Multiple Outbreaks and Flu Containment Plans

IN REPORTING ON OUR RECENT STUDY (1) ON THE RISK OF MULTIPLE OUTBREAKS OF PANDEMIC influenza, M. Enserink cites several scientific and political objections to our conclusions that a single introduction of pandemic flu might be followed by additional introductions in quick succession (“New study casts doubt on plans for pandemic containment,” News of the Week, 24 Feb., p. 1084).

Several commentators suggest that multiple introductions are unlikely, making analogies to other emerging infections, such as SARS. In fact, SARS is thought to have entered humans several times in 2003–04 (2, 3). Multiple infections have been suggested for HIV-1 (4), and clustered introductions have been observed for Ebola virus (5). The commentators suggest that the likelihood of a flu pandemic is not currently above its historical average of ~3% per year (6), so that containment will increase the time to a pandemic by a decade or more. Our analysis shows that containment will yield benefits on this scale only if the risk of introduction of a pandemic-capable strain is both (i) low, near its historical average, and (ii) constant over time. Neither seems likely. Although the process by which new pandemic strains emerge is poorly understood, the risk must increase with increasing encounters between livestock and humans, and populations of humans, pigs, and poultry have grown by an estimated 60%, 100-fold, and 1000-fold, respectively, in China alone since 1968 (7). Likewise, the past decade’s geographic spread of H5N1 influenza and other influenza strains in birds must increase the opportunities for encounters between H5N1-infected birds and humans (8).

We are disturbed by the implication from one commentator that our results should have been suppressed for fear of discouraging efforts at containment, particularly since we specifically advocate continued efforts at containment and suggest ways in which such efforts could be improved. Suppressing scientific findings or dissenting views more generally to achieve policy advocate continued efforts at containment and suggest ways in which such efforts could be suppressed for fear of discouraging efforts at containment, particularly since we specifically

We are disturbed by the implication from one commentator that our results should have been suppressed for fear of discouraging efforts at containment, particularly since we specifically advocate continued efforts at containment and suggest ways in which such efforts could be improved. Suppressing scientific findings or dissenting views more generally to achieve policy consensus is bad science and bad policy, for influenza (9) and in general (10).

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References
Reconsidering the Antiquity of Leprosy

LEPROSY HAS CLASSICALLY BEEN CONSIDERED a disease of evolutionarily recent times, with an epidemiology related to relatively high-density living. In their Report “On the origin of leprosy” (13 May 2005, p. 1040), M. Monot et al. propose a scenario in which leprosy was spread around the world during the dispersal of modern humans from Africa and by recent colonial movements. We welcome this innovative model but suggest that their data are equally compatible with a more recent origin and dispersal.

The basis of their Pleistocene dispersal model is that with a low rate of mutation among mycobacteria, the preferred phylogeny of the Mycobacterium leprae single nucleotide polymorphisms fits the dispersal of modern humans out of Africa. However, not only is there no paleopathological evidence for leprosy before the development of urban life (1), its appearance around the world shows sufficient chronological differentiation to be consistent with active spread during urbanization. M. leprae is an obligate pathogen (2) dependent on high levels of human contact to be maintained in a population (3). This suggests it was unlikely to have thrived during the Pleistocene, when human populations lived in highly mobile, low-density groups, under conditions of relative isolation (4, 5). Low host densities and the ecologically diverse geographic regions where M. leprae survives today indicate that mobility was the main factor determining the spread of the disease. Phylogenies should, therefore, be considered in the context of a post-Holocene pattern of dispersals associated with the appearance of higher density human populations. Finally, assessment of the coalescence of M. leprae strain sequences is dependent on both time and population size, and the expansion of human populations in the past 5000 years may be a critical part of the evolutionary history of the pathogen.

Relevant data on human migrations should be considered [see fig. 1; (6)]. Classical texts suggest that leprosy spread from the Indian subcontinent to Europe and the Middle East, possibly with the armies of Alexander the Great (7). The first phylogeny of Monot et al. suggests an East African origin. The second phylogeny suggests an Asian origin. If the origins and spread of M. leprae are prehistoric, an unlikely assumption, the first phylogeny is consistent with genomic analysis (8, 9) and some models of modern human dispersals (10). However, their second phylogeny is consistent with historical texts and is compatible with the patterns of movement, trade, and contact stretching back several millennia, associated with the rise of movements, trade, and contact stretching back several millennia, associated with the rise of

arly recent times, with an epidemiology related to relatively high-density living.

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References and Notes
6. SNPs in our figure are color-coded according to Monot et al.’s fig. 1b.

Species Diversity and Ecosystem Functioning

IN THEIR REPORT “NONRANDOM PROCESSES maintain diversity in tropical forests” (27 Jan., p. 527), C. Wills and colleagues provide strong
evidence that nonrandom processes play a key role in maintaining diversity in tropical forests, specifically that forest tree diversity increases as individuals age because of preferential survival by individuals of locally rare species. However, the implications are even greater than those proposed by Wills et al., as all three mechanisms supported by their results imply that species diversity increases ecosystem functioning.

