The role of louse-transmitted diseases in historical plague pandemics

Rémi Barbieri, Michel Drancourt, Didier Raoult

The rodent-murine ectoparasite-human model of plague transmission does not correspond with historical details around plague pandemics in Europe. New analysis of ancient genomes reveal that *Yersinia pestis* was unable to be transmitted by rat fleas until around 4000 Before Present, which challenges the rodent-murine ectoparasite-human model of plague transmission and historical details around plague pandemics in Europe. In this Review, we summarise data regarding *Y pestis* transmission by human lice in the context of genomic evolution and co-transmission of other major epidemic deadly pathogens throughout human history, with the aim of broadening our view of plague transmission. Experimental models support the efficiency of human lice as plague vectors through infected faeces, which suggest that *Y pestis* could be a louse-borne disease, similar to *Borrelia recurrentis*, *Rickettsia prowazekii*, and *Bartonella quintana*. Studies have shown that louse-borne outbreaks often involve multiple pathogens, and several cases of co-transmission of *Y pestis* and *B quintana* have been reported. Furthermore, an exclusive louse-borne bacterium, namely *B recurrentis*, was found to be circulating in northern Europe during the second plague pandemic (14th–18th century). Current data make it possible to attribute large historical pandemics to multiple bacteria, and suggests that human lice probably played a preponderant role in the interhuman transmission of plague and pathogen co-transmission during previous large epidemics, including plague pandemics.

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Introduction

Insights concerning historical plague pandemics have challenged assumptions about the ecology and transmission of the causative agent, *Yersinia pestis*, with cutting-edge technologies such as whole genomes sequencing of ancient samples giving us the ability to further explore this issue. The historical framework proposing transmission from rats to rat fleas to humans was initially proposed in three previous historical plague pandemics. The first pandemic began with the Plague of Justinian from circa 541 to 544 CE and continued for about two centuries in Continental Europe and the Mediterranean basin until 750 CE, killing probably between 0·1% and 50·0% of the population.[1] The second pandemic began with the so-called Black Death episode from 1346 to 1353,[2] claiming about 25 million deaths and devastating medieval Europe in an endemic way until the middle of the 18th century (the last epidemic reported in western Europe is the one affecting Marseille from 1720 to 1722). The current third pandemic began in 1772 in the Chinese province of Yunnan[2] before hitting Hong Kong in 1894 and then spreading around the world via railroads and steamboats.[3] It is estimated that this current pandemic has already claimed the lives of more than 13 million people.[4] Yet it is not clear whether the presence of rats and their fleas at the time of these pandemics were necessarily in sufficient abundance. In historical texts, the description of a fever associated with buboes (ie, swollen inflamed lymph nodes) has been pathognomonic of the plague since Justinian times, when it was clearly described by Procopius.[5] The *Y pestis* lineage responsible for the Plague of Justinian (541–750 CE)[6–9] represented a (now extinct) clade that was distinct from the Black Death episode that decimated Europe in the Middle Ages (1346–1353) during the second plague pandemic (14th–18th century).[10–16] Despite the independency of these strains, the clinical symptoms were similar during the first and second pandemics.[1,9,12,15] Indeed, the Black Death was rather a word coined to refer to plague epidemics in the symbolic register (with a negative connotation) than a denomination used by contemporaries to describe the clinical manifestation of the plague. Therefore, the Black Death was later wrongly associated with purpuric fever or haemorrhagic fever.[17]

In 1894, during the third pandemic, Alexandre Yersin's investigations done in Hong Kong led to the discovery of the *Y pestis* bacteria, the causative agent of the plague.[3] In 1898, Paul-Louis Simond completed the epidemiological cycle proposed 4 years earlier by Yersin.[18] He reported an indisputable mechanism by which infected fleas (*Xenopsylla cheopis*) could spread *Y pestis* from one murid to another.[19] The discovery of late-stage biofilm-dependent transmission by *X cheopis*[20,21] then made it possible to study 25 *Y pestis* genes involved in the transmission of the plague by fleas.[22] In particular, the *ymt* gene, which codes for a phospholipase D hydrolase and allows *Y pestis* to survive inside the flea's digestive tract, is considered to be essential.[23] These studies showed that *X cheopis* is the vector transmitting plague from rats to rats, with a possible accidental transmission to human beings. Later, new methods of whole genome sequencing of ancient DNA completely undermined this vision and molecular analysis traced the plague back to at least 5000 Before Present (BP),[24] detecting it not only on the arid shores of the Mediterranean but also in the northernmost part of Europe, hence in heterogeneous ecological environments.[24–30] This finding provided an unexpected opportunity to question the classic epidemiological transmission cycle from rats to rat fleas to humans. In this Review, we summarise data regarding *Y pestis* transmission by human lice in the context of genomic evolution and co-transmission of other major epidemic

deadly pathogens throughout human history, with the aim of broadening our view of plague transmission.

