Plague, malaria and demographics in past Italy:
recent acquisitions and open problems

LORENZO DEL PANTA
Alma Mater Studiorum – Università di Bologna

1. Introduction

In Italy, as elsewhere in Europe, the recurrence of severe and frequent plague epidemics, starting with the most violent and deadly in the mid-14th century, has strongly restricted population growth. Undoubtedly, the terrible catastrophes due to the plague caused the drastic reduction of the Italian population between the mid-14th century and the first decades of the 15th century. Their attenuation led to a subsequent demographic recovery, at first very slow and then more accelerated during the 16th century. Again, the great epidemics of plague, along with the less violent but more frequent and widespread ones of petechial typhus, caused the slowdown in demographic growth during the 17th century. Finally, we cannot ignore the influence that the attenuation of the crises (with the disappearance of the plague) had on the uninterrupted demographic growth that characterized a large part of the Italian territories from the second half of the 18th century and which became generalized in the following century.

Therefore, it is more than justified that historians and demographers have focused on the economic, demographic, social manifestations and consequences of the great epidemic crises. On the other hand, it must be recognized that it is much more complex, in the most remote centuries and also in relatively recent times[1], to investigate the role of many other diseases that have contributed to maintaining mortality at very high levels. Moreover, even the mortality gaps that can be highlighted between the populations of the different territories in Italy in the past cannot always be explained only by the greater or lesser impact of the major epidemic diseases.

In an essay dedicated to studying the sanitary conditions of Tuscany in the first decades of the 17th century, Carlo M. Cipolla (1989, 12) pointed out how the Health Magistracy mainly focused on the prevention and control of plague epidemics, while only occasionally «…they were worried about various diseases such as typhus, tertian fevers, smallpox, influenza epidemics…». Nevertheless, in this study, Cipolla specifically chose to analyse the medical reports sent to the Health Magistracy of Florence during a period (1608-1627) in which the Florentine state was immune to the plague (which then reappeared for the last time in 1630). From the reports of the Tuscan doctors, we can see a general picture of morbidity and mortality characterized by the massive prevalence of other infectious diseases. In

SIDeS, «Popolazione e Storia»,
1/2021, pp. 9-27. DOI: 10.4424/ps2021-1

particular, malaria, petechial typhus and gastrointestinal infections were present in the endemic state, occasionally resulting in epidemics.

In the conclusions of his essay, Cipolla (1989, 106-107), after recalling an observation by Grmek (1975, 75) that «…for too long historians and demographers have been fascinated by the spectacular devastation of the plague and have therefore neglected the impact of other diseases…», complains about the lack of «…a history of malaria that accurately specifies the geographical extent, levels and fluctuations of morbidity, and the cycles of recrudescence and remission». Cipolla pointed out, among other things, that the medical reports of the time indicated the spread of malaria in Tuscany well outside the traditional and more well-known Maremma coastal areas. Above all, he insisted that the presence of this endemic disease represented a severe economic (as well as health) problem, stating that «…malaria often does not kill but weakens humans and undermines their productivity, thus acting as a determining factor of misery and economic stagnation».

This paper is the result of various re-readings on the history and demographic impact of major historical diseases, to which I have recently dedicated myself, editing a new edition[2] of my older essay on the history of epidemics in Italy (Del Panta 1980). I intended to consider, among the factors that have conditioned the long-term evolution of the Italian population, not only the great plague epidemics but also, in parallel, the presence of endemics, starting with malaria[3], recognizing that the history of this disease, especially as regards its long-run demographic impacts, is still largely to be written.

2. The plague: notes on recent acquisitions regarding the nature and evolutionary history of the pathogenic germ

The plague has been responsible, in the history of humanity, for three major pandemics, which are attributed to possible variants of the same pathogen. The first pandemic affected the Mediterranean and Europe from the middle of the 6th century (the so-called *Justinian plague*). The second and perhaps best-known plague devastated Europe from 1348 onwards. Currently, the set of epidemics that, from that date, continued to hit the Mediterranean countries and Europe until the eighteenth century is considered as a single long pandemic cycle. The third pandemic, originating in China in the second half of the 19th century, grew massively and gained worldwide attention when it spread to Hong Kong in 1894. In this case, two scholars managed to isolate the bacterium responsible for the disease almost simultaneously and independently[4]. A few years later, in 1898, the French physician and biologist Paul-Louis Simond (1858-1947), fighting in Bombay against the epidemic, confirmed that the primary vector of the bacillus responsible for the epidemic was a flea. It was the *Xenopsylla cheopis*, a parasite of the *Rattus rattus*, the typical domestic rat. Today, the bacillus is known as *Yersinia pestis*, named after one of the two scientists who isolated it[5].

What is surprising today (Little 2011, 269) is the ease with which both scientists (Kitasato and Yersin) who identified the germ responsible for the plague hastened to declare, on the sole basis of the descriptions reported in the literature on the symptoms of the great epidemics of the past, that the epidemic waves that had

struck in the 14th century and in the following centuries in Europe and the East had been caused by the same pathogen. Since then, and for a good part of the 20th century, historians, demographers and scientists have not substantially questioned their assertion.

About ninety years since the discovery of Yersin and Kitasato, however, the first critical voice appeared. The zoologist Graham Twigg (1984) challenged the commonly accepted interpretation of the role played by mice during the medieval and modern epidemics and claimed that a different bacterium (anthrax) was responsible for the plagues that had struck Europe in the past. Some years later, Christopher Duncan and Susan Scott (2001, 2005) hypothesized a disease transmitted directly from human to human, much more contagious and lethal than the plague, which they defined as «viral hemorrhagic fever». The claims proposed by these authors have been contradicted by other epidemiological investigations (Alfani, Cohn 2007a; Alfani, Cohn 2007b; Alfani, Bonetti 2019) which, in any case, suggest ways of transmission of the epidemics of the 16th and 17th centuries other than those commonly accepted. These latest investigations raise doubts that the historical plagues had epidemiological characteristics corresponding to those of the *Yersinia pestis* recognized during the last pandemic, and suggest that the infection occurred mainly from man to man (Alfani 2010, 138).

The debate in the historical context (regarding the identification of the pathogen of plague epidemics and its mode of transmission) was very lively and lasted for many years[6]. Among the historians, Samuel Cohn held, with more conviction and for longer, a sceptical position regarding attributing responsibility for historical plagues to *Yersinia pestis* (Cohn 2002). On the opposite side, there was the criticism, even very harsh, by Ole Benedictow (known for his outstanding work in 2004 on the *Black Death* in Europe) to the theses expressed by Cohn (Benedictow 2010).

In the meantime, in the scientific field from the latter part of the 20th century, the first research projects aimed to reconstruct the evolutionary history of *Yersinia pestis* and verify whether the same microorganism was actually at the origin of the major historical pandemics. The first results obtained by a group of researchers of the Centre national de la recherche scientifique (CNRS) and the University of Marseille did not provide absolute certainty[7] and were contested by other researchers, mainly working in UK research centres[8], to whom the historians who contested the traditional thesis also referred.

The scientific literature on the subject is by now very rich and, at least in part, not easy for the layman to understand[9]. However, I attempt here to summarize the most crucial stages of the research that has evolved, in just over a decade, to provide a first sure (positive) answer regarding the identification of *Yersinia pestis* as the pathogen responsible for both the first and the second major pandemics. To do this, I follow the excellent essay by Lester Little (2011)[10], who reconstructs the chronology of the successive acquisitions of the various research groups initially in competition and then often in a collaborative relationship. This debate led (Haensch *et al*. 2010)[11] to a fixed point in 2010, demonstrating in an indisputable way that *Yersinia pestis* was the pathogen responsible for the *Black Death*.

Stepping back a decade or so, an important article by researchers from the Molecular Genetics Max Planck Institute in Berlin, together with other researchers at the Pasteur Institute in Paris, should be noted (Achtman *et al.* 1999). This study reports the results of an analysis of the genetic structure of three *Yersinia* species: *Y. pseudotuberculosis*, *Y. enterocolitica* and *Y. pestis*. The authors conclude that *Y. pestis* is a clone that emerged relatively recently (their estimate is between 1,500 and 20,000 years from the present time[12]) from *Y. pseudotuberculosis*.

