

Ebola in Antiquity?

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This article addresses whether Ebola may have been present in an urban setting in Athens in 430 BCE and explores the historical importance of the ancient outbreak. New knowledge from today's West African epidemic allows a more accurate assessment of whether Ebola may have caused the Athenian outbreak than was once possible. The Athenian disease, whose etiology remains unknown, developed abruptly with fevers, abdominal pain, vomiting, diarrhea, dehydration, and hemorrhage. It originated in sub-Saharan Africa and was especially contagious to doctors and caregivers. No remedies were effective. But the few survivors who were reexposed to diseased patients were not attacked a second time, suggesting protective immunity. What lessons can we learn from the ancient outbreak that bears a clinical and epidemiologic resemblance to Ebola? The historian Thucydides, an eyewitness and disease sufferer, described how the unsuspecting city panicked as it struggled to handle the rapidly spreading, devastating disease. Moreover, he stressed a theme that has relevance today—namely, that fear and panic intensified the disruption of society and damage to the individual that was directly caused by the disease. Moreover, fear amplified the spread of disease. The destructive nature of fear has remained a signature feature of pestilences that have subsequently caught ill-prepared societies off-guard—Bubonic plague in medieval times, AIDS in the 1980s, and Ebola today. The ancient Athenian epidemic is relevant for today's West African Ebola outbreak because it shows how fear and panic can endanger the individual, our society, and our efforts to handle the disease.

Keywords. Ebola; Athens; plague; fear; pandemic.

The medical and lay press portray today's current West African Ebola epidemic as unprecedented [1, 2]. This characterization is tenable, as this is the first time Ebola has unexpectedly appeared in overcrowded urban settings and continues to spread 1 year into its course [3]. Unlike previous self-limited Ebola outbreaks involving small populations that had suddenly appeared in different remote rural villages and then vanished in a matter of months [4], today's outbreak has spread through expanding routes of transportation into several large urban populations of adjacent nations [5]. Public health efforts that had been effective in handling prior Ebola epidemics—isolating cases, tracking contacts, and monitoring those people for symptoms—have been

hampered by the geographic extent of today's outbreak and inadequate community resources in impoverished countries [6]. These unique aspects of the current West African urban Ebola outbreak prompted Joanne Liu, President of Médecins Sans Frontières (Doctors Without Borders), to state, "We're making history, we're facing something we've never seen before" [2].

This article explores whether history has ever seen anything like today's Ebola outbreak. This inquiry is warranted in light of recent molecular data indicating that Ebola viruses are much older than previously thought and have an estimated lineage on the order of tens of millions of years. Evolutionary biologists searching for portions of viral DNA of Ebola within the genomes of animals found identical remnants in different species of rodents, including the mouse and the Norway rat [7]. On this basis, molecular virologists speculate that Ebola infected these animals early in evolution prior to the divergence of these rodent species at least 20 million years ago [7]. For most of that time, Ebola infected rodents and other mammals, possibly bats, millions of years before Ebola was first recognized in humans in 1976.

Received 4 March 2015; accepted 15 May 2015; electronically published 1 June 2015.

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Clinical Infectious Diseases® 2015;61(6):963–8

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DOI: 10.1093/cid/civ418

Could Ebola have spilled over into human populations during its long existence before 1976? Proof of such an outbreak would have been impossible as the virologic techniques required to detect Ebola were neither available prior to 1967 nor applied in a field setting until 1976 [8]. Nevertheless, we can use historic records to search for an epidemic whose features are compatible with Ebola. This article selects one epidemic that occurred in Athens in 430 BCE whose cause remains a longtime subject of conjecture among physicians and historians [9]. Although scholars have postulated typhus [10], smallpox [11], and even Ebola [12] as possible etiologies, they have been unable to agree on what the retrospective diagnosis might have been, in part because limited information about a disease like Ebola has been an obstacle for making comparisons [13]. New clinical and epidemiologic information now available from today's large West African epidemic, however, has filled this gap of knowledge about Ebola [14, 15] and permits a more accurate comparison of the Athenian outbreak with Ebola. In light of this new knowledge, I reexamine the Athenian outbreak to assess its compatibility with Ebola and to address what it can teach us about today's epidemic.

