Letter to the Editor

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When zoonosis mimics autoimmunity: arenavirus spillover, gut dysbiosis, and the case for community-level early warning systems

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To the Editor,

Rodent-borne viruses continue to represent a major, but often underestimated, source of emerging human infection, particularly in ecologically unstable and resource-limited settings. Among these, members of the Arenaviridae family deserve renewed attention not only because of their epidemic potential but also because of the diagnostic ambiguity they may create in clinical practice. Arenaviruses are traditionally recognized for causing febrile, hemorrhagic, or neurologic illness, yet their immunopathology also raises an important possibility: that some infections may present with atypical inflammatory phenotypes that overlap with autoimmune or rheumatologic syndromes before a zoonotic etiology is suspected[1].

Such concerns are even more relevant in endemic or spillover-prone regions, where exposure history may be underreported or clinically overlooked. Rodent-based surveillance studies have concluded that rodents are the potential reservoirs of many zoonotic diseases that are underdiagnosed or misdiagnosed in specific populations[2].

At the same time, host-response is evolving beyond pathogen detection alone. Increasing evidence suggests the role of the gut microbiome in reshaping a person's systemic immune responses, changes in inflammatory thresholds, and viral susceptibility. Experimental work has shown the influence of microbial composition on the severity and trajectory of immunological responses to viral infections through their effects on innate immunity[3]. Although arenavirus-specific human microbiome signatures remain insufficiently characterized, it is biologically plausible that gut dysbiosis in exposed populations may precede or accompany atypical inflammatory responses, especially in settings where repeated zoonotic exposure and environmental stressors coexist. In this sense, microbiome disruption may represent not merely a consequence of infection, but a potentially useful non-invasive early warning signal.

Furthermore, a pilot study has confirmed the presence of zoonotic pathogens in wastewater, suggesting their presence in the community. This highlights the need to expand wastewater surveillance beyond human pathogens by integrating broad, unspecific virus detection methods, metagenomics, and specific virus detection tools like PCR. This can lead to early detection and will help us better understand cross-species virus transmission[4].

For this reason, surveillance of rodent-associated viral threats should move beyond reactive outbreak confirmation toward hybrid early warning systems. We propose that endemic and high-risk communities may benefit from integrated wastewater and serosurveillance models, particularly in areas experiencing urban crowding, climate-driven habitat disruption, poor food storage, or intense human–rodent proximity. Such an approach would not only replace clinical diagnostics but could help identify ecological and immunologic signals of spillover risk before atypical inflammatory cases are misclassified as idiopathic autoimmune diseases or undifferentiated febrile illnesses.

As climate variability, land-use change, and zoonotic pressure intensify, future preparedness must become more ecologically literate and immunologically sensitive, particularly in light of continuing global inequities in surveillance capacity and data-sharing readiness[5]. Recognizing when a "rheumatologic" or inflammatory presentation may, in fact, signal a rodent-borne viral exposure is not only a diagnostic challenge; it is a surveillance opportunity. The next advance in zoonotic prevention may depend not only on detecting pathogens but on recognizing the host and environmental signatures that precede them.

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