

The past plague pandemics (Justinian, Black Death, Third) in light of modern Molecular Life Science insights

A meeting in the Norwegian Academy of Science and Letters, November 19th and 20th, 2014.

Summary

Our current understanding of the three plague pandemics has rapidly expanded in the last decade, largely due to ancient DNA analysis of medieval remains, and the sequencing of a large number of current-day plague strains. There is a great need to convey these newly gained modern insights to a broad spectrum of scientists, and provide them with access to these new MLS methods. In addition, though much progress has been made during the last few decades, much remains to be understood regarding the past plague pandemics: where did they originate from, what processes determined the timing of these pandemics, how did the disease spread? By inviting speakers from a broad spectrum of disciplines we seek new ways of further progress by taking advantage of the new tools of molecular biology which are available today.

Rationale for the conference

In November 2005, a meeting on plague was organized in the Norwegian Academy of Science and Letters ("Plague: bacteriology, evolution, epidemiology and its impact on human history"). One of the main insights gained from that earlier meeting was that we need to intensify and extend our scientific network to embrace the humanities and social scientists. Historians, anthropologists, geographers and archeologists are uniquely capable of contributing to the reconstruction of what has occurred during the past, beyond what is possible to infer from genetic studies, as its answers lie in the structure of human society and its response to pandemics. Current-day anthropologists are rapidly taking up these molecular life science techniques, including here in Oslo, where our quest is to understand infamous diseases such as the plague, which have been dispersed globally by human activities, yet whose dynamics are still strongly tied to animal reservoirs. Thus, inviting scholars from such a broad spectrum of disciplines from Norway, Europe, and beyond will create a unique and mutually beneficial opportunity to establish a groundbreaking multidisciplinary scientific collaboration. Such a meeting will certainly have broad scientific appeal.

Target group

The 2-day conference will be open for the public, and will offer ample opportunities for discussion between scientists, speakers and the public, allowing for a rewarding exchange of information.

The structure of the conference

The conference will start with two opening lectures, by *Prof. Herwig Leirs* and by *Prof. Lars Walløe*, who will bring the audience up to date on what we know of the biology and the history of plague: from its genetic

ancestry, to its natural host system, to the pandemics amongst humans that it has caused, and the countermeasures we historically took, and now still take to prevent new outbreaks.

After this introduction, the conference will focus on three recent developments in plague research that due to their novelty have not yet been integrated by plague researchers, and offer new roads into gaining important insights on the transmission, dynamics and lethality of the disease. The topics covered are the devastating impact of plague on Europe's medieval cities, and what we can learn from city mortality records about the mode of transmission of plague, to improved insight into the vectors of the disease that make it possible for *Y. pestis* to spread and persist globally, to the likely sites of origin of the three pandemics and the role that the conditions at these starting points have played in the shaping the disease. A recurring thread in these three sessions is the possibilities that are created by current molecular life science tools in different disciplines of science to further elucidate our past.

Finally, after a structured opportunity for discussion with the speakers, *Prof. Jared Diamond* (who has confirmed his attendance in Oslo) will reflect on the conference and give us his summarizing thoughts on the modern consequences of the past plague pandemics.

The sessions

Session 1. Plague and mortality within European cities

For 200 years during the first plague pandemic, and over 400 years during the second, Europe's cities frequently experienced disastrous plague outbreaks, despite preventive measures that were taken. The mechanism by which plague spread through these cities is still largely unknown, but now that detailed mortality records of cities are becoming available, several questions can be answered that could not before. Among these are the route by which plague was introduced into cities (through people, black rats, or trade goods, by ships, or through interactions with nearby wildlife), whether the mortality dynamics support one mode of plague transmission above another (by rodents and fleas, by air, or by human arthropod vector), and whether transient immunity in plague survivors can explain the timing and severity of the outbreak. The mortality records per city, but also the epidemics recorded throughout Europe create the possibility to look for the co-occurrence of plague outbreaks and other vector-borne diseases, such as typhus. Whether plague outbreaks coincided with other infections in plague victims is an area where modern molecular methods are capable of providing answers. Similarly, the growing collection of ancient DNA plague samples will shed light on the ability of plague to locally persist within large cities, or whether it was re-imported from outside the city boundaries.

Session 2. The role of plague vectors in transport and disease characteristics

The *Report of the Indian plague commission* concluded in 1901 that plague outbreaks in humans in British India were caused by flea bites from rat fleas during plague epizootics in rats. Combined with a later observation that *Y. pestis* blocked the fore-gut of infected fleas, strongly promoted the idea that plague depended on the relatively slow process of a flea vector capable of becoming blocked. The resulting slow speed of plague transmission was assumed to also apply to the first two plague pandemics, even though this assumption was not supported by historic records of plague transport in Europe, the Near East, or China, the epidemiology of medieval plague, and archeological records that indicated for example the absence of rats in northern Europe. The disease "plague" in the first two pandemics indeed differed so much from the plague of the third pandemic, that some scientists concluded that the former two pandemics were caused by another pathogen than *Yersinia pestis*. While that latter conclusion no longer

holds in Europe, thanks to advanced molecular life sciences techniques that led to the discovery of *Y. pestis* DNA in tooth samples of medieval plague victims, the pathological agent of large epidemics in medieval northwestern China is still uncertain, yet has characteristics of these epidemics share a resemblance with medieval plague in Europe. Comparative analysis of the transport characteristics, the speed with which epidemics spread through and between towns, and variation in disease pathology of *Yersinia pestis* across Eurasia will play an important role of establishing the role that the various modes of transmission of plague play in the plague pandemics.

