Epidemiological Status and Public Health Prevention Strategies of Plague

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Abstract. Yersinia pestis remains one of the few infectious agents not eliminated from natural reservoirs, despite over seventy years of effective antibiotics. It continues to threaten public health in many endemic regions. The epidemiological pattern has shifted in recent decades. Urban centers now see more pneumonic transmission. This review combines studies on the genetic evolution and transmission of Y. pestis. It assesses global surveillance data, focusing on the 2017 urban outbreak in Madagascar. It also evaluates prevention and control measures: ecological monitoring, clinical case management, and community-based interventions. The analysis indicates that recurrent outbreaks are not caused by a biologically novel pathogen. They result from weak health systems, reliance on short-term external aid, and conflicts between biomedical protocols and certain traditional practices in endemic communities. These findings point to the need for sustained investment in local laboratory infrastructure, health communication adapted to local cultures, and strategies designed for specific settings. Adapting new diagnostics and vaccines to field conditions in resource-limited areas remains difficult. Future research should focus on integrating climate, ecological, and epidemiological data into early warning systems. Such systems can enable faster, more targeted responses.

Keywords: Yersinia pestis, plague, epidemiology, Madagascar, zoonotic diseases.

1. Introduction

Y. pestis has had a severe and long-lasting demographic impact. Three pandemics—the Justinian Plague, the Black Death, and the modern-era outbreak—killed huge numbers of people and altered population structures and social orders across continents [1,2]. Streptomycin and tetracycline became available in the mid-20th century. These drugs turned plague from an almost invariably fatal disease into a treatable one. Many then assumed the threat was gone [3].

The early 21st century brought another major change. Historically, outbreaks occurred in remote rural settings. Most cases were bubonic. Human-to-human spread was limited. Outbreaks were contained quickly through isolation and vector control [4]. This pattern no longer holds. Rapid urbanization and large-scale population movement have dissolved the ecological buffers that once separated wild rodent foci from human settlements [5,6]. The 2017 pneumonic plague epidemic in Madagascar showed the consequences. The bacterium spread through crowded public transport and dense urban neighborhoods. Traditional control methods failed to stop these transmission chains [6,7]. The outbreak also exposed two deeper problems: the chronic weakness of primary health care in low-income settings, and friction between modern medical interventions and deeply rooted local customs around death and burial [8]. From 2000 to 2018, over 97% of notifiable plague cases were reported from African countries, mainly Madagascar and the Democratic Republic of the Congo. Central Asia, northwestern China, and western North America reported only sporadic bubonic cases [9]. This uneven distribution partly reflects who has the resources to detect and report. An outbreak in Switzerland would be recognized within hours. In rural Madagascar, the same outbreak could go unnoticed for weeks.

Microbiological knowledge of plague has expanded greatly. Genome sequencing has traced the evolution of Y. pestis in fine detail, revealing genetic diversity, the complexity of host-vector ecology, and the pathogen's ability to survive for long periods in the environment [1]. Earlier work systematized diagnostic algorithms, clarified the functions of virulence plasmids, and reviewed

conventional and next-generation vaccine candidates. Some of the vaccine assessments made at that time now appear too cautious, given the subsequent shifts in the vaccine landscape [10].

The 2017 Madagascar epidemic generated a large number of real-time investigations. One study traced transmission chains in detail through the intercity bus network. Another compiled case counts and described the coordination of multilateral outbreak response [6,7]. Both studies noted a critical limitation: only 390 of more than 2,400 suspected cases were laboratory-confirmed. Confirmed cases therefore represent only a fraction of the true disease burden [1]. A later regional review provided post-epidemic surveillance follow-up. It highlighted a damaging but often overlooked problem: sputum-based rapid tests used in peripheral health facilities have poor sensitivity. This almost certainly led to substantial undercounting of pneumonic cases [1]. The diagnostic gap harms individual patients and weakens the accuracy of the surveillance data on which outbreak responses depend.

This review examines the genetic evolution and multi-modal transmission of Y. pestis. It analyzes current epidemiological patterns, with emphasis on the 2017 urban outbreak in Madagascar. It also assesses the layered prevention and control framework: ecological source management, clinical diagnosis and treatment, community-based health interventions, and cross-border early warning systems.