THE 430 BCE OUTBREAK

In 430 BCE, the historian Thucydides described an unexpected, terrifying summer outbreak that ravaged Athens. When chronicling the Peloponnesian War between the rival city-states Athens and Sparta, the eyewitness Thucydides presented a systematic account of a disease whose symptoms began with an abrupt onset of fever, headache, fatigue, and pain in the stomach and extremities. This was accompanied by vomiting that "fasten[ed] . . . upon each sufferer [with] fury" [16]. For those who survived after 7 days of illness, the disease "descended into the bowels [and] severe diarrhea had set in" [16]. The disease also caused reddened eyes, hiccups (or "ineffectual retching") [17], and bleeding from the mouth. Seizures, confusion, cough, and a red livid rash, pustules, or ulcers that could lead to loss of digits (presumably due to gangrene) sometimes occurred [16]. As symptoms progressed, dehydration became so profound that men plunged themselves into wells in a futile attempt to quench their unceasing thirst. The fulminant disease frequently ended in death, typically occurring by day 7–9 of the illness. Medical treatment could not ameliorate the disease's severity or improve its bleak outcome, as the physicians "art . . . [was] utterly useless" [16]. Thucydides depicted a rapidly fatal clinical picture characterized by fever, vomiting, diarrhea, and hemorrhage.

Thucydides also portrayed a distinct epidemiology that highlighted the susceptibility of healthcare workers. Physicians, Thucydides said, were "among the first victims of the disease because they [most] often came into contact with it" [16]. He

said, "Appalling . . . was the rapidity with which men caught the infection, dying like sheep if they attended on one another, and this was the principal cause of mortality" [16]. The Roman poet Ovid also stressed physicians' susceptibility when he wrote about the epidemic, "Ph[ysicians] and Sur[geons] cureless cunning hurt themselves. The nearer any man approach[ed] his diseased friend . . . the sooner did he catch his bane" [18]. As true in Athens, caregivers of symptomatic Ebola patients today are especially susceptible as they come into contact with highly infectious bodily fluids; more than 270 healthcare workers have died from the disease [19]. In addition, the 5-year lifespan of the Athenian outbreak is within the realm of possibility for today's Ebola outbreak given its ongoing spread [20]. Furthermore, the congested locale of ancient Athens, with an estimated population of 315 500 people, mirrors the overcrowded urban settings in which Ebola now thrives [21]. Thus, epidemiologic features of the ancient outbreak—the population at risk, projected time course, and setting—are consistent with Ebola.

The geographic origin of the ancient disease also fits Ebola. The ancient malady began south of Egypt in a region Thucydides called "Aethiopia." Ancient Greeks used this term to refer to regions in sub-Saharan Africa, Sudan, and the Democratic Republic of the Congo—areas where Ebola outbreaks have occurred [22]. The ancient epidemic then raged in the Mediterranean before reaching Athens. In the ancient world, Africans from sub-Saharan regions migrated to Greece, where they found employment as farmers or servants [22]. Thus, the disease could have been spread by humans traveling along routes of transportation to an overcrowded urban center [23]. The sub-Saharan African origin of the ancient disease and its spread to a city is compatible with today's Ebola outbreak.

The composite clinical, epidemiologic, and geographic features of the ancient Athenian outbreak are consistent with our knowledge of Ebola today. In aggregate, the abrupt onset of generalized symptoms (fever, myalgias, headache, fatigue), development of specific symptoms (diarrhea, conjunctivitis, vomiting, confusion, hiccupping), fulminant nature resulting in death on day 7–10 following onset, high rate of spread to caregivers, and origin in sub-Saharan Africa are consistent with what we now know about Ebola [14, 15]. In addition, a variety of rashes are described for Ebola today, including petechia, hemorrhagic bullae, hematoma, and potentially gangrenous digits if disseminated intravascular coagulation is present [24]. Thus, the range of rashes that Thucydides described is not inconsistent with those of Ebola, especially considering that Thucydides' use of the word "pustule" in 430 BCE meant something different from our use of the term today. In addition, the patterns of diarrhea of the 2 diseases are not incompatible, as severe diarrhea is described to occur at days 3–7 of the Ebola illness in 70% of patients [15]. Furthermore, Thucydides' observation that "no one [in contact with a diseased individual] was

