurrently present (37)	Yes (38)	Yes (39)	Probably yes (known since the time of Hippocrates) (40)
<i>Listeria monocytogenes</i>	Listeriosis	Yes (41)	Yes (42)	No (43)	63% (42)	No (42)	Yes (42)	No (early 20 th century) (44)
<i>Orthopoxviridae</i>	Smallpox	No (45)	Yes (46)	Yes (47)	30% (48)	Yes (48)	Yes (48)	Yes (observations from 1100-1580 BC, even earlier phylogenetic origin) (49)
<i>Measles virus</i>	Measles	Yes (not reported in cows) (50)	Yes (51)	No (52)	15% (after encephalitis) (52)	Yes (52)	Yes (53)	No (not described BC, and recent phylogenetic analysis showed its origin in 11th–12th century AD) (54)
<i>Salmonella typhi</i>	Typhoid fever	No (55)	Yes (56)	NA	30% (when left untreated) (57)	No (58)	Yes (59)	Yes (60)
<i>Francisella tularensis</i>	Tularemia	Yes (mainly on rabbits, ticks, deerflies, squirrels) (61)	No (reported in sheep) (62)	NA	60% (63)	Yes (63)	Yes (63)	Probably yes (earliest outbreak credited, in 1715 BC Canaan) (64)
<i>Yersinia enterocolitica</i>	Gastroenteritis	No (mainly in pigs, dogs, cats, sheep and wild rodent strains) (65)	No (reported in sows, cattle) (66)	NA	50% (after septicemia) (67)	No (65)	Yes (68)	Probably not (<i>Yersinia</i> spp. is an ancient pathogen (3), first recognized reference to <i>Y. enterocolitica</i> in the USA in 1934 (69))
<i>Rickettsia prowazekii</i>	Epidemic typhus	No (mainly in flying squirrels) (70)	NA	NA	60% (70)	Yes (70)	Yes (71)	Yes (may have originated millions of years ago) (72)
<i>Lymphocytic Choriomeningitis Virus</i>	Choriomeningitis	No (mainly in rodents, house mice, pet hamsters) (73)	Yes (74)	NA	30% (among infants diagnosed with congenital infection) (74)	Yes (73)	Yes (75)	Probably yes (LCMV is quite ancient and the extensive diversity of the virus has accumulated over the past 1,000–5,000 years) (76)
<i>Aspergillus</i> spp.	Aspergillosis	Yes (77)	No (most frequent cause of abortions in cattle) (77,78)	NA	86% (treated immunocompromised patients) (77)	Yes (77)	Yes (79)	No (first introduced in 1729) (80)

*NA, not available; SARS, severe acute respiratory syndrome; LCMV, lymphocytic choriomeningitis virus; HEV, hepatitis E virus; BC, before Christ.

References

1. Stenseth NC, Atshabar BB, Begon M, Belmain SR, Bertherat E, Carniel E, et al. Plague: past, present, and future. *PLoS Med.* 2008;5:e3. [PubMed doi:10.1371/journal.pmed.0050003](#)
2. Perry RD, Fetherston JD. *Yersinia pestis*—etiologic agent of plague. *Clin Microbiol Rev.* 1997;10:35–66. [PubMed](#)
3. Freemon FR. Bubonic plague in the Book of Samuel. *J R Soc Med.* 2005;98:436. [PubMed doi:10.1258/jrsm.98.9.436](#)
4. Bern C, Courtenay O, Alvar J. Of cattle, sand flies and men: a systematic review of risk factor analyses for South Asian visceral leishmaniasis and implications for elimination. *PLoS Negl Trop Dis.* 2010;4:e599. [PubMed doi:10.1371/journal.pntd.0000599](#)
5. Pagliano P, Carannante N, Rossi M, Gramiccia M, Gradoni L, Faella FS, et al. Visceral leishmaniasis in pregnancy: a case series and a systematic review of the literature. *J Antimicrob Chemother.* 2005;55:229–33. [PubMed doi:10.1093/jac/dkh538](#)
6. Seaman J, Mercer AJ, Sondorp E. The epidemic of visceral leishmaniasis in western Upper Nile, southern Sudan: course and impact from 1984 to 1994. *Int J Epidemiol.* 1996;25:862–71. [PubMed doi:10.1093/ije/25.4.862](#)
7. Roberts LJ, Handman E, Foote SJ. Science, medicine, and the future: Leishmaniasis. *BMJ.* 2000;321:801–4. [PubMed doi:10.1136/bmj.321.7264.801](#)
8. Cox FE. History of human parasitology. *Clin Microbiol Rev.* 2002;15:595–612. [PubMed doi:10.1128/CMR.15.4.595-612.2002](#)
9. Levett PN. Leptospirosis. *Clin Microbiol Rev.* 2001;14:296–326. [PubMed doi:10.1128/CMR.14.2.296-326.2001](#)
10. Vijayachari P, Sugunan AP, Shriram AN. Leptospirosis: an emerging global public health problem. *J Biosci.* 2008;33:557–69. [PubMed doi:10.1007/s12038-008-0074-z](#)
11. Hankins DG, Rosekrans JA. Overview, prevention, and treatment of rabies. *Mayo Clin Proc.* 2004;79:671–6. [PubMed doi:10.4065/79.5.671](#)
12. Windiyarningsih C, Wilde H, Meslin FX, Suroso T, Widarso HS. The rabies epidemic on Flores Island, Indonesia (1998-2003). *J Med Assoc Thai.* 2004;87:1389–93. [PubMed](#)

