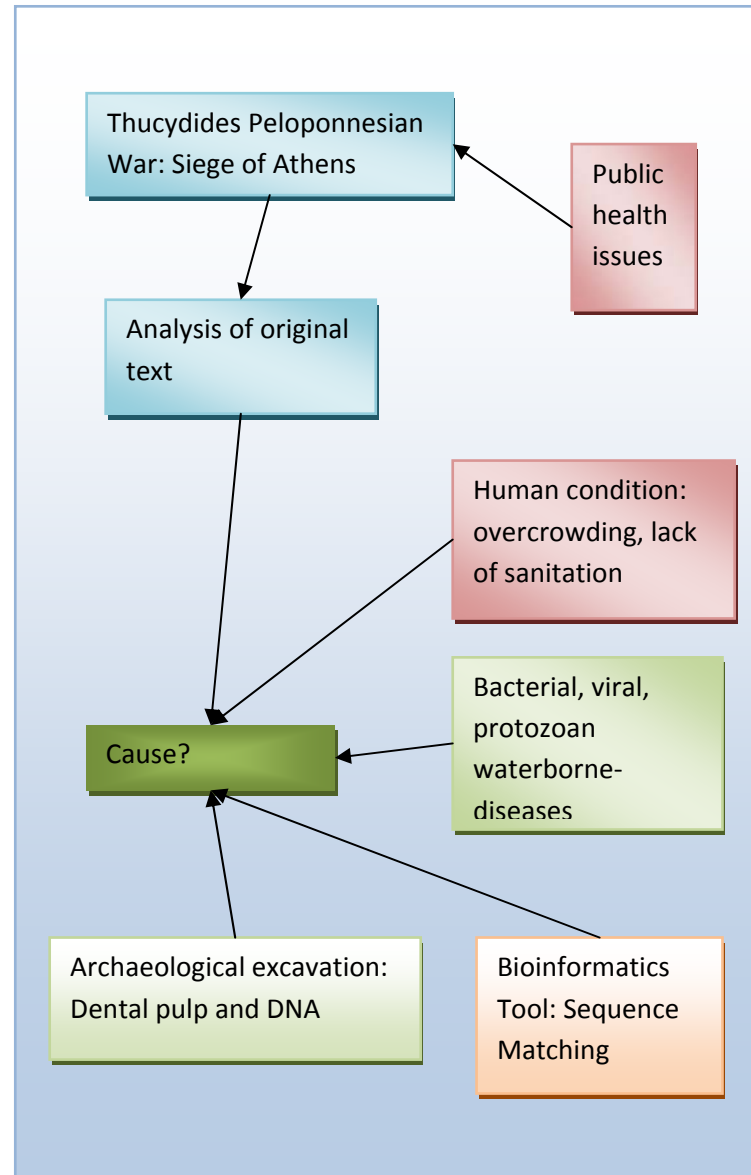


The Plague during the Siege of Athens

“As a rule, however, there was no ostensible cause; but people in good health were all of a sudden attacked by violent heats in the head, and redness and inflammation in the eyes, the inward parts, such as the throat or tongue, becoming bloody and emitting an unnatural and fetid breath. These symptoms were followed by sneezing and hoarseness, after which the pain soon reached the chest, and produced a hard cough. When it fixed in the stomach, it upset it; and discharges of bile of every kind named by physicians ensued, accompanied by very great distress. In most cases also an ineffectual retching followed, producing violent spasms, which in some cases ceased soon after, in others much later. Externally the body was not very hot to the touch, nor pale in its appearance, but reddish, livid, and breaking out into small pustules and ulcers. But internally it burned so that the patient could not bear to have on him clothing or linen even of the very lightest description; or indeed to be otherwise than stark naked. What they would have liked best would have been to throw themselves into cold water; as indeed was done by some of the neglected sick, who plunged into the rain-tanks in their agonies of unquenchable thirst; though it made no difference whether they drank little or much. Besides this, the miserable feeling of not being able to rest or sleep never ceased to torment them. The body meanwhile did not waste away so long as the distemper was at its height, but held out to a marvel against its ravages; so that when they succumbed, as in most cases, on the seventh or eighth day to the internal inflammation, they had still some strength in them. But if they passed this stage, and the disease descended further into the bowels, inducing a violent ulceration there accompanied by severe diarrhoea, this brought on a weakness which was generally fatal. For the disorder first settled in the head, ran its course from thence through the whole of the body, and, even where it did not prove mortal, it still left its mark on the extremities; for it settled in the privy parts, the fingers and the toes, and many escaped with the loss of these, some too with that of their eyes. Others again were seized with an entire loss of memory on their first recovery, and did not know either themselves or their friends.”