In their study of 1999, Achtman and colleagues accepted, with reference to *Y. pestis*, the distinction proposed a half-century earlier by Devignat (1951) in the three biovars: *Antiqua*, which would have generated the first pandemic; *Medievalis*, responsible for the second pandemic; *Orientalis*, the basis of the third pandemic. However, a subsequent article by Achtman *et al.* (2004) declared that the tripartite division of Devignat could not keep up with modern biomolecular analysis, admitting that it was premature to infer an association between any modern molecular grouping (biovar of *Y. pestis*) and any particular pandemic wave occurring before the 20th century. Since the classic division that attributed subsequent pandemics to three different variants has been abandoned, the picture has become increasingly complicated and detailed[13].

In any case, it seems useful to report, from a fine essay by Monica Green (2014, 27 ff.), a crucial clarification on the two distinct levels to consider when discussing the genetic research relating to the pathogen of the plague. Indeed, it is essential to know that, as regards the contemporary plague, directly known for the episodes that recently have occurred in different parts of the world, the first case of complete genome sequencing dates back to 2001 (Parkhill *et al.* 2001)[14]. From then, several variants have been identified, which are often associated with specific geographical areas[15].

The advances in research that finally led, in 2011 (Bos *et al.* 2011), to the complete sequencing of the genome obtained from skeletal findings referring to the period of the *Black Death* have been slower and more difficult. The result was only possible when the techniques that allow for the removal of the genetic material still preserved within the dental pulp were perfected.

Only in very recent years have these two different lines of research converged. The combination of the results of phylogenetic research (on contemporary DNA) with those deriving from the examination of ancient DNA (aDNA) has shown that the 14th-century genome is, in fact, inserted on a branch of the phylogenetic tree[16] in the position already postulated by analysing only the variants isolated in contemporary times.

Therefore, the most recent genetic research results have made it possible to construct phylogenetic trees that allow for the establishment of convincing evolutionary relationships between the various strains (or variants) of *Y. pestis*. Furthermore, there is now agreement that the origin of *Y. pestis* is Asia, most likely in an internal area of China (Qinghai-Tibet Plateau), and that its differentiation from *Y. pseudotuberculosis* dates back several thousand years from the present time (Cui *et al.* 2013)[17].

3. Recent historiography on plague epidemics in Italy: new results and new questions

The theme of the demographic incidence of epidemics is present in most of the studies dedicated to epidemic episodes or cycles of plague in Italy, even if, in most cases, it is not the primary one. In this regard, it is important to remember the remarkable study by Benedictow (2004) on the *Black Death* in Europe (1346-1353), which, for Italy, proposed a radical upward revision of the previous mortality estimates.

Generally speaking, all attempts to quantify the severity of individual epidemics, or even to estimate the demographic effect of recurring plagues over prolonged periods, collide with the general lack of reliable quantitative data, at least until the end of the 16th century. That is one reason for the more significant number of studies focused on the 17-century epidemics, which have primarily attracted scholars interested in their economic implications and social consequences, the history of health organisation systems and various cultural aspects.

Concerning the epochs preceding the first documents that can be used to conduct a quantitative evaluation of the mortality levels, the paleo-demographic analyses of the skeletal materials found in the necropolises of the ancient and medieval ages provide useful elements for understanding the demographic dynamics. For Italy, some works coauthored by Irene Barbiera (Barbiera, Dalla Zuanna 2007; Barbiera, Dalla Zuanna 2009; Barbiera *et al.* 2016) allowed for comparing the mortality levels across the first pandemic, the long centuries with the absence of the plague in Italy, and finally, the dramatic period of the Black Death and the following decades[18].

For the 16th century, Guido Alfani (2010) proposed an evolutionary scenario of the population of northern Italy based on an extensive database of serial data (births and deaths). The reconstruction of the overall demographic trends in the «long sixteenth century» obtained from Alfani appears very convincing, obliging a revision of the most accredited estimates hitherto. However, above all, it constitutes the basis for a more general reflection on the complex links between population and economy during the 16th century and in the first two decades of the following one, up to the great caesura caused by the plague of 1630.

Apart from the debate on the plague aetiology (now definitively resolved), Alfani's book offers several crucial and innovative results. Among them, we can point to the predominantly urban character of the 16th-century epidemics, which contrasts with the greater diffusion of the epidemics of the previous century, but, above all, with the tremendous territorial pervasiveness of the two terrible 17th-century epidemics[19].

The two severe epidemics of plague (1630-1631 and 1652-1657) that hit the Italian territories during the 17th century are certainly the most studied (leaving out perhaps the first serious catastrophe of 1348) both by historical demographers and historians of health systems, as well as by economic and social historians.

For the more specifically demographic aspects, and, in particular, the mechanisms of spread of the contagion and the evaluation of the possible differential aspects on the different strata of the affected populations, I recount here some

interesting studies based on the analysis of individual data, mainly obtained from parish sources.

A study that can be considered pioneering, at least for Italy, is that carried out by Corsini and Delille (1990) on Eboli (Salerno) in 1656. Their research was based on the analysis of individual data drawn from two *status animarum*, one (1656) before and one (1657) after the epidemic, and from the records of the deaths that occurred in the interval. The aim of the investigation was to assess the effect of the epidemic on family structures and to verify whether mortality levels were influenced by family size.

In a substantially similar way, the study by Manfredini, De Iasio and Lucchetti (2002) investigates, through the nominative *linkages* between *status* data and *movement* data (always from parish sources), the incidence and mechanisms of the plague spread (from 1630) at the family level units in two small parishes (Madregolo and Cella di Palmia) in the Parma area.

Following a similar approach from an interesting new perspective, Alfani and Cohn (2007b) and later Alfani and Bonetti (2019) attempted to investigate the aspects still not fully resolved regarding the possible modes of plague transmission.

The essay by Alfani and Cohn analyses the bio-demographic characteristics of the plague epidemic of 1630 in the Emilian community of Nonantola, using a housing structure reconstruction (by fires and by portions of the town) crossed with data taken from parish registers. Data relating to six epidemics in Milan between 1452 and 1523 were used to compare and verify the hypotheses formulated. As the main contribution, this research, based on an accurate analysis of the data, highlights the modalities of the epidemic spread. According to the authors, the plague diffusion was hardly compatible with the theory of pathogen transmission through rats and fleas[20].

The subsequent work on the same community of Nonantola (again regarding the plague of 1630) published by Alfani and Bonetti (2019) reaches similar conclusions. In this case, the authors applied to the database of the inhabitants of Nonantola[21] a statistical survival analysis that highlighted a strong positive relationship between the risk of death and the size of the family unit, which is undoubtedly compatible with the hypothesis of direct transmission of the bacillus from person to person.

As is known, after the great epidemics of 1630-1631 and 1652-1657, the plague did not wholly disappear from Italy. It had some other appearances but was eradicated with relative ease, except for the severe epidemic of Messina and Reggio of 1743 (Restifo 1984). Giuseppe Restifo is responsible for other crucial studies[22] on the latest plague epidemics that have affected the Mediterranean countries (sometimes even Italian seaside towns). These studies also recall a topic debated for a long time by researchers of various backgrounds (demographers, historians, epidemiologists, microbiologists): the reasons for the definitive plague disappearance from European territories between the end of the 18th and the first half of the 19th century.