Ancient plague transmission explained by paleomicrobiology

Palaeomicrobiology studies make it possible to consider another model of plague diffusion that does not feature rats and rat fleas. Indeed, between 2011 and 2020, 88 ancient *Y pestis* genomes were sequenced.[7–9,12–16,24–30] These genomes were all recovered from Eurasian samples of teeth or bones and dated from 5000 BP (Sweden)[24] to 1722 (France),[14] thus covering the first two historical pandemics. Complete genome analysis showed the systematic presence of plasmid virulence-associated genes, such as the *pla* gene (pPCP1 plasmid) that is coding for a plasminogen activator or the *CAF-1* gene that is responsible for antiphagocytic activity (pMT1 plasmid); both of these genes are associated with human mortality.[31,32] Furthermore, the archaeological identification of several individuals in the same grave, combined with the molecular presence of plague virulence-associated genes, indicated that plague was already a deadly epidemic disease during the Neolithic and Bronze Age, as further described during historical pandemics.[1,33] Whereas 72 of 88 available ancient genomes do harbour the pMT1-encoded *ymt* gene, 16 of 88 ancient *Y pestis* genomes dating from 5000 BP (Sweden) to 3701 BP (Russia) lack this gene,[24–27] which is involved in the survival of *Y pestis* in the flea's gut and is essential in effective plague flea transmission.[34] Spyrou and colleagues[30] indicate that the *ymt* gene probably appeared approximately 3800 years ago during the Early Bronze Age and that both the *Y pestis* flea-adapted and non-adapted variants circulated in Eurasia throughout the Bronze Age. These findings indicate that, for approximately 1200 years, fatal plague did not necessarily require rat fleas.[24–27,30] Regarding these results, *Y pestis* appears to be an old human pathogen present throughout Eurasia, even in the most northern part of Eurasia. Furthermore, the geographical location of the strains, combined with an absence of the *ymt* gene (in Austria, Croatia, Estonia, Germany, Lithuania, Norway, Poland, Russia, and Sweden),[24–27] does not seem to support a transmission mechanism mediated by rats and rat fleas.[35–37] The presence of the *pla* gene in all ancient genomes is an unequivocal indicator that plague could be bubonic and therefore transmitted by arthropods (ie, via the introduction of *Y pestis* in human tissues following biting).[23] Genetic and archaeological studies[38–40] provide evidence that the only known competent plague vectors present during the Neolithic and Bronze Ages in Eurasia were human fleas (*Pulex irritans*)[39,40] and the human louse (*Pediculus humanus* subspecies).[38,41,42] However, *P irritans* is known to be a poor plague vector[22,43] with a low blocking capacity.[44] Some authors have hypothesised that *P irritans* could have been involved in the spread of plague during the second pandemic[43–45] but currently, the transmission rates obtained in the laboratory using early phase transmission (0·14%) are too low to consider *P irritans* as an efficient vector.[20,22,46,47] Therefore, the most parsimonious hypothesis is that the human-to-human transmission of the plague at this time might have mostly involved human lice, given the absence of effective flea vector (such as *X cheopis*) and the presence of all associated virulence genes involved in deadly bubonic plagues.

The rat-and-flea model and the historical demography of the second pandemic

Beyond transmissions during the Neolithic and Bronze Age, the epidemiological rat–rat flea–human schema cannot explain the speed and magnitude of the Black Death, during which the spread was faster than during the current third pandemic.[36,43,48] In particular, this model is not compatible with the 1·5–6 km/day speed of dissemination of the Black Death as calculated using historical sources.[49] Occasionally, this scheme cannot even be implemented given the absence of its protagonist.[35] For example, in northern Europe, there are few archaeological records of *Rattus rattus* in the Middle Ages, which appears to have been unevenly distributed in coastal towns.[36,37] Current archaeozoological data do not appear to be compatible with the classic patterns of *Y pestis*[35–37,50] given the low density of rat bones found from medieval archaeological sites in Nordic countries.[36,37] Some authors argue, however, that the scarcity of rats in medieval Europe[51] is compatible with the classic model of transmission (from rats to rat ectoparasites) observed in India during the third pandemic.[33,52,53] These conclusions are based on unsupported assertions[47] or on mathematical models in which the plague can persist in relatively small rodent populations.[54] Nevertheless, the current parsimonious hypothesis is that it is very unlikely that rats could have played a meaningful role in vectorisation of the plague in Nordic countries.[36,37,47] For example, in the 15th century, two waves of plague killed approximately 50% of Icelanders despite an attested absence of rats.[35] However, this observation did not exclude the presence of other cold-resistant mammals that could have served as intermediate hosts. Finally, although it is acknowledged that the Oriental rat flea (*X cheopis*) has been the main vector of plague epidemics since the end of the 19th century, its role in disseminating the second pandemic is controversial because there are no fossil records of *X cheopis* in Europe. However, remains of *P irritans* have been discovered in these latitudes[55]—a finding that is consistent with the fact that the northern European climate might not be conducive to this Oriental flea species, which were adapted to the warmer climate of southern Europe, as evidenced by their involvement in the third pandemic's plague outbreak in four cities in southern Europe (ie, Barcelona, Malta, Marseille, and Ajaccio).[56]

