Editorial

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Plague in the modern world: Ecological persistence, epidemic containment, and the limits of public health preparedness

Liqin Sun[1,§], Haipeng Zhu[2,§], Qingsong Qi[2], Jin Li[2], Meina Tian[2], Fuxiang Wang[1,*], Jean-Pierre Routy[3,4,*], Jiaye Liu[5,*], Hongzhou Lu[1,*]

[1] Department of Infectious Diseases, National Clinical Research Center for Infectious Diseases, Shenzhen Third People's Hospital and The Second Affiliated Hospital of Southern University of Science and Technology, Shenzhen, Guangdong, China;
[2] Department of Infectious Diseases, The Ninth People's Hospital of Dongguan, Dongguan, Guangdong, China;
[3] Research Institute of the McGill University Health Centre, Montréal, QC, Canada;
[4] Chronic Viral Illness Service, McGill University Health Centre, Montréal, QC, Canada;
[5] School of Public Health, Shenzhen University Medical School, Shenzhen, Guangdong, China.

SUMMARY: *Yersinia pestis* persists across sylvatic rodent–flea reservoirs globally and is not currently amenable to eradication. Paleogenomic and paleoecological evidence indicates that historical plague pandemics reflected complex interactions among pathogen biology, environmental conditions, and societal vulnerabilities rather than pathogen virulence alone. Drawing a qualified epidemiological comparison to cholera, contemporary public health interventions show that effective disease control does not necessarily require eliminating a pathogen from its natural reservoirs; for plague, modern clinical and public health measures have substantially decoupled zoonotic spillovers from pandemic amplification. Whereas cholera control relies predominantly on water and sanitation barriers alongside clinical, vaccination, and surveillance programs, plague containment depends primarily on zoonotic monitoring, rapid diagnosis, early antimicrobial therapy, and contact management. The October 2026 unexplained fatal pneumonia in a Russian anti-plague laboratory worker illustrates both the capacity and the limitations of outbreak surveillance when targeted assays reported by national authorities are negative but etiology remains unresolved. With 97.7% of the 2646 confirmed human cases reported globally during 2019–2025 concentrated in two endemic countries, sustaining containment requires addressing healthcare inequities, maintaining clinical vigilance, monitoring antimicrobial resistance, and enforcing rigorous biosafety.

Keywords: Yersinia pestis; zoonotic spillover; transmission dynamics; antimicrobial resistance; International Health Regulations

1. Introduction

On October 2, 2026, the fatal acute pneumonia of a 28-year-old laboratory worker at an anti-plague research institute in Irkutsk, Russian Federation, prompted international public health inquiries regarding potential occupational exposure to Yersinia pestis (*1-3*). Local authorities placed approximately 200 healthcare and community contacts under medical observation (*1-3*). In its October 10, 2026 notification, the World Health Organization (WHO) stated that, according to information provided by the Russian authorities to WHO, more than 5500 laboratory tests were performed, with no detection of *Y. pestis* or other investigated high-consequence pathogens; no additional linked cases were reported among contacts during the completed observation period, and the primary illness remained classified as pneumonia of undetermined etiology (*1-3*). However, WHO noted that a key uncertainty remained the absence of a confirmed diagnosis in the deceased worker, leaving the exact cause of death—and whether the contact observation period sufficed to exclude all potential etiologies—independently unverified while public briefings and international news reports noted rapid multilateral queries alongside ongoing questions regarding diagnostic resolution and information transparency (*1-3*).

Rather than confirming that international surveillance and legal compliance mechanisms have fully succeeded, this episode illustrates both the capacity and the limitations of contemporary outbreak surveillance, particularly when initial laboratory findings reported by national authorities are reassuring but the underlying etiology remains unresolved (*1-3*). Negative targeted assays lower the likelihood of an immediate Y. pestis

outbreak but neither establish the cause of death nor validate every aspect of biosafety oversight and international risk communication (*1-3*). Beyond its immediate context, this event highlights a central question in infectious disease governance: how have modern medicine and public health institutions altered the epidemic potential of a pathogen entrenched in wildlife reservoirs, and how can containment capacity be sustained when human disease becomes globally rare yet geographically concentrated (*4*)?