13. Labrique AB, Thomas DL, Stoszek SK, Nelson KE. Hepatitis E: an emerging infectious disease. *Epidemiol Rev.* 1999;21:162–79. [PubMed](#)
14. Navaneethan U, Al Mohajer M, Shata MT. Hepatitis E and pregnancy: understanding the pathogenesis. *Liver Int.* 2008;28:1190–9. [PubMed](#)
[doi:10.1111/j.1478-3231.2008.01840.x](https://doi.org/10.1111/j.1478-3231.2008.01840.x)
15. Hosseini-Moghaddam SM, Zarei A, Alavian SM, Mansouri M. Hepatitis E virus infection: a general review with a focus on hemodialysis and kidney transplant patients. *Am J Nephrol.* 2010;31:398–407. [PubMed](#) [doi:10.1159/000294505](https://doi.org/10.1159/000294505)
16. Holmes KV. SARS coronavirus: a new challenge for prevention and therapy. *J Clin Invest.* 2003;111:1605–9. [PubMed](#)
17. Anderson RM, Fraser C, Ghani AC, Donnelly CA, Riley S, Ferguson NM, et al. Epidemiology, transmission dynamics and control of SARS: the 2002-2003 epidemic. *Philos Trans R Soc Lond B Biol Sci.* 2004;359:1091–105. [PubMed](#) [doi:10.1098/rstb.2004.1490](https://doi.org/10.1098/rstb.2004.1490)
18. Kahn JS, McIntosh K. History and recent advances in coronavirus discovery. *Pediatr Infect Dis J.* 2005 Nov;24(11 Suppl):S223-7, discussion S6.
19. Dos Reis M, Tamuri AU, Hay AJ, Goldstein RA. Charting the host adaptation of influenza viruses. *Mol Biol Evol.* 2010 Nov 25.
20. MacKenzie JS, Houghton M. Influenza infections during pregnancy: association with congenital malformations and with subsequent neoplasms in children, and potential hazards of live virus vaccines. *Bacteriol Rev.* 1974;38:356–70. [PubMed](#)
21. Mamelund SE. Effects of the Spanish Influenza pandemic on fertility and nuptiality in Norway. XXIV Conference on General Population; 2001 18-24 August; Salvador, Brazil; 2001.
22. Potter CW. A history of influenza. *J Appl Microbiol.* 2001;91:572–9. [PubMed](#) [doi:10.1046/j.1365-2672.2001.01492.x](https://doi.org/10.1046/j.1365-2672.2001.01492.x)
23. Guerra F. The earliest American epidemic. The influenza of 1493. *Soc Sci Hist.* 1988;12:305–25. [PubMed](#) [doi:10.2307/1171451](https://doi.org/10.2307/1171451)
24. Tellier R. Review of aerosol transmission of influenza A virus. *Emerg Infect Dis.* 2006;12:1657–62. [PubMed](#)
25. Martin PM, Martin-Granel E. 2,500-year evolution of the term epidemic. *Emerg Infect Dis.* 2006;12:976–80. [PubMed](#)

