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Abstract: Immune heterogeneity in wild host populations indicates that disease-mediated selection is common in nature. However, the underlying dynamic feedbacks involving the ecology of disease transmission, evolutionary processes, and their interaction with environmental drivers have proven challenging to characterize.

Plague presents an optimal system for interrogating such couplings: *Yersinia pestis* transmission exerts intense selective pressure driving the local persistence of disease resistance among its wildlife hosts in endemic areas. Investigations undertaken in colonial India after the introduction of plague in 1896 suggest that, only a decade after plague arrived, a heritable, plague-resistant phenotype had become prevalent among commensal rats of cities undergoing severe plague epidemics. To understand the possible evolutionary basis of these observations, we developed a mathematical model coupling environmentally forced plague dynamics with evolutionary selection of rats, capitalizing on extensive archival data from Indian Plague Commission investigations. Incorporating increased plague resistance among rats as a consequence of intense natural selection permits the model to reproduce observed changes in seasonal epidemic patterns in several cities and capture experimentally observed associations between climate and flea population dynamics in India. Our model results substantiate Victorian era claims of host evolution based on experimental observations of plague resistance and reveal the buffering effect of such evolution against environmental drivers of transmission. Our analysis shows that historical datasets can yield powerful insights into the transmission dynamics of reemerging disease agents with which we have limited contemporary experience to guide quantitative modeling and inference.

Model explained in detail and compared to historical data. Good references, but data not included in paper.

Keywords: differential equation, model, modeling, infectious disease, vector-borne disease, zoonosis, immunoecology