Concerning this debate, two old articles are particularly instructive (Appleby 1980; Slack 1981) that list and discuss in detail the various hypotheses on the plague's disappearance. Appleby, proceeding by exclusion, came to propose among the most probable hypotheses (while not excluding other possibilities) a

hypothetical partial immunity acquired by the rat populations, or at least their increased resistance to the plague[23]. Slack contested the validity of Appleby's thesis[24], and instead leaned towards the thesis (accepted by many) of the effectiveness of containment measures (sanitary cordons, quarantines, exchange of information between health magistracies). Ultimately, although these measures are not infallible and immediate in terms of their results, it is believed that, in the long run, they were probably decisive. This thesis also implies that the endemic reservoirs of wild rodents were extinguished in the meantime (between the 18th and 19th centuries), as they were supposed to be partially responsible for the repeated epidemics during the long centuries of the second pandemic[25].

4. The demographic impact of endemic diseases, from tuberculosis to malaria: a story yet to be written

As has already been pointed out, in Italy and most European countries, the statistics on the causes of death only begin in the second half of the 19th century. However, even in situations of a lack of complete data, it is possible to estimate the effects on mortality of the plague or other diseases that suddenly caused acute crises[26] in terms of the difference from the periods without such epidemics. It is much more difficult, though, to assess the actual weight of serious endemic diseases, such as tuberculosis or malaria, and the usual pathologies of the gastrointestinal and respiratory systems, which still in the 19th century represented very significant shares of overall mortality in Italy.

Among the diseases present in an endemic form in European and Italian areas in the past, tuberculosis and malaria were prevalent. One should remember that even today in the poorest countries (especially in Africa), these two diseases, together with HIV, are among those that claim the most victims, as the statistics of the World Health Organization report.

Let us now turn to the Italian situation for the period 1887-1889, the first years for which statistics on the causes of death are available for the entire Italian territory[27]. Deaths from all forms of tuberculosis accounted for nearly 8% of total deaths. Deaths from malaria, on the other hand, represented only 2.20% of the total. However, as in the more remote past, malaria was often the cause of indirect death and only affected a limited part of the Italian territory.

Thus, the burden of tuberculosis was certainly still relevant compared to the number of deaths attributed to the sum of *heart* and *circulatory system diseases* (together 11% of the total). The latter percentage is similar to that attributed to *gastroenteritis* and *colitis*, which killed mainly children at an early age. Instead, again in 1887-89, *pneumonia* and *bronchitis* represented 16% of all deaths[28].

In Italy, the phase of decline in mortality, also known as the *health transition*, began in the penultimate decade of the 19th century, to which the data just mentioned refer. This declining trend would also rapidly lead to a radical change in the nosological frame (Pozzi 2000). In 1881-1882, life expectancy in Italy was about 35 years, the risk of death in the first year of life was about 20% and the probability of survival to age 5 was just less than two-thirds of the generations of births. The levels of these indicators reveal a health situation perhaps closer to the most remote

centuries than to that which, fortunately, we find in Italy in the first and especially the second half of the 20th century.

Extrapolating backwards with what can only be verified with the data available for the contemporary age, we can return to reasoning about the past eras in which great epidemics frequently and abruptly altered the normal mortality tendencies. On the one hand, mortality has always been mainly concentrated in the infant group[29]. On the other hand, in all age groups, pathologies, today easily treatable, routinely claimed many victims. These pathologies were, in fact, the main culprits of the high mortality levels that characterized the populations of the past, even in periods not affected by severe epidemics[30].

As for the two endemic severe diseases mentioned above, namely tuberculosis and malaria, it must be said that both are very ancient diseases, certainly already present in the Mediterranean at the time of the first plague pandemic (6th-7th century AD) and then along the course of the second (from the mid-14th century onwards)[31].

Tuberculosis is caused by a group of phylogenetically closely related bacteria, collectively known as *Mycobacterium tuberculosis complex* (MTBC) (Gagneux 2012, 851)[32]. Within this group, by far the main one responsible for tuberculosis in humans is *M. tuberculosis*. However, we should also mention the *M. bovis*, a pathogen of cows capable of infecting humans. This infection occurs mainly through the ingestion of milk (not sterilized) from infected cows and through aerosols in rural areas where the populations are dedicated to raising livestock. In the past, it was believed that tuberculosis was a disease of animal origin (passed to humans with the Neolithic transition and the domestication of animals). Today, however, this hypothesis seems to be disproved by the most recent research (see e.g. Brites and Gagneux 2015, 7; Comas *et al.* 2013, 1177; Hershkovitz *et al.* 2015, 2), as certain human MTBC lineages are phylogenetically more basal (i.e. 'ancestral') than *M. bovis* (Brites and Gagneux 2015, 7).

However, it seems sure that the stable settlements of the Neolithic age represented the first phase of strong increase in the spread of tuberculosis in the history of humanity. As for Europe, favourable conditions for the tuberculosis pathogen propagation certainly occurred in the population growth and increasing urbanization phases preceding the plague's return in 1348. Nevertheless, even later, it is believed (McNeill 1982, 159; Stone *et al.* 2009, 70) that pulmonary tuberculosis has maintained a widespread presence, so much so that its prevalence has been considered a possible cause of the decline of leprosy, another disease caused by a pathogen belonging to the genus *Mycobacterium* (*M. leprae*)[33].

Since the 18th century, first in England and then in many other European countries, the rapid progress of industrialization and urbanization has increased crowding in homes and workplaces, creating the conditions for a greater spread of tuberculosis. This sharp increase in the disease has led some scholars to speak of its quasi-epidemic proportions (Hershkovitz *et al.* 2015, 1). It is also interesting to mention an estimate of the deaths caused by major infectious diseases worldwide over the past two centuries (Paulson 2013)[34]. In this ranking, tuberculosis is by far in first place with one million deaths followed at a great distance, in order, by small-

pox, malaria, plague, flu, cholera and AIDS. After all, between the 18th and 19th centuries, the countries most involved in the industrial revolution accounted for at least 20-25% of the deaths from tuberculosis (out of total deaths) (Donoghue 2009, 1159). As already mentioned, in the three years 1887-1889, that share in Italy was close to 8%. Nevertheless, in specific periods and areas, the percentage of deaths due to tuberculosis was undoubtedly much higher.

Regarding the history of malaria, its presence in large portions of the peninsular and insular Italian territory has been widely documented since very ancient times[35]. A splendid book by the microbiologist Robert Sallares (2002) deals with the history of the malaria endemic at the time of ancient Rome. Also reporting conflicting opinions of various scholars, Sallares (2002, 13 ff.) hypothesizes that the severe disease due to the *plasmodium falciparum* may have settled permanently in the countries of the northern Mediterranean shore only after the decline of the Etruscan civilization[36]. In any case, most scholars agree that the phases of geographic expansion (in the latitude direction) and the remission of malaria are linked, in addition to historical events that influenced the abandonment of cultivated land and the phenomena of land instability (and therefore the creation of favourable environments for mosquitoes of the genus *anopheles*), to long-term climatic variations. Hackett (1937, 7) suggested that in Italy, from the 9th to the 13th century, a long wave of malaria resurgence[37] would coincide in time with the phase of rising average temperatures of the 'medieval interglacial' period (Behringer 2013, 12). In the centuries at the turn of the first and second millennium, free from plague epidemics[38], the growth rates of the Italian population are compatible with relatively high mortality levels[39]. Even if these levels were lower than those estimated for the centuries affected by the most violent plague waves, the relatively high mortality could be due to the widespread presence of malaria.

However, an attempt to quantify the overall demographic impact of this disease is still missing, even for the long centuries in which the malaria endemic coexisted with the great epidemic waves caused by the plague. In this regard, it should be noted that some scholars, such as Sallares (2002), attempted to delineate a 'demography of malaria' for populations in the more or less remote past. However, they were obliged to infer the mortality intensity and structure (by sex, age, etc.) caused directly and indirectly by this scourge from investigations concerning recent times[40].