Session 3. Plague persistence and pandemics

Plague in human history is divided into the three large-scale plague pandemics, of which the third is still considered ongoing. In reality, the division between the pandemics is not that clear: the second and third pandemic overlapped during the late 18th and 19th century, during which the second pandemic was still present in northern Africa, the Middle east and Russia, and the third pandemic had already begun spreading through south-eastern China. Nor is it clear how many pandemics there have been: the third plague pandemic appears to have consisted of two pandemics with separate disease characteristics. While plague was spreading through southern China, a second pandemic broke out in northern China around 1905, with unknown origin. The latter pandemic had disease characteristics that were more similar to that of Europe's second medieval plague pandemic than to the comparatively mild characteristics of the southern third plague pandemic. In this session we start with looking at how far (and how trustworthy) current phylogenetic evidence can point us towards the sites of origin of the three pandemics.

One recurrent issue within plague's epidemiology and ecology is that we do not fully understand how the disease persists between outbreaks. Plague can be absent for years to decades from well-studied rodent ecosystems, only to suddenly reappear (or be re-introduced from elsewhere - something for Molecular life sciences to establish). At this level, the persistence of plague in fleas or in protozoa is being explored to reveal the mechanisms and the potential for plague to lie dormant. On longer timescales, the disease can be present at low intensity for centuries, and suddenly become a pandemic. Plague was festering at low intensity in the Yunnan province from the late 18th century, prior to its expansion through southern China in the mid-19th century, and there is tantalizing archeoentomological and literary evidence that plague might have been endemic for centuries as well in Egypt prior to the first pandemic. Complexing the issue is that locally endemic plague foci need not have been the source of plague in that region, but could have been supplanted by an epidemic strain.

What remains to be established is the circumstances under which plague becomes pandemic, and the determinants of the severity of the pandemic. It is tempting to speculate that the ecology at the different sites from which plague pandemics began might play a defining role in the differences between devastating pandemics, such as the second plague pandemic and the northern Manchurian plague epidemic (which, from current evidence, both appeared to have started in plague foci around 45°N latitude), versus the comparatively mild third pandemic came from a more southern 25°N latitude.

Workshop Programme

Venue: Academy of Science, open (up to capacity) for the public

Wednesday, November 19th, 2014. 8:30-22:00

Welcome

8:30 - 9:00 Coffee

9:00 - 9:15 Opening remarks by the Preses of the Academy, Prof. Nils Chr. Stenseth

9:15 - 9:45 Prof. Lars Walløe – *Introduction to the history of plague*

University of Oslo, Department of Physiology

9:45 - 10:15 Prof. Herwig Leirs – *Introduction to the biology of plague*

University of Antwerp, Department of Biology

Session 1: **Plague and mortality within European cities**

10:15 - 11:00 Dr. Neil Cummins – *Spatial and temporal patterns of birth and death in London from 1560 to 1665, a period dominated by outbreaks of plague*

London School of Economics, Economic History

11:00 - 11:45 Prof. John Henderson – *Death rates in the lazaretto, the parishes and mass graves of Florence during the plague of 1630-31*

University of London, Department of History, Classics and Archeology

11:45 - 12:30 Buffet Lunch

Session 2: **The role of plague vectors in transport and disease characteristics**

12:30 - 13:15 Dr. Anne Karin Hufthammer – *Rats cannot have been intermediate hosts for Yersinia pestis during medieval plague epidemics in Northern Europe.*

University of Bergen, Department of Osteology

13:15 - 14:00 Prof. Robert Hymes – Introducing the *inaugural issue of the Medieval Globe*, and his work therein on *the dispersal of 13th Century plague from the Qinghai-Tibet Plateau*

Columbia University, Department of History, Premodern Chinese History

14:00 - 14:45 Prof. Samuel Cohn – *The different disease expressions of Y. pestis, from historical medical descriptions of plague patients.*

University of Glasgow, Medieval History

14:45 - 15:00 Coffee

Continuation of Session 2

15:00 - 15:45 Prof. George Christakos – *Spatiotemporal modeling of bubonic plague epidemics*
San Diego State University, Department of Geography

15:45 - 16:30 Dr. Dionysios Stathakopoulos – *Traveling with the plague in the Byzantine empire*
King's College London, Centre for Hellenic Studies

Short session - Archeology and Surveillance: plague in Italy and Iran

16:30-16:50 Short presentations by Prof. Mauro Rubini and Dr. Abdolrazagh Hashemi Shahraki regarding their work on paleopathology and plague surveillance, respectively.

Discussion

16:50 - 18:15 Discussion and access to the speakers

Thursday, November 20th, 2014: 8:00-14:05

Welcome

8:00 - 8:30 Coffee

Session 3: Plague persistence and pandemics

8:30 - 9:15 Dr. Barbara Bramanti – *The current genetic evidence for sites of the origin of the three plague pandemics*

University of Oslo, Department of BioSciences

9:15 - 10:00 Dr. Christos Lynteris – *The perception of the plague epidemic in northern China*

University of Cambridge, Social Sciences and Humanities

10:00 - 10:45 Dr. Viveka Vadyvaloo – *Persistence and re-emergence of the plague using both fleas and protozoa as host models*

Washington State University, College of Veterinary Medicine

10:45- 11:30 Dr. Eva Panagiotakopulu – *Pharaonic Egypt and the Origins of Plague*

University of Edinburgh, School of Geosciences

11:30 - 12:15 Buffet Lunch

Discussion

12:15 - 13:15 Structured Discussion, followed by access for group discussions with the Speakers

13:15 - 14:00 Lecture "*Evolution of human infectious diseases*" and summarizing thoughts, by prof. Jared Diamond

14:00 - 14:05 Closing remarks by the Preses of the Academy, Prof. Nils Chr. Stenseth