2. The persistence of plague

A foundational reality of plague epidemiology is that Y. pestis is a complex zoonotic pathogen not currently amenable to eradication (*4,5*). Unlike smallpox, an obligate human viral infection eradicated through global vaccination, plague circulates independently of human populations within sylvatic rodent and flea networks across the Eurasian steppes, East African highlands, the Americas, and parts of Asia (*4-6*). Within these natural foci, transmission among mammalian hosts is mediated primarily by ectoparasitic fleas in which bacterial biofilm obstructs the proventriculus, promoting regurgitative transmission during blood meals (*5,6*). Epizootic amplification responds to fluctuations in precipitation, vegetation, and rodent density, although ecological lag phases vary substantially across ecosystems and geographic regions (*5,6*). When epizootic die-offs deplete wild rodents, infectious fleas seek alternative hosts, driving spillover into peridomestic animals and human settlements (*5,6*). Because humans are incidental hosts, curing human cases does not alter wildlife maintenance cycles, requiring public health systems to continuously monitor natural foci and manage the ecological interface between wildlife reservoirs and human communities (*4,5,7*).

3. Revisiting historical pandemics

Three historical plague pandemics have been documented: the First Pandemic (beginning with the Justinianic Plague, 541–750 AD), the Second Pandemic (initiated by the Black Death, 1346–1353), and the Third Pandemic, which spread globally from Asia in the nineteenth century (*5,6*). Ancient DNA analyses of fourteenth-century burial sites demonstrated that medieval Y. pestis strains carried the core virulence plasmids (pCD1, pMT1, and pPCP1) conserved in modern isolates (*8*), while phylogenomic reconstructions trace early Second Pandemic diversification to Central Eurasia around 1338 (*9*). Although paleogenomics provides no evidence for an extinct ancestral "super-strain", the absence of a distinct hypervirulent lineage does not exclude all historical differences in pathogen phenotype, nor does it justify attributing medieval mortality to societal factors alone (*8,9*).

For the First Pandemic, despite ancient genomic confirmations of *Y. pestis* (*10*), palaeoecological and documentary evidence does not support an empire-wide demographic collapse (*11*); for the Second Pandemic, pollen records indicate marked regional heterogeneity in land-use change and agricultural disruption across Europe (*12*). Historical plague mortality reflected the interaction between pathogen biology, ecological conditions, and societal vulnerability, rather than pathogen virulence alone (*5,8-12*).

Dense commensal rodent (such as *Rattus rattus*) and vector flea (such as *Xenopsylla cheopis*) populations, crowded housing, nutritional deficits, and the absence of etiological diagnosis or antimicrobial therapy allowed historical spillovers to amplify into major demographic crises (*5,6*), whereas nineteenth-century steamship trade dispersed the 1.ORI lineage globally and established secondary sylvatic foci before bacteriological control emerged (*5,13*).

4. Why catastrophic transmission has become less likely

Modern societies avoid pandemic amplification primarily because clinical care and public health interventions interrupt transmission chains and suppress the effective reproduction number (R_t) below unity (*4,7,14*). Clarifying how these interventions operate requires distinguishing between clinical forms and transmission pathways (*4,7,14*). Human infection typically presents as bubonic plague following a flea bite, or less commonly as primary septicemic or primary pneumonic plague (*4,7,14*). Untreated bubonic or septicemic infection can disseminate hematogenously to the lungs, causing secondary pneumonic plague; however, primary pneumonic plague also arises directly from inhaling infectious respiratory droplets—or, in high-risk laboratory or procedural settings, aerosols—from infected humans or animals (*4,7,14*). Early antimicrobial treatment may prevent progression from bubonic or septicemic plague to secondary pneumonic disease, while rapid identification, respiratory precautions, and contact management are essential to interrupt transmission from primary or secondary pneumonic cases (*4,7,14*).

Mathematical evaluations of historical primary pneumonic plague outbreaks estimate an average basic reproduction number (R_0) of approximately 1.3 (with variance = 3.1 for the fitted geometric secondary-case distribution, and outbreak-specific average secondary cases per primary case ranging from 0.7 to 3.0) (*15*) and an offspring dispersion parameter (κ) near 1.37 (90% CI: 0.88–3.53) (*16*). Because these estimates are derived from historical outbreak data and depend on study populations, case ascertainment, contact environments, and modeling assumptions, they should not be treated as universal biological constants of modern plague transmission, nor does a moderate

average R_0 preclude superspreading when care is delayed (*15,16*). Nevertheless, the rapid clinical progression of pneumonic plague following a brief incubation period (typically 1-4 days, within the general 1-7-day range for human plague), together with predominantly close-contact respiratory transmission in community settings, underscores the importance of early case recognition and prompt intervention (*4,7,14*).