In the three years 1887-1889, for which data are finally available to evaluate mortality from single causes for the whole national territory, malaria does not appear to have had a significant impact on the level of overall mortality: in Italy, with a crude death rate equal to 26.9 per thousand, the specific malaria mortality rate (0.6 per thousand) represents just over 2%. However, most interestingly, it is possible to draw precisely a geography of the malaria mortality for those years, which probably would not be very different from that of the very distant past. Thus, we find the areas most affected (for centuries) by the malaria endemic, where the direct incidence of malaria mortality could exceed 3-4 per thousand, as in the province of Cagliari. In that period, the most affected provinces in mortality terms constituted (apart from the province of Ferrara in northern Italy) a continuous area, including the Grosseto province and the strip along the Tyrrhenian Sea, Chieti

and the lands along the Adriatic Sea, including the whole of continental Southern Italy and the two major islands. Confirmations on the existence of opposing situations between the North and the South of the country, both in terms of spread of the disease and of mortality caused by malarial infection, are also offered by the cartographic representations of malaria produced at the end of the 19th century. For example, the *map of malaria of Italy* (Torelli 1882) highlighted, on the one hand, the prevalence of *mild malaria* in the northern part of the country (excluding the Veneto and Romagna coast), and, on the other hand, a vast *severe malaria* area including the Veneto-Romagna coast, the southern and significant part of the central regions, especially on the west coast with the Maremma and Lazio, and finally the two islands (Sicily and Sardinia)[41]. In any case, it is essential to underline that malaria has always been present in limited portions of the Italian territory. However, in the more remote past, there were surely periods in which the influence of malaria covered much wider territorial expanses than what are known as the malarial zones for the second half of the 19th century. That was due either to the change in climatic conditions or to historical events that caused the abandonment of the works to regulate the hydraulic systems in the areas subject to swamping.

Therefore, on the one hand, malaria did not affect the entire Italian territory, as did other diseases. On the other hand, however, in the past, historical malarial areas were characterized by very high levels of general mortality, often much higher than the surrounding areas free from this scourge. Tuscany represents an exemplary case of the differences in general mortality due to the presence or absence of malaria. For the Lorraine era, death and population statistics at the municipal level allow us to map the levels of general mortality in great detail and for the entire region.

These maps (Breschi and Salvini 1993, 368-369) clearly show for 1818-1837 a mortality gradient which, starting from the highest levels that characterized the areas of the Pisan and, above all, Grosseto Maremma, gradually showed a decrease in the levels of generic rates, which, in any case, still remained high in the Sienese hinterland. Mortality rates, on the other hand, were decidedly lower in the communities gravitating towards the Arno Valley and in those of the internal valleys (Garfagnana, Mugello, Casentino) and the Apennine Mountains. This gradient can be explained (Del Panta 1989, 18-19) by the presence of intense temporary mobility towards the Maremma areas. The short-lived summer migration came from the closest hinterland (mainly from the Siena and Pisa provinces). Undoubtedly, many seasonal workers contracted malaria in Maremma. They then died in their communities of origin due to malaria or other pathologies affecting individuals already weakened by malaria. From the distant Apennine communities (and also from many territories beyond the borders of the Grand Duchy) came winter immigration of longer duration, which exposed people very little to the risk of contracting malaria.

Another important aspect that is necessary to mention concerns the mortality structure by causes recorded in the malaria areas (Del Panta and Pozzi 2016). It is well known that the high mortality found in these areas is only partly attributable to the deaths directly caused by this disease[42]. In fact, the state of debilitation caused by malaria, even when this infection is not directly fatal[43], makes malarial subjects

easier prey to other morbid forms (mainly related to the respiratory and gastrointestinal systems). On the other hand, a malaria attack can aggravate other types of infections already in progress. Even the course of a malaria attack (especially in the case of relapses) could evolve more unfavourably if the human organism were already affected by other morbid forms. It should also be remembered that the children of malarial mothers were frequently born underweight and, even if they did not contract malaria, they were subject to exceptionally high risks of death, even after the first year of life, especially from gastrointestinal and lung infections[44]. Finally, malaria «can increase the body's susceptibility to respiratory infections such as tuberculosis» (Harper 2019, 111). More generally, it is believed (Enwere *et al.* 1999) that both asymptomatic and symptomatic malarial infections cause immunodeficiency, which predisposes the host to infection with other microorganisms[45].

Malaria is generally referred to as an endemic disease. In any case, it is interesting to note that in the literature, there are countless cases in which the term *epidemic* is used for malaria, citing episodes with very high peaks of malaria mortality in particular years (e.g. Hackett 1937, 221, 227, 230-231, 251; Bonelli 1966, 668; Sallares 2002, 68).

In fact, situations in which malaria mortality could assume such dimensions as to suggest an epidemic could occur in different contexts. On the one hand, sudden climatic variations in certain periods could probably generate particularly favourable conditions for the spread of mosquitoes and plasmodia. The case of a children's cemetery discovered in the abandoned ruins of a villa near Lugnano in Teverina (in Umbria, province of Terni) is frequently mentioned in the literature. The almost contemporary burial (5th century of the Common Era) of so many children who died at a very tender age can most likely be attributed to the severe resurgence of malaria, which was already present endemically there and in many other areas of peninsular Italy (Sallares, Gomzi 2001, 202 ff.).

However, we must also remember the countless episodes in which population groups came for the first time into contact with malarial environments, without having developed the typical degree of resistance of the native populations (Hackett 1937, 113). Cases of armies are well known, from Attila's Unni (Harper 2019, 250) to Frederick Barbarossa's troops, who were induced to retreat not in the face of fierce enemies but because they were prostrated by malaria.

Finally, the Lorraine colonies in Maremma offer a circumscribed but very illuminating example of the selective differential impact of malaria between indigenous populations and populations that recently immigrated to malarious areas. The documentation relating to the tragic attempt at repopulation conceived by the new Lorraine administration[46], starting from the end of the 30s of the 18th century, allows us to verify how the Lorraine micro-population was far more penalized by the presence of malaria in the context of a population, such as the Maremma one, already characterized by a worse mortality regime compared to the Tuscan standard. After the first impressive mortality crisis, which occurred during the first summer of stay in the Maremma territories, we can appreciate the rapid decline of the colonies of Massa Marittima and Sorano-Sovana, determined in part by the escape of the *colonists* but largely due to an absolutely unfavorable mortality regime.

In conclusion of this section and the entire essay, in order to underline the importance of the presence of malaria in Italy and other countries in the northern Mediterranean region in the past, I recall the words of Fernand Braudel (1986, vol. I, 50) who, in his great fresco on the societies of Mediterranean countries in the modern age, stated: «Although dangerous, the *plague*, imported from India and China through long-distance relations, is a passing stranger in the Mediterranean. *Malaria* has a permanent home there. It forms the background of the picture of the Mediterranean pathology».

[1] Except in exceptional cases, in Italy, it is not possible to have data on mortality by causes of death up to the 1880s.
[2] See Del Panta (2021). The volume reproduces the old edition, with the addition of an extensive preface written by the author. Several recent research acquisitions on the history of epidemics are taken into account, with particular attention to the contribution of microbiology in clarifying the evolutionary history of the pathogen responsible for plague epidemics. In the following paragraph, I have summarized some concepts more extensively illustrated in the preface to the volume.
[3] I will also mention in the following pages the significant presence of tuberculosis, another predominantly endemic pathology that has afflicted the Italian population from very ancient times until the first half of the 20th century.
[4] They are the Japanese physician and bacteriologist Shibasaburo Kitasato (1853-1931), who gained experience in the laboratory of Robert Koch in Berlin, and the Swiss physician and bacteriologist Alexandre Yersin (1863-1943), who worked until 1890 in the Pasteur Institute in Paris and subsequently moved to the East. For a clear and comprehensive summary of the research by Yersin and Kitasato, I suggest reading the section entitled *Knowledge of the plague* (written by the physician and epidemiologist Marco Geddes) contained (43 ff.) in the volume of Geddes da Filicaia C. and Geddes da Filicaia M. (2015).
[5] Initially, and until the mid-1950s, the bacillus was called *Pasteurella pestis*.
[6] A brief account of this debate, obviously limited to the years preceding the publication of that short note, can be read in Del Panta (2007).
[7] See Drancourt et al. (1998) and also Signoli *et al.* (2002).
[8] Gilbert et al. (2004).
[9] On the other hand, most published works are now readily available (almost all *open access)* on the Internet.
[10] Little is a distinguished historian, who has edited, among other things, a splendid collective volume on the pandemic of 541-750 (Little 2007), and who has the rare ability to deal with complex topics in a clear and rigorous form. Other important bibliographic review essays on the recent scientific research relating to the plague are those of Green (2014) and Seguy and Alfani (2017) which, among other things, give an account of some essential works published after Little's essay.
[11] Little points out, as an indication of the now prevalent capacity for international collaboration, that the article in question was signed by twelve authors representing seven different countries (France, Germany, Ireland, Italy, Madagascar, Holland and the United Kingdom).
[12] The lower limit estimated at 1,500 years from the present time would identify the bifurcation between *Y. pseudotuberculosis* and *Y. pestis* around the years of the first pandemic explosion. These estimates have been subsequently revised several times: Morelli *et al.* (2010, 1141) report a lower limit of at least 2,600 years, an epoch from which, from the *Root r*epresented in the phylogenetic tree by *Y. Pseudotuberculosis*, the story of *Y. pestis* with subsequent branches would have originated.
[13] See, among others, Haensch *et al.* (2010), Cui *et al.* (2013), Hymes (2014) and finally the most recent article by Spyrou *et al.* (2019).
[14] The genoma was sequenced using an organic sample from a patient who had contracted pneumonic plague in Colorado in 1992 (Doll *et al.* 1994).