26. Sampathkumar P. West Nile virus: epidemiology, clinical presentation, diagnosis, and prevention. *Mayo Clin Proc.* 2003;78:1137–43, quiz 44. [PubMed doi:10.4065/78.9.1137](#)
27. Hayes EB, Komar N, Nasci RS, Montgomery SP, O’Leary DR, Campbell GL. Epidemiology and transmission dynamics of West Nile virus disease. *Emerg Infect Dis.* 2005;11:1167–73. [PubMed](#)
28. From the Centers for Disease Control and Prevention. Laboratory-acquired West Nile virus infections—United States, 2002. *JAMA.* 2003;289:414–5. [PubMed doi:10.1001/jama.289.4.414](#)
29. Galli M, Bernini F, Zehender G. Alexander the Great and West Nile virus encephalitis. *Emerg Infect Dis.* 2004;10:1330–2, author reply 2–3. [PubMed](#)
30. Gubler DJ. Dengue and dengue hemorrhagic fever. *Clin Microbiol Rev.* 1998;11:480–96. [PubMed](#)
31. Nandi S, Negi BS. Bovine ephemeral fever: a review. *Comp Immunol Microbiol Infect Dis.* 1999;22:81–91. [PubMed doi:10.1016/S0147-9571\(98\)00027-7](#)
32. Carroll ID, Toovey S, Van Gompel A. Dengue fever and pregnancy—a review and comment. *Travel Med Infect Dis.* 2007;5:183–8. [PubMed doi:10.1016/j.tmaid.2006.11.002](#)
33. Malavige GN, Fernando S, Fernando DJ, Seneviratne SL. Dengue viral infections. *Postgrad Med J.* 2004;80:588–601. [PubMed doi:10.1136/pgmj.2004.019638](#)
34. Pappas G, Akritidis N, Bosilkovski M, Tsianos E. Brucellosis. *N Engl J Med.* 2005;352:2325–36. [PubMed doi:10.1056/NEJMra050570](#)
35. Khan MY, Mah MW, Memish ZA. Brucellosis in pregnant women. *Clin Infect Dis.* 2001;32:1172–7. [PubMed doi:10.1086/319758](#)
36. Olsen S, Tatum F. Bovine brucellosis. *Vet Clin North Am Food Anim Pract.* 2010;26:15–27. [PubMed doi:10.1016/j.cvfa.2009.10.006](#)
37. Langmuir AD, Worthen TD, Solomon J, Ray CG, Petersen E. The Thucydides syndrome. A new hypothesis for the cause of the plague of Athens. *N Engl J Med.* 1985;313:1027–30. [PubMed doi:10.1056/NEJM198510173131618](#)

38. Ergonul O, Celikbas A, Tezeren D, Guvener E, Dokuzoguz B. Analysis of risk factors for laboratory-acquired brucella infections. *J Hosp Infect.* 2004;56:223–7. [PubMed doi:10.1016/j.jhin.2003.12.020](#)
39. Markovic-Denic L, Trifunovic VS, Zugic V, Radojic D, Stevanovic G. The first outbreak of brucellosis in the region of Sabac. *Vojnosanit Pregl.* 2010;67:634–7. [PubMed doi:10.2298/VSP1008634M](#)
40. Kyebambe PS. Acute brucella meningomyeloencephalo-spondylosis in a teenage male. *Afr Health Sci.* 2005;5:69–72. [PubMed](#)
41. Troutt HF, Osburn BI. Meat from dairy cows: possible microbiological hazards and risks. *Rev Sci Tech.* 1997;16:405–14. [PubMed](#)
42. Silver HM. Listeriosis during pregnancy. *Obstet Gynecol Surv.* 1998;53:737–40. [PubMed doi:10.1097/00006254-199812000-00004](#)
43. Gomez-Mampaso E, Baquero Mochales F, de Rafael Nerpel L, Michaux Oquinena L, Garcia-Villalba A. [Listeriosis and fertility (author's transl)]. *Reproduccion.* 1980;4:309–14. [PubMed](#)
44. Seeliger HP. Listeriosis—history and actual developments. *Infection.* 1988;16(Suppl 2):S80–4. [PubMed doi:10.1007/BF01639726](#)
45. Baum SG. Zoonoses—with friends like this, who needs enemies? *Trans Am Clin Climatol Assoc.* 2008;119:39-51; discussion -2.
46. Constantin CM, Martinelli AM, Foster SO, Bonney EA, Strickland OL. Smallpox: a disease of the past? Consideration for midwives. *J Midwifery Womens Health.* 2003;48:258–67, 302–4. [PubMed doi:10.1016/S1526-9523\(03\)00084-9](#)
47. Phadke AM, Samant NR, Dewal SD. Smallpox as an etiologic factor in male infertility. *Fertil Steril.* 1973;24:802–4. [PubMed](#)
48. Breman JG, Henderson DA. Diagnosis and management of smallpox. *N Engl J Med.* 2002;346:1300–8. [PubMed doi:10.1056/NEJMra020025](#)
49. Li Y, Carroll DS, Gardner SN, Walsh MC, Vitalis EA, Damon IK. On the origin of smallpox: correlating variola phylogenics with historical smallpox records. *Proc Natl Acad Sci U S A.* 2007;104:15787–92. [PubMed doi:10.1073/pnas.0609268104](#)
50. Coulibaly ND, Yameogo KR. Prevalence and control of zoonotic diseases: collaboration between public health workers and veterinarians in Burkina Faso. *Acta Trop.* 2000;76:53–7. [PubMed doi:10.1016/S0001-706X\(00\)00090-5](#)
51. Stein SJ, Greenspoon JS. Rubella during pregnancy. *Obstet Gynecol.* 1991;78:925–9. [PubMed](#)