Within this operational window, the 2021 WHO plague management guidelines and the 2024 WHO operational manual recommend bedside Fraction 1 capsular antigen rapid diagnostic tests (F1-RDT) to accelerate clinical triage and isolation; however, WHO notes that these F1-RDT recommendations rest on very-low-certainty evidence, and imperfect specificity in pneumonic screening necessitates confirmation by bacterial culture or validated molecular assays before an outbreak is officially verified (*7,14*). Prompt effective antimicrobial therapy—with the 2021 WHO guidelines adding fluoroquinolones (ciprofloxacin, levofloxacin, moxifloxacin) to first-line streptomycin and gentamicin for pneumonic or septicemic plague, and to first-line streptomycin, gentamicin, and doxycycline for bubonic plague—reduces mortality and transmission risk; respiratory isolation and droplet precautions remain essential during the initial 48 hours of treatment and until clinical improvement (*7,14*). Concurrently, personal protective equipment (PPE) during post-mortem handling prevents funeral-associated transmission, while seven-day post-exposure prophylaxis with oral doxycycline or ciprofloxacin protects close contacts (*7,14*). Because no plague vaccine is currently WHO-recommended for general use—with older whole-cell and live-attenuated formulations exhibiting notable reactogenicity and limited durability, restricting any use to selected high-risk occupational groups in some countries—and because insecticidal flea control must precede rodent control to prevent displaced fleas from biting humans, operational containment relies heavily on diagnostic, vector-control, and therapeutic readiness (*4-7,14*).

The 2017 urban plague epidemic in Madagascar highlights both the utility of coordinated response and the complexity of outbreak data (*17*). Of 2414 clinically suspected plague cases notified nationally, 1878 were clinically classified as pneumonic plague: 32 (1.7%) were laboratory-confirmed, 386 (20.6%) were probable, and 1460 (77.7%) remained suspected (*17*). While unconfirmed status does not exclude plague among all suspected cases, heightened urban concern likely expanded syndromic reporting of non-plague respiratory illnesses (*17*). The decline in notified cases may have reflected a combination of outbreak-control measures, changes in case ascertainment, and diagnostic reclassification; the relative contribution of each cannot be determined from these data (*17*).

Conceptually, both cholera and plague demonstrate that effective disease control does not necessarily require elimination of the pathogen from its environmental or animal reservoirs; however, the extent of control depends on sustained public health infrastructure, healthcare access, and surveillance capacity (*4,5,7,14*). Rather than representing a rigid dichotomy between passive infrastructure versus active suppression—which oversimplifies cholera programs that also require surveillance, treatment, oral vaccination, and maintenance—they represent distinct primary barrier architectures: cholera control relies predominantly on water, sanitation, and environmental exposure barriers, whereas plague containment depends primarily on zoonotic surveillance, rapid diagnosis, antimicrobial therapy, and contact management (*4,5,7,14*).

5. Remaining vulnerabilities

Global reductions in average plague risk obscure severe geographic disparities (*18*). According to the September 2026 WHO surveillance report covering 2019-2025, 10 countries reported 3860 suspected human plague cases; 6 of these countries reported 2646 confirmed cases and 423 deaths, corresponding to a crude case-fatality ratio of 11.0% using the 3847 suspected cases from those 6 countries as the denominator rather than laboratory-confirmed cases alone (*18*). Notably, the Democratic Republic of the Congo and Madagascar accounted for 97.7% of all reported confirmed cases globally during 2019–2025, although WHO noted that identical suspected and confirmed case counts in some national reports indicate that independent laboratory confirmation cannot be assumed for every reported confirmed case (*18*). These findings highlight the geographic concentration of reported plague cases and raise important questions about how differences in ecological exposure, diagnostic access, case classification, and health-system capacity shape the observed disease burden (*7,18*) (Table 1).

Addressing these vulnerabilities under conditions of global rarity and focal endemicity requires sustained institutional commitment across four interconnected priorities (*4,7,14,18*).

First, closing healthcare delivery gaps in endemic rural foci—by decentralizing F1-RDT stockpiles, strengthening specimen transport networks for culture and molecular confirmation, coordinating sequential flea and rodent control, and guaranteeing uninterrupted access to frontline fluoroquinolones and aminoglycosides at primary health centers—is essential to prevent sporadic bubonic spillovers from progressing to fatal septicemic or secondary pneumonic clusters (*7,14,18*).