[15] It is also important to clarify that much of the data on *Yersinia* accumulated and analysed by researchers in recent years (see e.g. Cui *et al.* 2013) comes from infected animals (usually rodents). These data were found in areas where outbreaks have persisted from time immemorial. Presumably, the previous pandemics that have affected humanity also originated from these areas.
[16] See Cui *et al.*, 2013 (fig. 1 on page 578). I indicate below the link to download (*open access*) the article in which the phylogenetic tree is illustrated: https://www.researchgate.net/publication/233999975_Historical_variations_in_mutation_rate_in_an_epidemic_pathogen_Yersinia_pestis.
[17] Scholars are still debating the possible relationship between climatic variations and the explosion and spread of epidemics. Furthermore, the discussion focuses on the possible long-term stay of *Y. pestis* in Europe after its entry in the mid-14th century. Nevertheless, some scholars mainly consider the frequent episodes between the 14th and 17th–18th centuries as new entrances from Asian outbreaks. The two positions are not necessarily in total antithesis. However, researchers with equally convincing arguments firmly support the first thesis (Carmichael 2014) or the second one (Schmid *et al.* 2015). For a brief review of the different positions on these issues, see the preface to Del Panta (2021).
[18] The cited articles describe the technical modalities to evaluate the mortality levels, using the estimates of the age at death.
[19] This aspect of the great "pervasiveness" of the contagion in the Italian territories, much more accentuated than in the countries of Northern Europe, was then taken up and developed by the same author (Alfani 2013) with reference precisely to the epidemics of the 17th century.
[20] In this context, it is helpful to point out the remarkable book by the archaeozoologist Frédérique Audoin-Rouzeau (2003), which, in my opinion, is the most complete and exhaustive work on the ways of transmission of *Yersinia pestis* to man through the different species of fleas and rats.
[21] The data concerning the population of Nonantola come from two primary sources: the parish registers of baptisms and burials and a register of the salt tax (*boccatico*) dated to 1629 (before the beginning of the epidemic).
[22] Two volumes (Restifo 1994; 2005) deal with the Mediterranean epidemics between the 18th and 19th centuries. Furthermore, a seminar held in Messina in May 1998 (Restifo 2001) involved scholars of the plague from various Mediterranean countries.
[23] In this case, the transition from epizootic to epidemic would not be generated, as fleas would not need to search for alternative hosts to rats.
[24] Incidentally, Appleby died before Slack's criticism of this article was published.
[25] See Carmichael (2014, 177 ff.).
[26] In reality, it cannot be excluded (see e.g. Little 2011, 289) that the plague was superimposed, on certain occasions, by other epidemic diseases, starting from petechial typhus.
[27] A summary collection of mortality data by causes, at the national and regional level, for 1887-1955, can be found in ISTAT (1958).
[28] It is actually not very correct to combine these two categories. Children more frequently died because of bronchitis (two-thirds of bronchitis deaths occur in children under five years of age), whereas this is not case with pneumonia.
[29] To compare infant mortality in the past among several countries (including Italy), see Bideau, Dejardins, Pérez Brignoli, 1997. See also Corsini and Viazzo (1997) and Breschi and Pozzi (2004).
[30] In the absence of complete data to correctly measure the levels and structure of mortality, historical demographers still have at their disposal a variety of techniques for reconstructing the evolutionary mechanisms of past populations and for estimating the main parameters of fertility and mortality (e.g. Reher, Schofield 1993).
[31] See, for tuberculosis, Achtman (2016), and for malaria Sallares and Gomzi (2001) and Sallares *et al.* (2004).
[32] In the field of genetics and microbiology, research is constantly evolving. In terms of its interest in this context, I mention only the facts and results on which scientists today seem to agree. Here, I indicate some of the many studies relating to the possible evolutionary scenarios of the disease, starting from its, almost certainly, African origin: Brosch *et al.*, 2002; Wirth *et al.* 2008; Gagneux, 2012; Brites, Gagneux 2015; Donoghue 2019; Henneberg *et al.* 2021.
[33] The issue of the possible relationship between the spread of tuberculosis and the decline of lep-

rosy in Europe in the late Middle Ages has been addressed in numerous studies (e.g. Chaussinand 1948; Manchester 1991; Stone *et al.* 2009; Donoghue 2019).

[34] The estimates proposed by Paulson are cited, among others, by Saelens *et al.* (2019).

[35] Among the many texts that deal with the history of malaria in Italy, I focus on only five (the first two also concern other European countries), in chronological order of publication: Hackett (1937), Bruce-Chwatt and De Zulueta (1980), Coluzzi and Corbellini (1995), Sallares (2002) and Tognotti (2008).

[36] Even Bruce-Chwatt and De Zulueta (1980, 13-19) believe that the *plasmodium falciparum* was not consistently present in Europe before the Greek-Roman era.

[37] It should be noted that Hackett attributes the authorship of the graph shown on page 7 (and, above all, the identification of a series of centuries-old waves of increase and reductions in the spread and aggressiveness of malaria) to Angelo Celli, without mentioning a precise bibliographic reference.

[38] See Lo Cascio, Malanima (2005) and Del Panta, Livi Bacci, Pinto and Sonnino (1996). Lo Cascio and Malanima have significantly adjusted the previous estimates of the evolution of the Italian population in the long term, from the Roman age to the end of the second millennium. However, the differences are largely due to a different estimate of the initial population amount at the beginning of the Christian era (see Lo Cascio and Malanima, 2005, 16).

[39] See Barbiera and Dalla Zuanna (2007) and Barbiera *et al.* (2016).

[40] Robert Sallares (2002) cites several times a short essay of mine (Del Panta 1989). In this essay, I had widely used, for the 1840s (therefore for a period prior to the publication, at the national level, of the statistics on the causes of death), the data on sick people and the deaths due to malaria reported in the *Saggio illustrativo le tavole della statistica medica delle Maremme toscane* [Illustrative essay on the tables of the medical statistics of the Tuscan Maremmas] drawn up by the physician and malariologist Antonio Salvagnoli Marchetti (1844, 1845) (see also Del Panta, 2019).

[41] In the years immediately following the publication of Torelli's map, it was understood how that distinction corresponded to the presence of *plasmodium vivax* (areas of mild malaria) and of *plasmodium falciparum* (often together with *p. vivax*) in the severe malarial areas. The greater sensitivity of the *p. falciparum* at temperatures, when it is hosted inside the mosquito, explains why this species is less suitable than the other for a considerable diffusion in geographic areas characterized by long winters. On the relation between temperatures and diffusion of the different plasmodic species in Italy, even in the very remote past, see Sallares (2002, 101-103) and Hackett (1937, 202-208).