2. Microbial Evolution and Multi-modal Transmission of Yersinia pestis

2.1. Genetic Background and Core Virulence Determinants

Y. pestis evolved from Yersinia pseudotuberculosis, an enteric pathogen. Over roughly 10,000 to 40,000 years, it acquired genes through horizontal transfer and lost others through chromosomal deletions. This turned a mild gastrointestinal bacterium into one of the most lethal infectious agents in history [1,3].

The pYV plasmid encodes a type III secretion system. This system injects bacterial effector proteins into host macrophages and disables their immune response [3]. The pFra plasmid carries the ymt gene, which helps bacteria survive in the flea gut, and directs synthesis of the F1 capsular antigen. F1 is a key anti-phagocytic factor that gives the bacterium a surface resistant to engulfment. The pPst plasmid produces plasminogen activator Pla, a protease that aids systemic spread after the bacterium breaches the skin barrier [3]. Together, these plasmids allow Y. pestis to evade immune clearance, survive, and spread effectively.

The traditional biovar scheme divided Y. pestis into Antiqua, Medievalis, and Orientalis, each initially linked to one of the three historical pandemics [1]. Whole-genome sequencing has revealed more complex phylogenetic relationships. These relationships often cut across the classical biovar categories. This finding matters beyond taxonomy: if historical outbreaks cannot be reliably tied to specific bacterial lineages, the understanding of long-term transmission dynamics rests on shakier ground than previously thought.

Environmental persistence adds another layer to the pathogen's adaptability. Virulent strains can remain viable in saline and dry soils for up to 280 days. They can adopt a dormant L-form state that withstands temperature extremes and osmotic stress [1]. Soil-dwelling amoebae may serve as transient intracellular hosts. This offers a plausible explanation for sporadic human cases with no known animal exposure [1]. The amoeba hypothesis has laboratory support but has not been confirmed in field settings. Its implications for surveillance still need to be established.

Multidrug-resistant isolates have appeared in Madagascar in recent years. Resistance determinants are carried on conjugative plasmids and can transfer across bacterial species [8]. Some Malagasy isolates already show reduced susceptibility to streptomycin, the first-line drug. Fully resistant strains remain uncommon [8].

2.2. Animal Reservoirs and Flea-Mediated Transmission

Y. pestis persists in nature through enzootic cycles involving mammalian reservoirs and flea vectors. More than 200 mammal species can serve as reservoirs. The dominant host species vary by region. Marmots are central in Central Asian foci. Black rats drive transmission in Madagascar and the African savanna. Prairie dogs play the equivalent role in North America [1]. A marmot-based focus differs ecologically from a rat-based one. They have different seasonal patterns, human exposure risks, and options for intervention.

Fleas transmit plague in two main ways. Early-phase transmission can occur within hours of an infected blood meal. Its overall efficiency is relatively low [1]. Biofilm-blockage transmission involves bacterial aggregates that form a plug in the flea's proventriculus. The blocked flea repeatedly tries to feed and regurgitates pathogen-laden blood into the bite site. This method delivers a much more effective infectious dose [1].

Seasonal dynamics shape outbreak risk. In high-altitude settings, rodent breeding and flea activity typically peak during the rainy season. This creates conditions for epizootic amplification [8]. The seasonal rhythm is consistent across Madagascar and the Democratic Republic of Congo. It provides a predictable window for intensified surveillance. Resource-constrained health systems have only partly used this opportunity [8]. The predictable pattern means outbreaks can be anticipated. Failures to act reflect not a lack of foresight but a failure to set priorities.

2.3. Human Infection Routes and Interhuman Transmission

People can acquire plague through several routes. The flea bite remains the most common route and causes bubonic plague [3]. Direct contact with infected animal carcasses during hunting, skinning, or butchering offers another route. Eating undercooked contaminated meat is a third pathway [1]. In some Central Asian communities, traditional remedies that use raw marmot bile have been linked to transmission, though this route is hard to quantify.

The most dangerous route is respiratory. Primary pneumonic plague spreads via infectious droplets over roughly one meter. It bypasses the bubonic stage. Without prompt antibiotics, the case-fatality rate approaches 100% [3]. If antibiotics are not given within 24 to 48 hours, survival is virtually impossible [8].