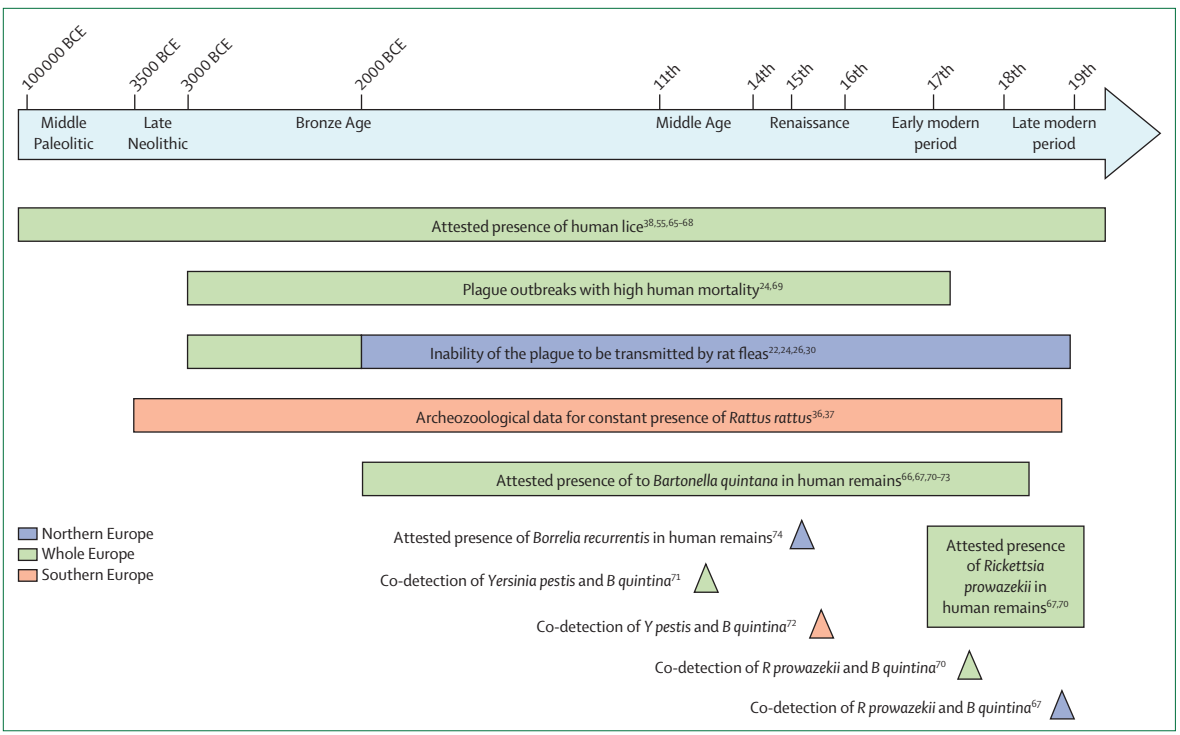

Figure 1: **Timescale of paleomicrobiological data related to louse-borne pathogens from 100 000 BP to the 19th century**