ever attacked a second time” [16] is compatible with the protective immunity known to accompany Ebola survivors today [25]. Furthermore, Thucydides and Ovid noted that animals also developed the Athenian malady [16, 18]. Thucydides remarked that the death of animals in addition to humans was “one circumstance in particular which distinguished [the Athenian disease] from ordinary diseases” [16]. Because neither author specified the spectrum of animal species involved, their observation is consistent with Ebola as well as other zoonotic infections as the possible cause of the Athenian epidemic.

As the true nature of the Athenian outbreak has not been definitively established, we must consider how infections other than Ebola fit Thucydides’ description. Table 1 lists the aggregate features of the epidemic according to infections hypothesized by scholars. Although typhus, bubonic plague, and anthrax involve animals, none of those diseases account for the vomiting, diarrhea, conjunctivitis, or preferential spread to healthcare workers. Furthermore, the absence of buboes and the generalized rash do not fit bubonic plague; the hemorrhaging would be unlikely with typhus; and the absence of a necrotic ulcer would be atypical for anthrax [26]. It is noteworthy that hiccupping is associated with Ebola but with no other disease [14, 26]. The summertime occurrence would be unusual for epidemic typhus, which ordinarily occurs during winter times of crowding. The involvement of animals excludes infections that involve humans exclusively (ie, smallpox, measles, toxic shock syndrome). Although no disease outlined in Table 1 fits the clinical or epidemiologic pattern and geographic location as closely as Ebola, definitive proof of the ancient disease would require genetic analysis of skeletal remains. Until those studies are performed, Ebola is a plausible, if not likely, cause of the disease Thucydides described.

One question remains: If the ancient plague was due to Ebola, why did it not reappear until 1976? One possible explanation is that diagnostic tests for Ebola were not introduced until the 1970s. Thus, an earlier epidemic due to Ebola in Africa or elsewhere would have gone unrecognized. Another possible explanation is that the clinical features of a particular disease vary over time, as those of Ebola have done over the past 30 years. The mortality rate of Ebola, for example, has ranged from 30% to 90% during this period, and the percentage of patients with particular symptoms, including hemorrhage, has also varied among outbreaks [14, 15]. Thus, Ebola may have reappeared before this time in Africa or elsewhere in a pattern that was not as devastating as the Athenian plague. Furthermore, because the features of a particular disease can evolve over time, the clinical pattern as we know it today may not match perfectly with the manifestations described in the past. Syphilis, for example, is one disease where the predominant cutaneous manifestation during its description in 1492—vesicles—are no longer associated with this disease today [27]. In light of these considerations,

one cannot exclude the possibility that Ebola reappeared prior to 1976. As a corollary, even though no disease listed in Table 1 precisely matches each clinical feature of the Athenian plague, Ebola accounts for the overall features—fever, vomiting, diarrhea, dehydration, and high mortality occurring at week 1 of illness—as well or better than other conditions listed in Table 1.

SOCIETAL RESPONSE

After describing the disease, Thucydides explored society’s response to the epidemic. He focused on the destructive nature of fear and asserted that fear and panic compounded damage to society and to the individual caused by the disease itself. He stated that anxious citizens disregarded civic authority and violated laws and customs that “had hitherto been observed” [16]. As a consequence of the social disorder, the highly disciplined Athenian democratic society unraveled as citizens abdicated their accountability to family and government. As they abandoned their work, a famine ensued. There may have been other causes of the Athenian famine, including failure of crops to be cultivated and harvested as a result of a military decision by the Athenian general Pericles to seclude citizens within the city’s walls during the battle. Nonetheless, as healthy but anxious citizens abdicated their responsibilities to care for their ill family members, the ill found isolation at a time when they most needed support. Thucydides and, later, Ovid described the isolation of disease sufferers, whom citizens believed may have contracted the disease by drinking well water poisoned by the invading Peloponnesians or by displeasing the vengeful goddess Juno [16, 18]. Regarding the isolation experienced by disease sufferers, Thucydides said, “When men were afraid to visit one another, the sufferers died in their solitude . . . [and] from want of care” [16].