[42] On this important topic, the understanding of which is decisive for correctly interpreting both the differences in mortality between malarial and non-malarial areas, and also those between malarial areas in which different species of plasmodia prevailed, I find particularly clear the work of Mary Dobson (1980, 375-376; 1997, 331-336) and Robert Sallares (2002, 123 ff.)

[43] It should be remembered that the lethality rate varies depending on the species of plasmodium that causes the malarial attack. It is much higher for *p. falciparum*, as it frequently kills mainly children at the first attack, while generally the lethality of *p. vivax* does not exceed 5%. However, through the mechanism of relapses, malaria leads the body to such a state of debilitation that it is much more exposed (compared to a healthy body) to succumb to several other infections.

[44] See Sallares (2002, 125-126). It also appears that pregnant women, in particular, attract mosquitoes. In addition, possible immunity from *p. falciparum*, acquired after previous attacks, decreases from the second or third month of pregnancy. Finally, the risk of spontaneous abortion is high in malarial women.

[45] In their essay, Enwere *et al.* (1999) consider the possible ways in which malaria-induced immune impairment could affect the host's response to *Mycobacterium tuberculosis* infection.

[46] The sources to reconstruct this story are reported in the essays by Parenti (1937), Mortara (1938), Rombai (1985) and Del Panta (1985, 1999).

References

M. Achtman, K. Zurth, G. Morelli, G. Torrea, A. Guiyoule, E. Carniel 1999, *Yersinia pestis, the cause of plague, is a recently emerged clone of Yersinia tuberculosis*, «Proceedings of the National Academy of the Sciences of the United Nations of America», 96(24), 14043-14048.

M. Achtman, G. Morelli, P. Zhu, T. Wirth, I. Diehl, B. Kusecek, A.J. Vogler, D.M. Wagner, C.J. Allender, W.R. Easterday, V. Chenal-Francisque, P. Worsham, N.R. Thomson, J. Parkhill, L.E. Lindler, E. Carniel, P. Keim 2004, *Microevolution and history of the plague bacillus, Yersinia pestis*, «Proceedings of the National Academy of the Sciences of the United Nations of America», 101(51), 17837-17842.

M. Achtman 2016, *How old are bacterial pathogens?*, «Proceedings of the Royal Society B: Biological Sciences», 283, 20160990.

G. Alfani 2010, *Il Grand Tour dei Cavalieri dell'Apocalisse. L'Italia del «lungo Cinquecento» (1494-1629)*, Marsilio, Venezia.

G. Alfani 2013, *Plague in Seventeenth Century Europe and the decline of Italy: an Epidemiological Hypothesis*, «European Review of Economic History», 17(4), 408-430.

G. Alfani, M. Bonetti 2019, *A survival analysis of the last great European plagues: The case of Nonantola (Northern Italy) in 1630*, «Population Studies», 73:1, 101-118.

G. Alfani, S.K. Cohn 2007a, *Households and Plague in Early Modern Italy*, «Journal of Interdisciplinary History», 38, 177-205.

G. Alfani, S.K. Cohn 2007b, *Nonantola 1630, Anatomia di una pestilenza e meccanismi del contagio*, «Popolazione e storia», 2, 99-138.

A.B. Appleby 1980, *Epidemics and Famine in the Little Ice Age*, «The Journal of Interdisciplinary History», 10(4), 643-663.

F. Audoin-Rouzeau 2003, *Les Chemins de la peste. Le rat, la puce et l'homme*, Presses Universitaires de Rennes.

I. Barbiera, G. Dalla Zuanna 2007, *Le dinamiche della popolazione nell'Italia medievale. Nuovi riscontri su documenti e reperti archeologici*, «Archeologia Medievale», XXXIV, 2007, 19-42.

I. Barbiera, G. Dalla Zuanna 2009, *Population Dynamics in Italy in the Middle Ages: New Insights from Archeological Findings*, «Population and Development Review», 35(2), 367-389.

I. Barbiera, M. Castiglioni, G. Dalla Zuanna 2016, *La mortalità ai tempi della peste nera: indagine paleodemografica dell'Italia del XIV secolo*, «Archeologia Medievale», XLIII, 2016, 33-40.

W. Behringer 2013, *Storia culturale del clima. Dall'era glaciale al riscaldamento globale*, Bollati Boringhieri, Torino (first edition: *Kulturgeschichte des Klimas. Von der Eiszeit zur globalen Erwärmung*, Verlag C. H. Beck oHG, München, 2010).

O.J. Benedictow 2004, *The Black Death 1346-1353. The Complete History*, The Boydell Press, Woodbridge.

O.J. Benedictow 2010, *What Disease was Plague? On the Controversy over the Microbiological Identity of Plague Epidemics of the Past*, Brill, Leiden.

A. Bideau, B. Desjardins, H. Pérez Brignoli (eds.) 1997, *Infant and Child Mortality in the Past*, Clarendon Press, Oxford

F. Bonelli 1966, *La malaria nella storia demografica ed economica d'Italia*, «Studi storici», VII, 4, 659-687.

K.I. Bos, V.J. Schuenemann, G.B. Golding, H.A. Burbano, N. Waglechner, B.K. Coombes, J.B. McPhee, S.N. DeWitte, M. Meyer, S. Schmedes, J. Wood *et al.* 2011, *A draft genome of Yersinia pestis from victims of the Black Death*, «Nature», 478(7370), 506-510.

F. Braudel 1986, *Civiltà e imperi del Mediterraneo nell'età di Filippo II*, 2 Vols., Piccola Biblioteca Einaudi, Torino.

M. Breschi, L. Pozzi (eds) 2004, *The determinants of infant and child mortality in past European populations*, Forum, Udine.

M. Breschi, S. Salvini 1993, *Differenze territoriali nella mortalità del Granducato di Toscana nella prima metà dell'800*, in Società Italiana di Demografia Storica (SIDES), *La popolazione delle campagne italiane in età moderna*, CLUEB, Bologna, 363-387.

D. Brites, S. Gagneux 2015, *Co-evolution of Mycobacterium tuberculosis and Homo sapiens*, «Immunological Reviews», 264, 6-24.

R. Brosch, S.V. Gordon, M. Marmiesse, P. Brodin, C. Buchrieser, K. Eiglmeier, T. Garnier, C. Gutierrez, G. Hewinson, K. Kremer, L.M. Parsons *et al.* 2002, *A new evolutionary scenario for*