The 2017 Madagascar epidemic showed the dynamics of pneumonic spread. The index case was a 31-year-old man. He developed symptoms and boarded a crowded intercity bus traveling from the central highlands to Toamasina. He died during the journey. His infection spawned secondary cases among fellow passengers, and the chain eventually reached several urban centers [6,7]. When he got on the bus, he was symptomatic but not severely ill. He looked no different from any other passenger with a cough. By the time his infection was confirmed, he had already seeded transmission across a network spanning hundreds of kilometers [8].

Interhuman spread is not only a modern phenomenon. Historical research confirms that human body lice and human fleas can also mediate transmission. Bacteria in louse feces enter the host through skin breaks caused by scratching. This pathway helps explain the rapid spread of the Black Death in medieval Europe, where rat epizootics were not always obvious [1]. Some historians have questioned the rat-centric model of the Black Death. Louse-mediated transmission offers a plausible alternative that needs further microbiological study [1].

For all suspected pneumonic cases, thorough contact tracing and early isolation are essential. Putting these measures into practice depends heavily on local health system capacity. This remains a persistent challenge in resource-limited settings [6,8].

3. Current Epidemiological Status and Impact

3.1. The Three Major Historical Pandemics

Three plague pandemics are recorded in history. The first, the Justinian Plague (541–750 AD), began in Egypt and spread along Mediterranean trade networks. It caused an estimated 25–50 million deaths [1]. The second, the Black Death (1346–18th century), emerged in Central Asia and moved along the Silk Road. Between 1346 and 1353 it killed about one-third of Europe's population. Recurrent outbreaks continued in Europe until the 18th century [2,12]. The third pandemic started in Yunnan, China, in 1772. By the late 19th century, steamships and railways carried it to port cities across Asia, Africa, the Americas, and Oceania. It established permanent natural foci in many regions [1]. These pandemics were not driven by a single bacterial lineage. In each case, expanding transport networks spread the disease faster than public health systems could respond. The link between plague spread and trade routes has been consistent. Changes in transportation have always shaped the speed and reach of epidemics. This pattern remains relevant today.

3.2. Contemporary Global Epidemiological Patterns

From 2000 to 2018, WHO consolidated surveillance recorded 26,237 notified human plague cases worldwide. Of these, 97% were concentrated in African countries, particularly Madagascar and the Democratic Republic of the Congo [9]. Bubonic plague accounts for 80–95% of all clinical forms. With standard treatment, its case-fatality rate is 10–20%. Untreated primary pneumonic plague kills nearly all patients [3,4]. All endemic areas share common environmental features: high altitude, arid or saline soils, and dense wild rodent populations [1]. The most notable epidemiological shift in the 21st century is the movement of outbreak sites from remote rural areas into densely populated cities [5,6]. Along with this shift, the proportion of pneumonic cases has risen. In traditional rural foci, pneumonic plague typically represents less than 5% of cases. In the 2017 Madagascar epidemic, it reached 77% [8].

3.3. The 2017 Madagascar Urban Pneumonic Plague Epidemic

Between August and November 2017, Madagascar recorded 2,417 suspected plague cases. Pneumonic plague accounted for 77% of them. Only 390 cases were laboratory-confirmed by F1 antigen rapid test and PCR [1]. The index case was a 31-year-old man. After developing symptoms, he boarded a crowded intercity bus traveling from the central highlands to the eastern city of Toamasina and died en route. Secondary infections occurred among passengers and eventually led to large-scale intercity transmission [6,7].

Several factors kept the epidemic expanding. First, grassroots health workers lacked systematic training in plague recognition. Diagnosis and isolation were delayed. More than 80 health workers became infected during the outbreak [6]. Second, local funeral traditions require washing the body of the deceased. This forced healthy residents into prolonged close contact with infected corpses and created hidden transmission chains [8]. Third, peripheral health facilities had limited laboratory capacity. Sputum-based diagnostic tests had low sensitivity. Many suspected cases were never confirmed [1].

For the emergency response, the Madagascar government created a high-level task force chaired by the prime minister. The WHO Global Outbreak Alert and Response Network coordinated support from the Pasteur Institute and the International Red Cross. It delivered more than 1.2 million doses of antibiotics and complete personal protective equipment to affected areas [6]. Nine neighboring countries were designated high-risk zones, and airport entry screening was put in place to block cross-border spread [6].