Second, countering clinical amnesia in low-incidence regions requires integrating high-consequence zoonoses into continuing medical education and emergency triage algorithms, as unfamiliarity with rare primary pneumonic or septicemic presentations frequently causes delays in initiating effective treatment within the narrow therapeutic window and heightens nosocomial

Table 1. From historical plague pandemics to modern containment: Changing determinants of epidemic risk

Dimension	Historical vulnerability	Modern change and remaining limitation
Ecological reservoirs	Persistent sylvatic rodent–flea maintenance cycles and unmonitored epizootic spillovers (*5,6*)	Natural foci remain permanent; integrated ecological and vector surveillance reduces but cannot eliminate spillover exposure (*4-7*)
Clinical management	Absence of etiological diagnosis or pathogen-directed therapy (*5*)	Prompt aminoglycoside and fluoroquinolone therapy reduces mortality and transmission risk; diagnostic delays and rural access gaps persist (*4,7,14,18*)
Transmission control	Limited diagnostic, respiratory isolation, post-mortem precaution, and contact management capacity (*5*)	Rapid clinical recognition, respiratory precautions, post-mortem PPE, contact management, and post-exposure prophylaxis reduce opportunities for onward transmission; uneven availability persists (*7,14,17*)
Societal conditions	Variable sanitation, commensal rodent density, crowded housing, nutrition, and medical knowledge (*5,8-12*)	Greater health-system capacity globally, yet 97.7% of reported confirmed cases remain concentrated in endemic settings facing resource constraints (*4,7,18*)
Surveillance	Limited pathogen identification and outbreak intelligence (*5*)	Integrated laboratory and international IHR (2005) surveillance; incomplete verification, syndromic misclassification, and unresolved diagnostic uncertainty (*4,7,17,18*)

Note: Numbers in parentheses correspond to the manuscript reference list. IHR (2005), International Health Regulations (2005); PPE, personal protective equipment.

transmission risk (*4,7,14*).

Third, systematic genomic and phenotypic resistance surveillance remains vital following the emergence of transferable IncC plasmid-mediated multidrug resistance (pIP1202) (*19,20*) and chromosomal *rpsL* streptomycin resistance in clinical Y. pestis isolates from Madagascar, including documented person-to-person transmission of streptomycin-resistant pneumonic plague (*21*). Although experimental flea co-infection models suggest that IncC plasmid carriage may incur competitive fitness costs during vector colonization while retaining full virulence and vector-transmission competence in single-strain infections (*20*), laboratory findings offer mechanistic hypotheses rather than guarantees of natural containment, underscoring the necessity of routine susceptibility monitoring and validated therapeutic alternatives (*7,14,20,21*).

Fourth, because reference laboratories and research institutes maintain extensive collections of viable Y. pestis strains, stringent biosafety governance must be coupled with transparent etiological investigation and timely notification under the International Health Regulations (2005) of events that may constitute a public health emergency of international concern (PHEIC), including pneumonic plague and clusters of unexplained severe respiratory illness (*1,4,7*).

6. Conclusion

The enduring presence of *Y. pestis* across sylvatic reservoirs underscores a fundamental epidemiological principle: the ecological survival of a zoonotic pathogen does not dictate the scale of human disease (*4–6*). Whereas historical plague pandemics emerged from the convergence of pathogen biology, environmental perturbations, and premodern societal vulnerabilities (*5,8-12*), contemporary diagnostic, antimicrobial, and public health interventions have greatly reduced, but not eliminated, the probability that wildlife spillover will amplify into a large epidemic or pandemic (*4,7,14-17*). Yet this decoupling remains incomplete, neither self-sustaining nor globally equitable; its durability is contingent on sustained surveillance, timely diagnosis and treatment, accessible frontline healthcare in endemic margins, continuous resistance monitoring, and rigorous biosafety governance (*4,7,14,18-21*). As illustrated by the recent unexplained fatal respiratory illness in a laboratory worker, credible outbreak intelligence requires transparent etiological investigation without premature attribution or institutional reassurance (*1-3*). Ultimately, when an entrenched pathogen cannot be eradicated from nature, public health success must be measured by two interconnected benchmarks: sustainably reducing the human disease burden in endemic regions while preserving long-term capacities for risk identification, diagnosis, treatment, and transmission control across the world's most vulnerable health systems (*4,7,14,18*).

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[§]These authors contributed equally to this work.
**Address correspondence to:*
Hongzhou Lu and Fuxiang Wang, Department of Infectious Diseases, National Clinical Research Center for Infectious Diseases, Shenzhen Third People's Hospital and The Second Affiliated Hospital of Southern University of Science and Technology, Shenzhen, Guangdong, China.
E-mail: luhongzhou@fudan.edu.cn (HL), wangfuxiang999@163.com (FW)

Jiaye Liu, School of Public Health, Shenzhen University Medical School, Shenzhen, Guangdong, China.
E-mail: liujiaye1984@163.com

Jean-Pierre Routy, Division of Hematology, Chronic Viral Illness Service, and Research Institute of the McGill University Health Centre, Montreal, QC, Canada.
E-mail: jean-pierre.routy@mcgill.ca

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