the Mycobacterium tuberculosis complex, «Proceedings of the National Academy of the Sciences of the United Nations of America», 99(6), 3684-3689.
L.J. Bruce-Chwatt, J. De Zulueta 1980, *The rise and fall of malaria in Europe. A historico-epidemiological study*, Oxford University Press.
A.G. Carmichael 2014, *Plague Persistence in Western Europe: A Hypothesis*, «The Medieval Globe», I, 2014, 157-19.
R. Chaussinand 1948, *Tuberculosis and Leprosy-Antagonistic Ilnesses*, «International Journal of Leprosy», 16, 431-438.
C.M. Cipolla 1989, *Miasmi e umori. Ecologia e condizioni sanitarie in Toscana nel Seicento*, Il Mulino, Bologna.
S.K. Cohn 2002, *The Black Death Transformed*, Arnold, London.
M. Coluzzi, G. Corbellini 1995, *I luoghi della mal'aria e le cause della malaria*, «Medicina nei secoli. Arte e Scienza», VII, 3, 575-598.
I. Comas, M. Coscolla, T. Luo, S. Borrell, K.E. Holt, M. Kato-Maeda, J. Parkhill, B. Malla, S. Berg, G. Thwaites, D. Yeboah-Manu *et al.* 2013, *Out-of-Africa migration and Neolithic co-expansion of Mycobacterium tuberculosis with modern humans*, «Nature genetics» 45(10), 1176-1182.
C.A Corsini, G. Delille 1990, *«Né si scorgeva altro per le strade che condurre sacramenti agl'infermi e cadaveri alle sepolture». Eboli e la peste del 1656*, in Società Italiana di Demografia Storica (SIDES), *Popolazione, società e ambiente. Temi di demografia storica italiana (secc. XVII-XIX)*, CLUEB, Bologna, 581-593.
C.A. Corsini, P.P. Viazzo (eds.) 1997, *The decline of infant and child mortality. The European experience: 1750-1990*, UNICEF, Kluwer Law International, The Hague, The Netherlands.
Y. Cui, C. Yu, Y. Yan, D. Li, Y. Li, T. Jombart, L.A. Weinert, Z. Wang, Z. Guo, L. Xu, Y. Zhang *et al.* 2013, *Historical variations in mutation rate in an epidemic pathogen, Yersinia pestis*, «Proceedings of the National Academy of the Sciences of the United Nations of America», 110(2), 577-582.
L. Del Panta 1980, *Le epidemie nella storia demografica italiana (secoli XIV-XIX)*, Loescher Editore, Torino.
L. Del Panta 1985, *Una fonte per lo studio delle colonie lorenesi in Maremma: i libri parrocchiali di Massa Marittima*, «Bollettino della Società Storica Maremmana», 49, 95-105.
L. Del Panta 1989, *Malaria e regime demografico: la Maremma grossetana nell'Ottocento preunitario*, Il Professore Editore, Messina.
L. Del Panta 1999, *La colonia lorenese di Massa Marittima: aspetti demografici*, in A. Contini, M.G. Parri (ed.), *Il Granducato di Toscana e i Lorena nel secolo XVIII*, Leo S. Olschki Editore, Firenze, 621-631.
L. Del Panta 2007, *Per orientarsi nel recente dibattito sull'eziologia della 'peste': alcune indicazioni bibliografiche e un tentativo di riflessione*, «Popolazione e storia», 2, 139-149.
L. Del Panta 2019, *Malaria, migrazioni e bonifiche negli scritti sulla Maremma di Antonio Salvagnoli Marchetti*, «Popolazione e storia», 2, 9-19.
L. Del Panta 2021, *Le epidemie nella storia demografica italiana*, Biblioteca Clueb, Bologna.
L. Del Panta, M. Livi Bacci, G. Pinto, E. Sonnino 1996, *La popolazione italiana dal Medioevo a oggi*, Laterza, Roma-Bari.
L. Del Panta, L. Pozzi 2016, *La malaria in Italia: geografia e struttura della mortalità nel passaggio tra Otto e Novecento*, in A. Fornasin, C. Lorenzini (eds.), *Per una storia della popolazione italiana nel Novecento*, Forum, Udine, 405-416.
R. Devignat 1951, *Variétés de l'espèce Pasteurella pestis. Nouvelle hypothèse*, «Bulletin of the World Health Organization» 4, 247-263.
M. Dobson 1980, *"Marsh Fever" – the geography of malaria in England*, «Journal of Historical Geography», 6, 4 (357-389).
M. Dobson 1997, *Contours of death and disease in early modern England*, Cambridge University Press.
J.M. Doll, P.S. Zeitz, P. Ettestad, A.L. Bucholtz, T. Davis, K. Gage 1994, *Cat-transmitted fatal pneumonic plague in a person who traveled from Colorado to Arizona*, «The American journal of tropical medicine and hygiene», 51, 109-114.
H.D. Donoghue 2009, *Human tuberculosis: an ancient disease, as elucidated by ancient microbial biomolecules*, «Microbes and Infection», 11(14-15), 1156-1162.

H.D. Donoghue 2019, *Tuberculosis and leprosy associated with historical human population movements in Europe and beyond – an overview based on mycobacterial ancient DNA*, «Annals of Human Biology», 46(2), 120-128.
M. Drancourt, G. Aboudharam, M. Signoli, O. Dutour, D. Raoult 1998, *Detection of 400-years-old Yersinia pestis DNA in human dental pulp: An approach to the diagnosis of ancient septicemia*, «Proceedings of the National Academy of the Sciences of the United Nations of America», 95, 12637-12640.
C. Duncan, S. Scott 2001, *Biology of Plagues*, Cambridge University Press.
C. Duncan, S. Scott 2005, *What Caused the Black Death?*, «Postgraduate medical journal», 81, 315-320.
G.C. Enwere, M.O. Ota, S.K. Obaro 1999, *The host response in malaria and depression of defence against tuberculosis*, «Annals of Tropical Medicine & Parasitology», 93(7), 669-678.
S. Gagneux 2012, *Host-pathogen coevolution in human tuberculosis*, «Philosophical Transactions of the Royal Society B: Biological Sciences», 367, 850-859.
C. Geddes da Filicaia, M. Geddes da Filicaia 2015, *Peste. Il flagello di Dio fra letteratura e scienza*, Edizioni Polistampa, Firenze.
M.T.P. Gilbert, J. Cuccui, W. White, N. Lynnerup, R.W. Titball, A. Cooper, M.B. Prentice 2004, *Absence of Yersinia pestis-specific DNA in human teeth from five European excavations of putative plague victims*, «Microbiology», 150, 341-354.
H.M. Green 2014, *Taking «Pandemic» Seriously: Making the Black Death Global*, «The Medieval Globe», I, 27-61.
M.D. Grmek 1975, *Metodi nuovi nello studio delle malattie antiche*, «Scienza e Tecnica», 75, Milano.
L.W. Hackett 1937, *Malaria in Europe. An Ecological Study*, Oxford University Press, Oxford.
S. Haensch, R. Bianucci, M. Signoli, M. Rajerison, M. Schultz, S. Kacki, M. Vermunt, D.A. Weston, D. Hurst, M. Achtman, E. Carniel, B. Bramanti 2010, *Distinct Clones of «Yersinia pestis» Caused the Black Death*, «PLoS Pathogens», VI, e1001134.
K. Harper 2019, *Il destino di Roma. Clima, epidemie e la fine di un impero*, Einaudi, Torino (first edition: *The Fate of Rome. Climate, Disease and the End of an Empire*, Princeton University Press, 2017).
M. Henneberg, K. Holloway-Kew, T. Lucas 2021, *Human major infections: Tuberculosis, treponematoses, leprosy – A paleopathological perspective of their evolution*, «PLoS ONE», 16(2), e0243687.
I. Hershkovitz, H.D. Donoghue, D.E. Minnikin, H. May, O.Y.C. Lee, M. Feldman, E. Galili, M. Spigelman, B.M. Rothschild, G.K. Bar-Gal 2015, *Tuberculosis origin: The Neolithic scenario*, «Tuberculosis», http://dx.doi.org/10.1016/j.tube.2015.02.021.
R. Hymes 2014, *A Hypothesis on the East Asian Beginnings of the Yersinia pestis Polytomy*, «The Medieval Globe», I, 285-308.
ISTAT 1958, *Cause di morte 1887-1955*, A.BE.T.E., Roma.
L.K. Little (ed.) 2007, *Plague and the End of Antiquity. The Pandemic of 541-750*, Cambridge University Press.
L.K. Little 2011, *Review article: plague historians in lab coats*, «Past&Present», 213, 267-290.
E. Lo Cascio, P. Malanima 2005, *Cycles and Stability. Italian Population before the Demographic Transition (225 B.C. - A.D. 1900)*, «Rivista di Storia Economica», XXI(3), 5-40.
K. Manchester 1991, *Tuberculosis and leprosy: Evidence for interaction of disease*, in D.J. Ortner, A.C. Aufderheide (eds.), *Human Paleopathology. Current Syntheses and Future Options*, Smithsonian Institution Press, Washington and London, 23-34.
M. Manfredini, S. De Iasio, E. Lucchetti 2002, *The plague of 1630 in the territory of Parma: Outbreak and effects of a crisis*, «International Journal of Anthropology», 17, 41-57.
W.H. McNeill 1982, *La peste nella storia. Epidemie, morbi e contagio dall'antichità all'età contemporanea*, Einaudi, Torino (first edition: *Plagues and Peoples*, Anchor Press/Doubleday, 1976).
G. Morelli, Y. Song, C.J. Mazzoni, M. Eppinger, P. Roumagnac, D.M. Wagner, M. Feldkamp, B. Kusecek, A.J. Vogler, Y. Li, Y. Cui *et al.* 2010, *Yersinia pestis genome sequencing identifies patterns of global phylogenetic diversity*, «Nature Genetics», 2(12), 1140-1145.
A. Mortara 1938, *Un tentativo di colonizzazione agraria in Maremma al tempo della Reggenza lorenese*, «Nuova rivista storica», XXII, fasc. I-II, 40-63 and fasc. V-VI, 338-394.