In China, natural plague foci are concentrated on the Qinghai-Tibet Plateau, Xinjiang, and Inner Mongolia. Himalayan marmots serve as the core reservoir species [1]. Most sporadic human cases are linked to hunting and skinning infected wild rodents. With standard isolation and contact

management protocols, the risk of large-scale human-to-human pneumonic transmission remains under control [1,9].

4. Prevention and Control Strategies

4.1. Ecological Source Control

The goal of ecological source control is to interrupt the transmission cycle of Y. pestis in the environment. Long-term monitoring of carnivorous sentinel animals is a key method. Wild carnivores become exposed by eating infected rodents. Serological testing of these animals indirectly samples hundreds of rodents [1]. Regular insecticide applications around residential areas can lower the risk of flea bites. Flea control must be coordinated with rodent control. If rodents are eliminated without flea control, fleas may turn to human hosts [4]. San Francisco's experience in eradicating plague shows the value of urban environmental reconstruction. Sealing basements with concrete, paving streets, and renovating sewage systems removed rodent breeding habitats. These measures were more effective than chemical rodent control alone [11,12]. In areas with saline soils where Y. pestis can survive for months, targeted environmental remediation should also be carried out [1].

4.2. Clinical Diagnosis, Treatment, and Pharmaceutical Interventions

Streptomycin is the standard first-line drug for all forms of plague. Gentamicin is an alternative in resource-limited settings [3]. Oral doxycycline and ciprofloxacin can be used for mild bubonic plague and for mandatory post-exposure prophylaxis of close contacts of pneumonic patients. Chloramphenicol is specifically indicated for plague meningitis [3]. All confirmed patients must complete a 10- to 14-day treatment course. Delaying antibiotics in pneumonic plague pushes the case-fatality rate above 50%. Starting treatment within 24 hours of symptom onset lowers it below 25% [6,8].

Common point-of-care diagnostic tools include F1 antigen rapid test strips, which are suitable for remote endemic areas, and multiplex PCR targeting the pla and caf1 genes [3]. Bacterial culture and bacteriophage lysis testing remain the gold standard for confirmation [1]. The low sensitivity of sputum testing severely limits accurate diagnosis of pneumonic plague in African primary-care hospitals. During the 2017 Madagascar epidemic, only 32 pneumonic cases were laboratory-confirmed [1].

Traditional inactivated whole-cell vaccines and live attenuated vaccines cause significant systemic side effects. They do not confer effective protection against pneumonic plague [3]. F1-LcrV subunit vaccines have reached phase II clinical trials. mRNA and aerosol neutralizing antibody vaccines are still in preclinical research [10].

5. Conclusion

Plague has not been eradicated in the 21st century, even with more than 70 years of effective antibiotics. Urban pneumonic plague, transmitted directly between people, has emerged. This is a departure from the rural bubonic pattern that long dominated the literature. This review examined the genetic evolution and transmission of Y. pestis, analyzed surveillance data with an emphasis on the 2017 Madagascar outbreak, and evaluated current prevention frameworks. The Madagascar experience highlights several points. Urban pneumonic plague presents a different challenge from rural bubonic plague. Crowded transport, delayed diagnosis in areas unfamiliar with the disease, and funeral customs all amplified transmission beyond what rodent-focused control could contain. More fundamentally, the outbreak exposed structural weaknesses in low-income endemic regions: weak health infrastructure, chronic underfunding of primary care, and dependence on short-term external aid. These factors allow epidemics to recur despite the availability of effective treatments. International assistance should move beyond occasional delivery of drugs and diagnostics. It should support sustained investment in laboratory capacity, workforce development, and community

engagement that fits local cultural contexts. Plague in many endemic areas has a predictable seasonality. This provides an underexploited chance to strengthen surveillance during high-risk periods. However, published surveillance data likely undercount true cases because of diagnostic limitations in resource-poor settings. The focus on Madagascar may also limit how far the findings apply to regions with different ecologies and cultures. Future work should focus on affordable point-of-care diagnostics for peripheral facilities, next-generation vaccines that give durable protection against pneumonic forms, and predictive models that combine climatic, ecological, and epidemiological data. Integrated approaches offer the best chance to break the cycle of recurrent outbreaks and achieve lasting disease control.

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