52. Elliman D, Sengupta N, El Bashir H, Bedford H. Measles, mumps, and rubella: prevention. *Clin Evid (Online)*. 2007;2007.
53. Siegfried N, Wiysonge CS, Pienaar D. Too little, too late: measles epidemic in South Africa. *Lancet*. 2010;376:160. [PubMed](#)
[doi:10.1016/S0140-6736\(10\)61100-2](https://doi.org/10.1016/S0140-6736(10)61100-2)
54. Furuse Y, Suzuki A, Oshitani H. Origin of measles virus: divergence from rinderpest virus between the 11th and 12th centuries. *Virology*. 2010;7:52. [PubMed](#) [doi:10.1186/1743-422X-7-52](https://doi.org/10.1186/1743-422X-7-52)
55. Gorbach SL, Bartlett JG, Blacklow NR. *Infectious Diseases*. 3rd ed. Philadelphia: Lippincott Williams & Wilkins; 2004.
56. Awadalla SG, Mercer LJ, Brown LG. Pregnancy complicated by intraamniotic infection by *Salmonella typhi*. *Obstet Gynecol*. 1985;65(Suppl):30S–1S. [PubMed](#)
57. Crump JA, Luby SP, Mintz ED. The global burden of typhoid fever. *Bull World Health Organ*. 2004;82:346–53. [PubMed](#)
58. Meltzer E, Schwartz E. Enteric fever: a travel medicine oriented view. *Curr Opin Infect Dis*. 2010;23:432–7. [PubMed](#)
[doi:10.1097/QCO.0b013e32833c7ca1](https://doi.org/10.1097/QCO.0b013e32833c7ca1)
59. Cabello F, Springer AD. Typhoid fever in Chile 1977-1990: an emergent disease [in Spanish]. *Rev Med Chil*. 1997;125:474–82. [PubMed](#)
60. Papagrigorakis MJ, Yapijakis C, Synodinos PN, Baziotopoulou-Valavani E. DNA examination of ancient dental pulp incriminates typhoid fever as a probable cause of the Plague of Athens. *Int J Infect Dis*. 2006;10:206–14. [PubMed](#) [doi:10.1016/j.ijid.2005.09.001](https://doi.org/10.1016/j.ijid.2005.09.001)
61. Geiger JC. Tularemia in cattle and sheep. *Cal West Med*. 1931;34:154–6. [PubMed](#)
62. O'Toole D, Williams ES, Woods LW, Mills K, Boerger-Fields A, Montgomery DL, et al. Tularemia in range sheep: an overlooked syndrome? *J Vet Diagn Invest*. 2008;20:508–13. [PubMed](#) [doi:10.1177/104063870802000417](https://doi.org/10.1177/104063870802000417)
63. Feldman KA, Ensore RE, Lathrop SL, Matyas BT, McGuill M, Schriefer ME, et al. An outbreak of primary pneumonic tularemia on Martha's Vineyard. *N Engl J Med*. 2001;345:1601–6. [PubMed](#) [doi:10.1056/NEJMoa011374](https://doi.org/10.1056/NEJMoa011374)
64. Trevisanato SI. The biblical plague of the Philistines now has a name, tularemia. *Med Hypotheses*. 2007;69:1144–6. [PubMed](#)
[doi:10.1016/j.mehy.2007.02.036](https://doi.org/10.1016/j.mehy.2007.02.036)