G. Parenti 1937, *La popolazione della Toscana sotto la Reggenza lorenese*, Scuola di Statistica della R. Università di Firenze.
J. Parkhill, B.W. Wren, N.R. Thomson, R.W. Titball, M.T.G. Holden, M.B. Prentice, M. Sebaihia, K.D. James, C. Churcher, K.L. Mungall, S. Baker *et al.* 2001, *Genome sequence of Yersinia pestis, the Causative Agent of Plague*, «Nature», CDXIII, 523-27.
T. Paulson 2013, *A mortal foe. Tuberculosis is one of the world's most lethal infectious diseases. Further progress in consigning it to the past is a massive challenge*, «Nature», 502, S2-S3.
L. Pozzi 2000, *La lotta per la vita. Evoluzione e geografia della sopravvivenza in Italia fra '800 e '900*, Forum, Udine.
D.S. Reher, R. Schofield (eds.) 1993, *Old and New Methods in Historical Demography*, Clarendon Press, Oxford.
G. Restifo 1984, *Peste al confine. L'epidemia di Messina del 1743*, Epos, Palermo.
G. Restifo 1994, *Le ultime piaghe. Le pesti nel Mediterraneo (1720-1820)*, Selene Edizioni, Milano.
G. Restifo (ed.) 2001, *Epidemie e società nel Mediterraneo di età moderna*, Armando Siciliano Editore, Messina.
G. Restifo 2005, *I porti della peste. Epidemie mediterranee fra Settecento e Ottocento*, Mesogea, Messina.
L. Rombai 1985, *"Un tragico ed inutile scupìo di dolore, di vite umane e di denaro": la "Colonia Lorena" di Sovana (1739-1745)*, «Bollettino della Società Storica Maremmana», 49, 78-94.
J.W. Saelens, G. Viswanathan, D.M. Tobin 2019, *Mycobacterial Evolution Intersects with Host Tolerance*, «Frontiers in Immunology», 10:528. doi: 10.3389/fimmu.2019.00528.
R. Sallares 2002, *Malaria and Rome. A History of Malaria in Ancient Italy*, Oxford University Press.
R. Sallares, S. Gomzi 2001, *Biomolecular Archaeology of Malaria*, «Ancient Biomolecules», 3, 195-213.
R. Sallares, A. Bouwman, C. Anderung 2004, *The Spread of Malaria to Southern Europe in Antiquity: New Approaches to Old Problems*, «Medical History», 48, 311-328.
A. Salvagnoli Marchetti 1844, *Saggio illustrativo le tavole della statistica medica delle Maremme toscane*, Le Monnier, Firenze.
A. Salvagnoli Marchetti 1845, *Saggio illustrativo le tavole della statistica medica delle Maremme toscane. Secondo biennio: anni 1842-43 e 1843-44*, Le Monnier, Firenze.
B.V. Schmid, U. Büntgen, W.R. Easterday, C. Ginzler, L. Walløe, B. Bramanti, N.C. Stenseth 2015, *Climate-driven Introduction of the Black Death and Successive Plague Reintroductions into Europe*, «Proceedings of the National Academy of the Sciences of the United Nations of America», 112(19), 3020-3025.
I. Seguy, G. Alfani 2017, *La peste: bref état des connaissances actuelles*, «Annales de Démographie Historique», 2, 15-38.
M. Signoli, I. Séguy, J.N. Biraben, O. Dutour 2002, *Paléodémographie et démographie historique en contexte épidémique: La peste en Provence au XVIIIe siècle*, «Population», 57(6), 821-847.
P. Slack 1981, *The Disappearance of Plague: An Alternative View*, «The Economic History Review», New Series, 34(3), 469-476.
M.A. Spyrou, M. Keller, R.I. Tukhbatova, C.L. Scheib, E.A. Nelson, A.A. Valtueña, G.U. Neumann, D. Walker, A. Alterauge, N. Carty, C. Cessford *et al.* 2019, *Phylogeography of the second plague pandemic revealed through analysis of historical Yersinia pestis genomes*, «Nature Communications», 10, 4470.
A.C. Stone, A.K. Wilbur, J.E. Buikstra, C.A. Roberts 2009, *Tuberculosis and Leprosy in Perspective*, «Yearbook of Physical Anthropology», 52, 66-94.
E. Tognotti 2008, *Per una storia della malaria in Italia. Il caso della Sardegna*, Seconda edizione riveduta e ampliata, Franco Angeli, Milano.
L. Torelli 1882, *Carta della malaria d'Italia illustrata da Luigi Torelli senatore del Regno*, Pellas, Firenze.
G. Twigg 1984, *The Black Death: A Biological Reappraisal*, Schocken, London.
T. Wirth, F. Hildebrand, C. Allix-Béguec, F. Wölbeling, T. Kubica, K. Kremer, D. Van Soolingen, S. Rüsch-Gerdes, C. Locht, S. Brisse, A. Meyer *et al.* 2008, *Origin, Spread and Demography of the Mycobacterium tuberculosis Complex*, «PLoS Pathogens», 4(9), e1000160.

Riassunto

Peste, malaria e demografia nell'Italia del passato: acquisizioni recenti e problemi aperti

Con questo breve saggio l'autore ha inteso in primo luogo riconsiderare la bibliografia che testimonia del dibattito degli ultimi decenni, in ambito storico, circa la natura delle grandi epidemie di peste, mettendo in evidenza il valore delle ricerche più innovative riguardo alle possibili differenti modalità di trasmissione di *Yersinia pestis*. Nell'articolo si è anche cercato di sintetizzare, e di esporre con un linguaggio accessibile anche ai non specialisti della materia, il percorso delle ricerche nel campo della microbiologia che hanno consentito, negli ultimi due decenni, di ricostruire la storia evolutiva dei germi patogeni (a partire da quello della peste) e di chiarire molti interrogativi cui gli storici non avevano dato risposta. L'ultimo paragrafo dell'articolo accenna infine all'importanza che anche le malattie a carattere endemico (a partire dalla tubercolosi e dalla malaria) hanno avuto nel condizionare, nel lungo periodo, l'evoluzione della popolazione italiana, e sottolinea altresì la carenza di studi in grado di fornire stime affidabili, per i secoli passati, riguardo alla mortalità provocata da tali patologie.

Summary

Plague, malaria and demographics in past Italy: recent acquisitions and open problems

With this short essay, the author intends, in the first place, to reconsider the bibliography that testifies to the debate of recent decades, in the historical context, about the nature of the great plague epidemics, highlighting the value of the most innovative research regarding the possible different modalities of transmission of *Yersinia pestis*. The article also attempts to summarize and expose, in a language accessible even to non-specialists of the subject, the path of research in the field of microbiology that has allowed scholars, in the last two decades, to reconstruct the evolutionary history of pathogenic germs (starting from that of the plague) and to clarify many questions that historians had not previously answered. Finally, the last paragraph of the paper mentions the importance that even endemic diseases (starting from tuberculosis and malaria) have had in influencing, in the long term, the evolution of the Italian population. The article also underlines the lack of studies that allow reliable estimates, for the past centuries, of the mortality caused by these pathologies.

Parole chiave

Pandemie; Peste; Malaria; Tubercolosi; Italia.

Keywords

Pandemics; Plague; Malaria; Tuberculosis; Italy.