First, the Janzen-Connell model (1, 2) predicts that species escape their specialist herbivores, predators, and pathogens when they are locally rare, whereas common species are more readily attacked. Losses of carbon and nutrients to natural enemies result in lower growth rates and thus lower primary productivity (3). Second, niche complementarity occurs when species exploit resources in different ways and results in more complete resource utilization and thus higher productivity (4) and has been shown to contribute to increased functioning with diversity (5, 6). In tropical forests, tree species may differ in their ability to acquire soil resources, resulting in more complete resource capture and thus higher productivity. Third, facilitation occurs when one species directly benefits another but experiences no harm (7) and has been shown to contribute to increases in ecosystem functioning with diversity (8, 9). In tropical forests, a tree species might fix nitrogen that becomes available to its neighbors. In this case, the tree’s neighbors will experience increased growth rates if nitrogen is limiting.

When any of these three nonrandom mechanisms are operating, species extinctions will result in a decrease in productivity due to increased losses to natural enemies, failure to fully utilize essential resources, or the loss of direct benefits of facilitation. In contrast, neutral models of species coexistence (10–12) assume species are functionally equivalent, and therefore ecosystem functioning will not be dependent on species diversity. Wills and colleagues provide strong circumstantial evidence that even in highly diverse tropical forests, biodiversity enhances ecosystem functioning.

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References

Response
Bunker and Naeem correctly identify the key result of our analyses, i.e., that local frequency-dependent processes contribute to the maintenance of diversity in tropical forests. The commentary on our Report by E. Pennisi (“Rare tree species thrive in local neighborhoods,” News of the Week, 27 Jan., p. 452) may have given readers the erroneous impression that plot-wide or forest-wide diversity increased during the census periods. Our results concerned multispecies cohorts of trees within small-scale quadrats (100 to 2500 m²) in which species-level diversity increased through time as the result of higher mortality of locally common species. This result does not conflict with the possibility that the local (quadrat) diversity of recruits (i.e., the individuals that set the bounds within which diversity may vary for a given cohort) fluctuates through time.

Bunker and Naeem also suggest that our results support the hypothesis that tropical tree diversity may be positively correlated with
“ecosystem functioning.” Even though our data and analyses do not directly address this important hypothesis, it is a testable idea. A positive relationship between biodiversity and productivity (or other ecosystem-level variables) would have important implications for tropical forest conservation.

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Increase in Foreign Grad Students

IN THE NEWS OF THE WEEK ARTICLE “FOREIGN grad students show renewed interest” (K. Unger, 31 Mar., p. 1845), university administrators seem to have overlooked possibly the most important reason for the recent increase in graduate school applications from foreign students. For many skilled foreigners, a change of the H-1B “work visa” quota system 2 years ago made it very difficult to obtain the necessary authorization to work in the United States. However, foreigners who hold a Master’s or Ph.D. degree from a U.S. school fall under a separate quota allotment, and thus it is far easier for them to obtain the necessary H-1B visa to work in the United States. In other words, many foreigners who want science or engineering jobs in this country no longer have the option of obtaining graduate degrees in their home countries. They are applying to graduate schools here in increasing numbers because they must obtain a graduate degree from the United States to have a reasonable chance of acquiring the necessary U.S. work visa without a certain delay of one or more years. It is perhaps ironic that raising the bar on granting work visas has had the side effect of increasing the number of foreign grad student applicants.

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Letters to the Editor

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FULL TEXT AT www.sciencemag.org/cgi/content/full/312/5775/848b

RESPONSE TO COMMENT ON “Evidence for Positive Epistasis in HIV-1”

Sebastian Bonhoeffer, Colombe Chappey, Neil T. Parkin, Jeannette M. Whitcomb, Christos J. Petropoulos

Wang et al. analyzed artificially biased data to show that our results can be explained by a bias against sequences with low fitness. We explicitly acknowledged this potential caveat in our original study. Showing that an artificially introduced bias can produce a spurious signal of positive epistasis does not demonstrate that such bias exists in our original data.

Full text at www.sciencemag.org/cgi/content/full/312/5775/848c

TECHNICAL COMMENT ABSTRACTS

COMMENT ON “Evidence for Positive Epistasis in HIV-1”

Kai Wang, John E. Mittler, Ram Samudrala

Bonhoeffer et al. (Reports, 26 November 2004, p. 1547) presented evidence for positive epistasis in a clinical data set of HIV-1 mutants and corresponding fitness values. We demonstrate that biases in the original and simulated data sets may lead to erroneous evidence for epistasis. More rigorous statistical tests must be used to account for such biases before one can infer epistasis.

Full text at www.sciencemag.org/cgi/content/full/312/5775/848b

REFERENCE FOR TECHNICAL COMMENT ABSTRACTS

Wang et al. analyzed artificially biased data to show that our results can be explained by a bias against sequences with low fitness. We explicitly acknowledged this potential caveat in our original study. Showing that an artificially introduced bias can produce a spurious signal of positive epistasis does not demonstrate that such bias exists in our original data.

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