(History of the Peloponnesian War. Thucydides. Chapter 7.
<http://www.gutenberg.org/dirs/etext04/plpwr10.txt>)



Background

The Peloponnesian war (431 BC to 404 BC) between the Athenian Empire and the Peloponnesian League was documented by Thucydides in the book *History of the Peloponnesian War*. The above excerpt from Thucydides' book describes the "plague" that ravaged Athens in 430 BC. Consult the following web pages (and others) about the Peloponnesian War and learn more about the "plague" that killed about a quarter of the densely populated city Athens. Note that in classical times, epidemics were frequently referred to as the plague regardless of the actual disease due to a lack of knowledge that would have allowed classification of the diseases.

<http://www.crystalinks.com/peloponnesianwar.html>

http://en.wikipedia.org/wiki/Peloponnesian_War

<http://www.mlahanas.de/Greeks/History/PeloponnesianWar.html>

The "Plague"

In-class discussion: Describe the symptoms of the disease according to Thucydides.

There is no agreement on what caused this plague. The following diseases and their disease agents (in parentheses) are among the ones that have been implicated according to Papagrigorakis et al. 2006 and references therein (there are many more candidates—see Table 1 in Papagrigorakis et al. 2006): Bubonic plague (*Yersinia pestis*), typhus (*Rickettsia prowazekii*), anthrax (*Bacillus anthracis*), and typhoid fever (*Salmonella enteric* serovar Typhi).

Group projects: Divide the students in four groups. Each group picks one of the four diseases, and determines the causative disease agent, the symptoms, and transmission mode. Based on this information, each group should evaluate the strength of the evidence for or against the disease being the cause of the Plague of Athens.

In-class discussion: Groups report their findings in class. The class then compares the strength of evidence for each disease as the likely candidate for the "plague" that ravaged Athens in 430 BC.

Microbial DNA Fragments Narrow the List of Candidates

Papagrigorakis et al. (2006a) examined microbial DNA fragments retrieved from dental pulp of human skeletal remains found in a mass burial site that has been linked to the outbreak of the Plague of Athens. They compared the ancient DNA sequence to a number of other sequences and found that it is most closely related to *Salmonella enteric* serovar Typhi, which is the causative agent of typhoid fever. Their findings are published in Papagrigorakis et al. (2006a). Shapiro and Gibert (2006) disputed their conclusion [see also reply by Papagrigorakis et al. (2006b)]. The causative agent thus still remains a mystery.

Papagrigorakis et al. (2006a) published the DNA sequence of the *narG* gene region that they obtained by PCR amplification. The *narG* gene encodes for the alpha chain of the nitrate reductase 1, which is an important enzyme in anaerobic respiration.

Here is the sequence according to Papagrigorakis et al. (2006a):

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GTTCACTTCCTGCCATGAGGAGCGAACAAAACCACCACGACCACGCGCCTGTTTGAAGCTTTTGGCTTTATCGGCA  
TCTTCAATGATGGAGGCCCATGCCTCTACCGGATCGCGGTGCAGTTTCTTGGCCTCGCGCCACAGTTTGATCAGGC  
GTTTGGCGCATCAGCGGGTATTTTCAGGCGGTTGGCGCTGTACAGATAACCAGGAGTAACTGGCGCCACGTGGGCAAC  
CGAGCCGTTTCATGGTTGGGCAAGTCCGGGCGGGTACGCGGATAATCGGTTTGCTGGGTTTCCCAGGTCACCAGGC  
CATTTTTACATAAATTTTCCAGCTACAGGAGCCGGTGCAGTTCACCCCATGGGTTGA
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The Module “Bioinformatics: Searching Online Databases for DNA Sequences” contains instructions on how to find closely related sequences using the search tool BLAST.

References

Papagrigoakis, M.J., C. Yapijakis, P. N. Synodinos, and E. Baziotopoulou-Valvani. 2006a. DNA examination of ancient pulp incriminates typhoid fever as a probable cause of the Plague of Athens. *International Journal of Infectious Diseases* 10: 206-214.

Papagrigoakis, M.J., C. Yapijakis, P. N. Synodinos, and E. Baziotopoulou-Valvani. 2006b. Insufficient analysis may not exclude candidacy of typhoid fever as a probable cause of the Plague of Athens (reply to Shapiro et al.). *International Journal of Infectious Diseases* 10: 335-336.

Shapiro, B. and M.T.P. Gilbert. 2006. No proof that typhoid caused the Plague of Athens (a reply to Papagrigorakis et al.). *International Journal of Infectious Diseases* 10: 334-335.