Studies have shown the incapacity and inefficiency of *Y pestis* transmission when *X cheopis* is exposed to low temperatures (≤12·5°C).[57–59] This finding questions the causes of the plague, suggesting that the plague has been caused by haemorrhagic fever viruses[60] without any scientifically identified causative agent. Accumulated evidence in favour of *Y pestis* indicates that the plague had the same clinical features and mortality and dissemination rates without rats and rat fleas, as illustrated by the northern epidemics.[35,50] Furthermore, studies on plague and climate seem to indicate that the timing of the second plague pandemic is correlated with hot Mediterranean summers in southern Europe, which are compatible with flea transmission.[61] By contrast, in the southern Baltic states and Iceland, plague was driven by a cold climate (<10°C)[57] or a climate consistent with the Little Ice Age (ie, a period of cooling that occurred after the Medieval Climatic Optimum).[62] Such temperatures are completely incompatible with rat flea transmission but consistent with transmissions through other vectors, such as human lice, which can live in the heat of clothes and could have been an effective *Y pestis* vector following the 1·5–6km/day speed of plague dissemination[49] that corresponds to human travel through Eurasia to the most northern places in Europe.[55] In summary, in the context of the plague epidemic, the two main methods of transmission are ectoparasites and aerosols. Considering that interhuman transmission of plague through aerosols has shown to be ineffective unless particular conditions are met,[63,64] the most plausible form for the ancient plagues is the bubonic form. Particularly during plague outbreaks in Nordic countries, lice are the most plausible vector proposed (figure 1).

History and role of lice in human infection

Lice are among the oldest human ectoparasites recorded. Lice are estimated to have appeared around 100 million years ago, and speciation between chimpanzee lice (*Pediculus schaeffi*) and human lice (*P humanus* subspecies) occurred approximately 5·6 million years ago.[38] Ancient human lice have been recovered from all continents with the exception of Oceania. Lice dated as being 9000 years old were retrieved from textiles in Israel.[65] Lice have also been directly identified on mummified human bodies in Egypt and pre-Columbian America.[75,76] Regarding European prehistory, ancient lice have been found in textiles in Austria.[66]

Based on these observations, one of the main candidates (with *P irritans*) for a vector of plague in the Bronze Age are human lice. Furthermore, the same model can probably be applied to the great medieval epidemics in northern Europe, where the presence of lice has been shown.[55] These outbreaks had a high rate of mortality and led to the decline of northern populations.[35,50]

Louse-borne diseases are able to cause immense epidemics, as evidenced by contemporary observations. For example, during the Napoleonic wars, approximately 30% of Napoleon's soldiers died of typhus when they were infested with lice in Vilnius, Lithuania, during the Russian campaign.[67] Millions of people also died of louse-borne

relapsing fever, typhus, and probably trench fever transmitted by lice during the Russian Revolution and World War 2.[77] The last severe outbreak of louse-borne diseases was observed in Burundi in 1997, causing probably 10 000 deaths and 100 000 infections.[78]

The role of lice as a vector of *Rickettsia prowazekii* was first identified by Charles Nicolle, who earned a Nobel Prize for this finding. Nicolle noted that patients whose clothes were removed and who were bathed during hospital admission did not transmit typhus to other people in the hospital, including health-care workers.[79] Examining the clothes of patients revealed the only possible vector and source of transmission, the louse. Later, the louse was found to be responsible for trench fever during World War 1.[80] Finally, the presence of *Borrelia recurrentis* (the causative agent of relapsing fever) in lice was identified as early as the 19th century in Ireland.[81]

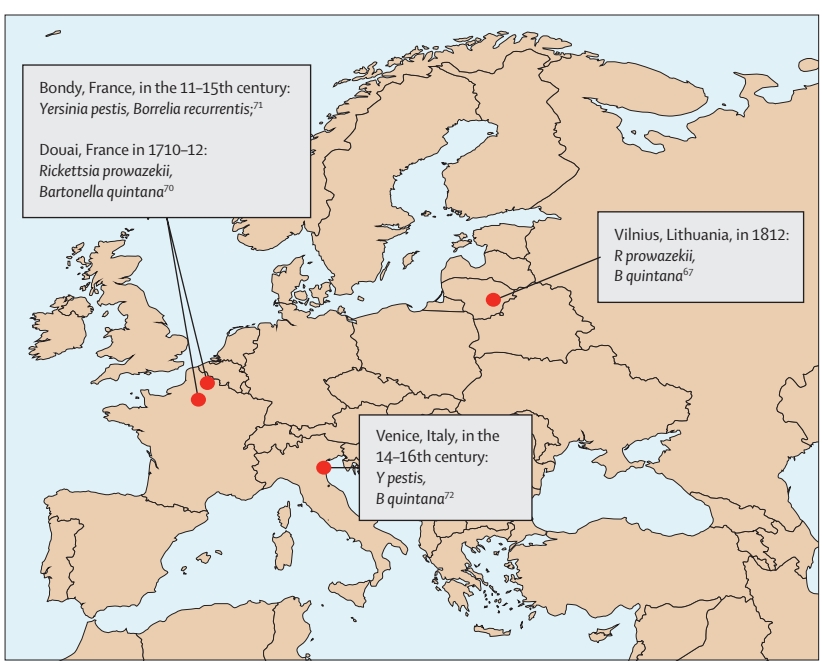

Figure 2: **Map of detection of presumably co-transmitted ancient louse-borne bacteria in Europe from the 11th to the 19th century**