65. Fredriksson-Ahomaa M, Stolle A, Korkeala H. Molecular epidemiology of *Yersinia enterocolitica* infections. FEMS Immunol Med Microbiol. 2006;47:315–29. [PubMed doi:10.1111/j.1574-695X.2006.00095.x](#)
66. Platt-Samoraj A, Szweda W, Procajlo Z. The influence of experimental *Yersinia enterocolitica* infection on the pregnancy course in sows— preliminary studies. I. Bacteriological examination. Pol J Vet Sci. 2009;12:317–22. [PubMed](#)
67. Vento S, Cainelli F, Cesario F. Infections and thalassaemia. Lancet Infect Dis. 2006;6:226–33. [PubMed doi:10.1016/S1473-3099\(06\)70437-6](#)
68. Gourdon F, Beytout J, Reynaud A, Romaszko JP, Perre D, Theodore P, et al. Human and animal epidemic of *Yersinia enterocolitica* O:9, 1989–1997, Auvergne, France. Emerg Infect Dis. 1999;5:719–21. [PubMed doi:10.3201/eid0505.990516](#)
69. Bottone EJ. *Yersinia enterocolitica*: the charisma continues. Clin Microbiol Rev. 1997;10:257–76. [PubMed](#)
70. Bechah Y, Capo C, Mege JL, Raoult D. Epidemic typhus. Lancet Infect Dis. 2008;8:417–26. [PubMed doi:10.1016/S1473-3099\(08\)70150-6](#)
71. Raoult D, Ndiokubwayo JB, Tissot-Dupont H, Roux V, Faugere B, Abegbinni R, et al. Outbreak of epidemic typhus associated with trench fever in Burundi. Lancet. 1998;352:353–8. [PubMed doi:10.1016/S0140-6736\(97\)12433-3](#)
72. Andersson SG, Zomorodipour A, Andersson JO, Sicheritz-Ponten T, Alsmark UC, Podowski RM, et al. The genome sequence of *Rickettsia prowazekii* and the origin of mitochondria. Nature. 1998;396:133–40. [PubMed doi:10.1038/24094](#)
73. Fischer SA, Graham MB, Kuehnert MJ, Kotton CN, Srinivasan A, Marty FM, et al. Transmission of lymphocytic choriomeningitis virus by organ transplantation. N Engl J Med. 2006;354:2235–49. [PubMed doi:10.1056/NEJMoa053240](#)
74. Jamieson DJ, Kourtis AP, Bell M, Rasmussen SA. Lymphocytic choriomeningitis virus: an emerging obstetric pathogen? Am J Obstet Gynecol. 2006;194:1532–6. [PubMed doi:10.1016/j.ajog.2005.11.040](#)
75. Baum SG, Lewis AM Jr, Rowe WP, Huebner RJ. Epidemic nonmeningitic lymphocytic-choriomeningitis-virus infection. An outbreak in a population of laboratory personnel. N Engl J Med. 1966;274:934–6. [PubMed doi:10.1056/NEJM196604282741704](#)
76. Albarino CG, Palacios G, Khristova ML, Erickson BR, Carroll SA, Comer JA, et al. High diversity and ancient common ancestry of lymphocytic choriomeningitis virus. Emerg Infect Dis. 2010;16:1093–100. [PubMed doi:10.3201/eid1607.091902](#)

77. Latge JP. *Aspergillus fumigatus* and aspergillosis. Clin Microbiol Rev. 1999;12:310–50. [PubMed](#)
78. McCausland IP, Slee KJ, Hirst FS. Mycotic abortion in cattle. Aust Vet J. 1987;64:129–32. [PubMed](#) [doi:10.1111/j.1751-0813.1987.tb09659.x](https://doi.org/10.1111/j.1751-0813.1987.tb09659.x)
79. Buffington J, Reporter R, Lasker BA, McNeil MM, Lanson JM, Ross LA, et al. Investigation of an epidemic of invasive aspergillosis: utility of molecular typing with the use of random amplified polymorphic DNA probes. Pediatr Infect Dis J. 1994;13:386–93. [PubMed](#)
[doi:10.1097/00006454-199405000-00011](https://doi.org/10.1097/00006454-199405000-00011)
80. Andrade-Filho Jde S, Pena GP. Analogies in medicine: fungus and liturgy. Rev Inst Med Trop Sao Paulo. 2010;52:288. [PubMed](#)
[doi:10.1590/S0036-46652010000500014](https://doi.org/10.1590/S0036-46652010000500014)