Fear, Thucydides showed, not only accentuated the damage caused by the disease to society and the individual, it also exacerbated disease spread. Fearful citizens who fled their homes, he noted, obtained shelter by residing in congested urban huts. The overcrowding intensified disease spread, “. . . [and the] mortality among them was dreadful” [16]. Afterward, the dead laid unburied “one upon another” in the streets, as people were fearful of approaching them to provide customary burials. Based on today’s knowledge of Ebola, unattended corpses lying uncovered in the street may have intensified disease spread as bodily fluids after death remain contagious to those living in proximity, particularly in overpopulated regions of the city [1]. Thucydides did not mention whether these overcrowded regions were also impoverished, as in the case of spread of Ebola today, or whether it occurred most often among Athenian soldiers who resided in close proximity to one another. Nevertheless, unlike Ebola today, where adherence to traditional funeral customs (eg, touching and washing of the deceased body)

Table 1. Clinical and Epidemiologic Features of 430 BCE Athenian Outbreak According to Possible Etiologies

Athens Outbreak ^a	Ebola	Epidemic Typhus	Anthrax	Typhoid Fever	Bubonic Plague	Smallpox	Measles	Toxic Shock Syndrome
Clinical feature								
Fever	+	+	+	+	+	+	+	+
Vomiting, diarrhea, stomach pain	+	–	–	+	–	–	–	+
Headache, myalgia	+	+	–	–	–	–	–	+
Rash (pustular/bullous)	+/–	–	+	–	–	+	–	–
Conjunctivitis	+	–	–	–	–	–	–	–
Bleeding from mouth	+	–	–	–	–	–	–	–
Seizures, forgetfulness	+	–	+	–	–	–	–	–
Hiccups	+	–	–	–	–	–	–	–
Loss of digits	+ ^{b,c}	–	–	–	+ ^{b,c}	–	–	–
Clinical course								
Acute, fulminant	+	–	+ ^b	+ ^b	+	–	–	+
High mortality; death on day 7–9	+	+ ^b	+ ^b	–	+ ^b	+ ^b	+ ^b	+
Survivors protected from reinfection	+	+	–	–	–	+	+	–
Epidemiology								
Origin south of Egypt (Sudan)	+	+ ^b	–	–	–	–	–	–
Notable spread to HCWs	+	–	–	–	–	+	+	–
Involves animals	+ ^d	+	+	+	+	–	–	–
Summertime illness	+	–	–	–	+ ^b	+ ^b	–	–
Comments	Accounts for all clinical/epidemiologic features	Accounts for some features, not spread to HCWs	Accounts for some features, not spread to HCWs	Accounts for few features, not spread to HCWs	Does not fit clinical/epidemiologic pattern	Does not fit clinical/epidemiologic pattern	Does not fit clinical/epidemiologic pattern	Does not fit epidemiologic pattern

Abbreviations: +, feature typically present in the indicated disease; –, feature not accounted for by indicated disease; HCW, healthcare worker.

^a Clinical, epidemiologic, and geographic features of the Athenian outbreak that Thucydides described in 430 BCE.

^b Feature that may accompany the indicated disease.

^c If accompanied by disseminated intravascular coagulation.

^d Involves primates and rodents.

facilitates disease spread, it was the violation of traditional individual burial customs that may have exacerbated the spread of the ancient epidemic. Nonetheless, Thucydides' insights into the detrimental consequences that fear had for society, the individual, and spread of disease would be echoed in lethal pestilences that were to emerge.