Among louse-borne outbreaks, therefore, it is generally difficult to determine which diseases are caused by which pathogens. Indeed, among Napoleon's soldiers, *R prowazekii* and *Bartonella quintana* were identified retrospectively as co-occurring during the same epidemic, but *B recurrentis* was not tested for.[65] In Burundi, the cocirculation of *R prowazekii* and *B quintana* during the same epidemic was highlighted, but *B recurrentis* was not tested for.[67] In historical studies in Douai, France, done by molecular testing of the dental pulp, the co-occurrence of *R prowazekii* and *B quintana* was highlighted.[70] These studies represent the first evidence of *R prowazekii* in Europe. The cocirculation of *Y pestis* and *B quintana* has also been observed in Venice, Italy, and Bondy, France,[71,72] suggesting a coupled epidemic (figure 2). Thus, given that many infectious diseases might be transmitted by the same mechanism, epidemic agents could be considered responsible by association (figure 2).

The discovery of two microorganisms during the same pandemic is probably indicative of the fact that both pathogens have the same mechanism of transmission, allowing us to hypothesise that *Y pestis* and *B quintana* were co-transmitted by body lice in Venice and Bondy.

Possible role of lice in ancient plague outbreaks

Observation of the natural infection of body lice (*Pediculus humanus humanus*) from plague-infected humans began at the beginning of the 20th century when the spontaneous infection of head lice with plague (*Pediculus humanus capitis*) was found. With regards to body lice, Swellengrebel and Otten[82] recovered infected body lice from the clothes of a plague victim and from an inhabitant of a plagued house in 1914, and in 1935, the capacity of body lice to be infected by ingesting plague-contaminated blood was finally shown. The first known observation of human contamination by body lice was made among Andean Indians who had pharyngeal plague after consumption of

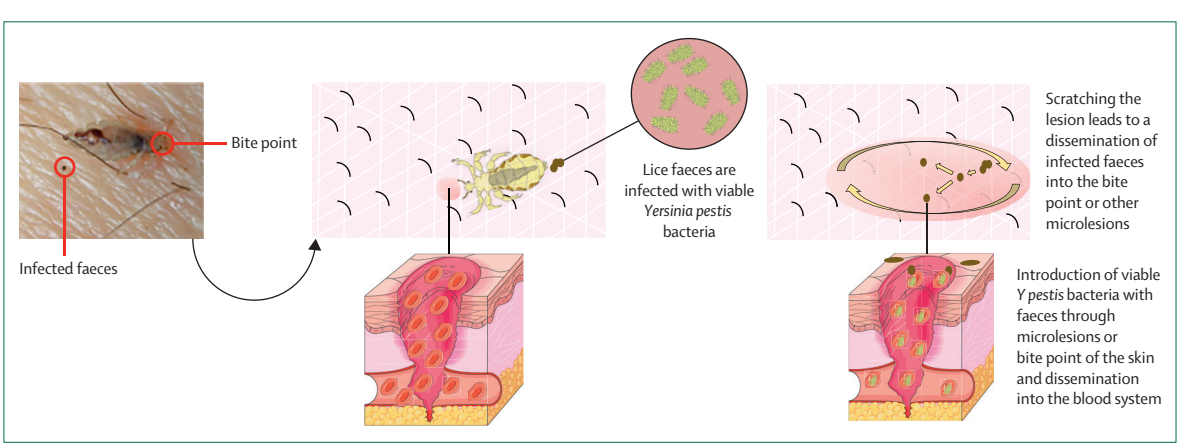

Figure 3: **Schematic view of *Y pestis* lice-to-human transmission mechanisms**

contaminated lice,[83] although it is not known if the bacterial load present in infected body lice can cause pharyngeal plague that was observed by John D Long after the consumption of infected lice.[84] The vectoral capacity of lice by contamination of their faeces was discovered by Blanc and Baltazard,[85] but their observations and experiments were forgotten and then rediscovered. In 2006, we unambiguously showed the plague-vector potential of body lice by faecal contamination with viable *Y pestis* bacteria in an experiment with rabbits (figure 3).[86]

We also found *Y pestis* in head and body lice during one of the last endemic outbreaks in Congo.[87,88] Experimental studies done both in the 1950s and in 2006 highlighted the vectoral capacity of lice for *Y pestis* in rabbits.[85,86,89] Current models that integrate lice into plague transmission models in the Middle Ages are able to explain the spread that could not be explained when exclusively using the rat–rat flea–human transmission model.[90] All these studies could also shed light on the role played by clothing in the dispersal of *Y pestis* in an epidemic context, as medieval populations were infested with lice until the modern period (1492–1850; (appendix pp 2–3).[68]

In the past, authors wrote about the danger posed by the clothing worn by people with plague when it came to the spread of the plague, especially during the epidemics of Marseilles (1720–22)[91] and Moscow (1771).[69] These observations foreshadowed the role of lice and their infected faeces that was demonstrated in 1909 during an epidemic typhus outbreak by Nobel Prize winner Charles Nicolle.[79] Further investigations might address whether such a mode of transmission might apply to pneumonic plague contamination (appendix pp 2–3).

Historical interhuman transmissions of *Y pestis*

We reviewed historical texts dealing with plague to consider the role of lice in the transmission of deadly infections, including plague. The first mention of lice as putative vectors of plague was found in a treatise written by Nicolas Hartsoeker in 1722.[92] This text was written at the end of the Great Plague of Marseille (1720–22) and refers directly to this outbreak.[92] Hartsoeker argued that plague is not transmitted by air but by the bite of microscopic insects, such as lice, which find refuge in rags, clothes, and bedding. He described them as follows: "I conjecture that the plague is caused only by invisible insects which hide themselves willingly in these stuffs (tatters, goods or clothes and make their nests inside; that these insects multiply extremely in a very short time [...] that these insects do not fly, or at least they do not fly very far, but that they do rather like lice that we win easily when those who are infected; that their bite is in proportion to their size, which is at least as dangerous as that of vipers; and that their numbers compensate for their smallness".[92] The hypothetical role of lice in the plague was also mentioned during the Moscow plague epidemic in 1771 by Russian scientists on the basis of the role that clothing played in the contagion of the disease.[69,91] The absence of reported cases of animal plague during some large outbreaks, such as in Marseille (1720–22) or Moscow (1771), revealed that there was probably a mostly interhuman transmission, which cannot be explained by pneumonic plague because of its low transmission rate.[69] Although more than 200 mammal species are susceptible to plague,[93] in some cases, no major epizootics were observed during plague outbreaks.[69,91] Furthermore, regarding ancient historical texts about second pandemic plague outbreaks, the great majority of reported cases were bubonic.[47] Bubo (meaning swelling of lymph glands in Latin, coming from the ancient Greek word *boubōn* which means groin or swelling in the groin) is an adenitis and was common during the 15th century (appendix pp 4–5).

During the Plague of Marseille (one of the most documented plague episodes [1720–22]), lymphadenopathies were given different names according to their location on the body, thereby lymphadenopathy of the glands around the ears was named parotid. Lymphadenopathies on inguinal and axillary parts of the body were known as buboes, and lymphadenopathies located on other parts of the body were known as abscesses.[94] In the modern semiology of the plague, these three terms are grouped under the term buboes. During the second pandemic, buboes were primarily reported on the inguinal parts of the body or on axillary parts of the body, depending on the source;[47,91] these locations are compatible with human lice bites (appendix pp 6–7). The most common location of bubo, the groin, offers a refuge for body lice in the underwear (appendix pp 6–7), whereas popliteal adenitis might occur from fleabites on the legs. At this time, underwear commonly covered the thighs. In the modern era, scratching lesions following plague infection are usually found in the underwear area. After the second pandemic, human body lice became rarer thanks to increased hygiene; however, on rare occasions, body lice could have been involved in plague transmission during the third pandemic, as evidenced by the bubonic outbreaks in Glasgow, UK,[95] in 1900 and in Congo in 2010.[88]

See Online for appendix

The future of the plague in the context of louse-borne diseases

The disappearance of massive *Y pestis*, *B recurrentis*, and *R prowazekii* outbreaks in countries with a high level of hygiene is most likely evidence of the pronounced disappearance of body lice and anthropophilic fleas (*P irritans*), another potential vector for interhuman transmission of plague.[44] Rats are still common in high-income countries where body lice are scarce, and plague foci persist in low-income countries, such as Congo and Madagascar.[96,97] However, sporadic cases have been reported in the USA and northern Africa.[98,99] The 2018 discovery and sequencing of *B recurrentis* that was recovered from two teeth samples from Oslo, Norway, in