In 1348, the Italian writer Giovanni Boccaccio wrote about the effects of fear on European society during an untreatable bubonic plague epidemic. He noted that "fears [took] root in the minds of those who were still alive and well" [28]. Society became disorderly as frightened citizens grew to disregard their affairs and disrespect authority. Customary burials in individual plots were substituted by mass burials where people died "more like animals than human[s]" [28]. Moreover, a famine ensued when fearful citizens "abandoned their city and headed for the countryside. . . [and] crops lay abandoned" [2]. Furthermore, the anguished well "[ran] away from the sick" and their relatives as "though they did not belong to them" [28]. As scared citizens relinquished their familial responsibilities, the ill "languished away with virtually no one to nurse them. . . and [died]. . . in isolation because the healthy were too terrified to approach them" [28]. Echoing Boccaccio's observations, the medieval French surgeon Guy de Chauliac admonished his undutiful peers who "did not dare visit the sick for fear of infection" [29].

In 1981, fear that accompanied another unexpected, incurable epidemic, AIDS, again had negative repercussions for society, the individual, and efforts to control the epidemic. Anxious citizens rejected scientific evidence that the virus was transmitted only through body fluids and remained unconvinced that it could not be transmitted casually [30, 31]. AIDS patients were denied the medical care they needed or were shunned by those who feared becoming infected by casual contact even though medical evidence told them otherwise [32]. There was anxiety about the potential for the epidemic to breach its stigmatized risk groups and cause widespread deaths among the entire population [33]. Accompanying this panic were calls of permanent quarantines that disregarded scientific recommendations [34]. The distress of being shunned and fears of discrimination in the workplace deterred some from seeking healthcare, taking their antiretroviral drugs, or practicing safe sex—behaviors that encouraged the spread of AIDS [35].

The historical accounts of Thucydides, Boccaccio, and AIDS help us recognize the detrimental costs that fear of Ebola has today. Fear of disease has shut down transportation systems and kept people away from their jobs [23]. With citizens fleeing affected communities and with travel restrictions, businesses and schools have closed, road construction has declined, and the food supply has become endangered [36]. Due to fear of catching disease, there has been an inadequate supply of health-care workers willing to provide care for sick patients or workers

willing to transport or bury bodies [23]. In West Africa today, fear of Ebola has contributed to its continued spread as there are not enough workers to carry out the tasks required to control the disease, and patients die in solitude without receiving basic medical care [37, 38]. Moreover, talk of mandatory quarantines of asymptomatic healthcare workers returning to the United States that reject scientific evidence are based on fear of disease rather than scientific knowledge of how the disease actually spreads [39]. These restrictive measures have the potential to discourage volunteering and reduce humanitarian assignments that are needed to handle disease spread in West Africa [40]. These responses show that a scientific understanding of diseases such as Ebola and AIDS today, as well as the knowledge of factors that place a person at risk of acquiring these infections, did not lessen society's response of fear and fright that had been evident during the Athenian plague and subsequent epidemics. Furthermore, as was the case in prior epidemics, fear today is intensifying the damage to society and individuals caused by Ebola itself and interfering with efforts to control its spread.

CONCLUSIONS

For Ebola today, it is important to explore linkages with rather than ruptures from the past. During today's epidemic, attention by the medical and lay press have aptly focused on the pandemic's distinct features—the need to quickly develop a coordinated international response to perform surveillance, isolate cases, deliver appropriate gear to protect healthcare providers, and provide therapies to help manage victims. While acknowledging the necessity of addressing these unique features of today's Ebola outbreak, it is also important to address how past epidemics can provide wisdom and insights for us today. A look back to an ancient outbreak that resembled Ebola on the basis of clinical, epidemiologic, and geographic similarities shows us how society's panic-stricken responses to pestilences have intensified the damage and devastation directly caused by the disease itself. From antiquity to medieval times to Ebola today, society's response of anxiety has worsened the suffering of the individual, disrupted society, marginalized civic or scientific authority, decimated economies, and intensified the spread of epidemics. For current and past epidemics, suffering and deprivation have been caused by the image of pestilence with its associated fear, flight, and isolation as well as by the microbe itself.

Note

Potential conflict of interest. Author certifies no potential conflicts of interest.

The author has submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

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