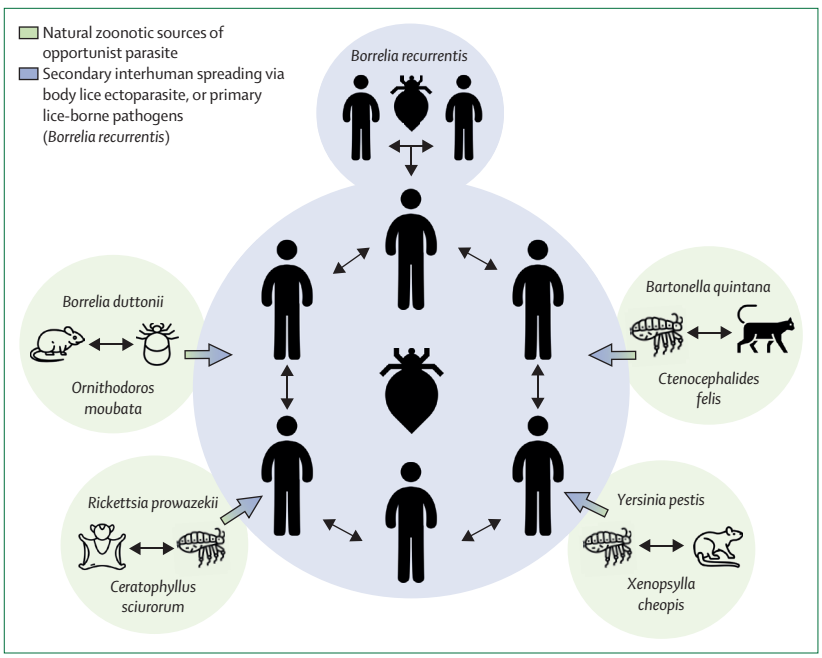

Figure 4: **Schematic scenario showing how zoonotic agents might be transmitted among human populations via body lice**

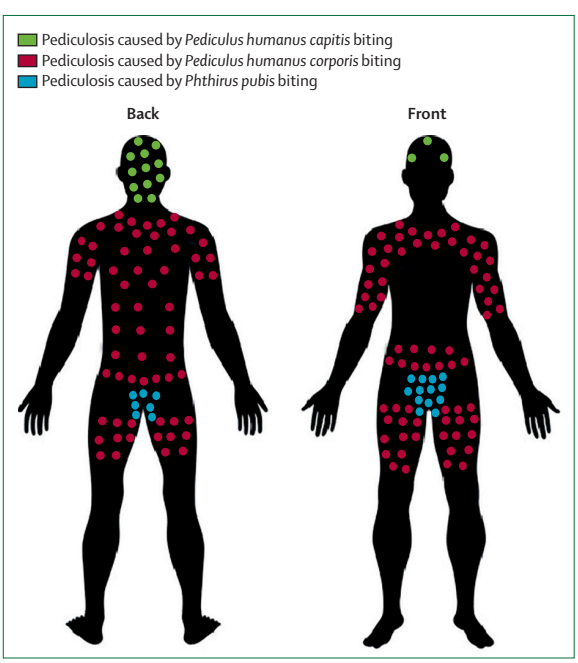

Figure 5: **Repartition of pediculosis on human body**
Pediculosis is caused by human lice bites. Here, we reconstructed pediculosis body repartition documented from more than 500 photographs of modern pediculosis cases, taken by health-care workers in the Institut Hospitalo-Universitaire, Marseilles, France.

the 15th century, a time when the plague was endemic,[74] offers evidence of the circulation of both pathogens and body lice in the late medieval period. *B recurrentis* was circulating at the same time as *R prowazekii*, but in different locations.[67,74] Moreover, *B recurrentis* is transmitted by lice faeces, similar to *R prowazekii* and *B quintana*.[100] A zoonotic agent, such as the murine soft-tick-transmitted *Borrelia duttonii*,[101] might become an interhuman-transmitted pathogen, such as *B recurrentis*, after a louse becomes contaminated after biting a bacteraemic patient. Thus, *B recurrentis* is probably a model organism for lice-transmitted pathogens, and the circulation of plague has probably more to do with human hygiene and the presence of body lice than with the transmission of the bacterium as a purely zoonotic pathogen. Moreover, the *pla* gene, which is considered a key factor in *Y pestis* transmission, is unspecific and has been found in some strains of *Citrobacter koseri* isolated from rats or in *Escherichia coli*.[102,103] This gene coding for a protease can partly explain human pandemics, but the success of *Y pestis* as a zoonotic agent is rather caused by the murine toxin, the *ymt* gene.[93]

We can construct a scenario for the passage of pathogens detected in wild animals, vectored by arthropods that occasionally bite humans and are responsible for zoonosis (figure 4). Among these pathogens, *B quintana* can remain for years in human organisms and populations.[104] Similarly, typhus can relapse in the form of Brill-Zinsser disease up until 40 years after the initial infection with *R prowazekii*, indicating that humans can host the pathogen and transmit it through lice throughout their lifetimes.[105,106] *B recurrentis* is also an endemic relapsing fever pathogen that persists in individual human beings.[107] However, because *Y pestis* is not a persisting pathogen in the human organism and populations, plague is the louse-transmitted disease that manifests itself in successive waves, resulting in multiple introductions in Europe because of the absence of a human reservoir.[61]

Lice can considerably amplify the spread of microbes, leading to the creation of a hypervirulent clone with a reduced genome size and massive interhuman transmission.[108] Thus, *R prowazekii*, which is well identified in flying squirrels in the USA, is likely to occasionally transmit infections to humans via its arthropods, resulting in a situation in which a new typhus cycle can begin. Causative agents of recurrent tick-borne borreliosis, such as *B duttonii* or *B crocidurae*, have a high genetic homogeneity. *B recurrentis* clearly appears as an emerging clone of *B duttonii* with a reduced genome.[101] In some cases, *B duttonii* is transmitted to humans,[109] and human-to-human transmission could lead to the selection of a hypervirulent clone with a reduced genome size in epidemics of pediculosis. We have shown that *B quintana* is also a zoonosis affecting cats.[110] The transmission of *B quintana* from cats to humans can be made through fleas, and its further spread by lice can occur on a considerable scale. However, *B quintana* has been found in individuals who died approximately 2000 years BCE in Europe—at a time when cat fleas were probably not the main vector.[66,111] In Poland, *B quintana* was propagated on a large scale in

Search strategy and selection criteria

We used PubMed and Google scholar to search for articles dealing with plague or lice, or both, that were published between May 1, 1720, and March 1, 2020, and written either in French or English. We used the search terms "Yersinia", "lice", "Pestis", "Pediculus", "ancient", "plague", or "Medieval". Additionally, we reviewed relevant articles cited in references of identified literature and included them as primary sources when appropriate.

volunteers who were feeding lice for typhus-producing lice colonies to produce a vaccine against epidemic typhus, as previously reviewed.[112] The hyper-specialisation of *B quintana* and its high transmission rates have been associated with a reduced genome.[113] Finally, the same model can be suggested for plague, because plague is a zoonotic disease that can affect several animals (murids, camels, sheep, and cats)[93] and rat fleas are likely to bite humans during epizootics. Although most plague cases result from the ectoparasite-borne transmission of *Y pestis*, the pathogen can also be efficiently transmitted by contaminated food.[114–116] In situations of epidemics of pediculosis, such as those in eastern Congo,[96] this sporadic form can be followed by a micro outbreak. In special situations, body lice epidemics could occur. This type of epidemic happened in concentration camps during World War 2. It was also observed during the civil war in Rwanda and Burundi as well as in eastern Congo where 100% of the refugee population was infested with lice and where two epidemics—epidemic typhus and trench fever—developed simultaneously.[78] The nature and persistence of epidemics of pediculosis outside the contemporary era are difficult to evaluate, as few texts allow them to be analysed; however, it is probable that during these epidemics of pediculosis, several pathogens were transmitted (figure 5). In addition to the cases that are authentically attributable to plague, with the presence of buboes, cases of severe fever sometimes associated with jaundice (such as cases infected with *B recurrentis*) are likely to indicate one of several epidemics that are transmitted by lice.

Conclusion

In summary, current paleomicrobiological data provide an understanding of past pandemics transmitted by lice, which have probably been the vector, together with mosquitoes, of the most deadly and widespread pandemics in human history. The discovery of *B recurrentis* from the 15th century in northern Europe highlights the vast circulation of human body lice during this period in this area and suggests that the louse was a competent vector; the louse was probably linked with plague-related outbreaks in the late medieval period, as proposed by field studies, experimental studies, and models. Moreover, the cocirculation of the plague with other louse-borne diseases suggests that multiple pathogens could have been identified as the plague. Furthermore, modelling of ancient plague epidemics shows that transmission by rats and rat fleas is not consistent with major outbreaks during the second pandemic. These postulations, combined with the rediscovery and demonstration of the efficiency of lice as a plague vector, provide substantial evidence on which to base a new theory around *Y pestis* transmission in medieval Europe. There is sufficient evidence to suggest that lice played a major role in plague transmission and spread following the same schema as other louse-borne diseases. This proposed framework change allows for a better understanding of past and future epidemics.

Contributors

DR and MD contributed to the conception of the Review. RB, MD, and DR did the literature search. RB created figures. DR provided photography. RB, MD, and DR wrote the manuscript. All authors contributed to the interpretation of the data and revision of the manuscript.

Declaration of interests

We declare no competing interests.

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