

NEWS AND VIEWS

PERSPECTIVE

West Nile virus may have hitched a ride across the Western United States on *Culex tarsalis* mosquitoes

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West Nile virus spread rapidly from east to west across North America, despite the north-south migratory flyways of its avian hosts. In this issue, Venkatesan & Rasgon (2010) present new data on the population genetics of *Culex tarsalis*, the dominant West Nile virus vector in the Western United States, suggesting that patterns of mosquito gene flow may better reflect the virus's expansion from the Midwest to the Pacific than patterns of bird movement. These findings suggest a more significant role for vector dispersal in arboviral range expansion than has previously been appreciated, and they highlight the value of molecular genetic studies of insect vector populations for understanding epidemiology and disease ecology.

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Public perception of most emerging infections tends to follow a predictable trajectory, beginning with surprise and panic, progressing to intense worry, and settling eventually on nervous acceptance. West Nile virus is no exception. This virus, still the world's most widely distributed arbovirus ('arthropod-borne virus', an ecological rather than phylogenetic classification) (Kramer *et al.* 2008), seems to have lost its 'au courant' vibe, overshadowed by newer and more frightening infectious threats such as swine flu and Anthrax. As the paper by Venkatesan & Rasgon (2010) in this issue of *Molecular Ecology* demonstrates, however, there's still a lot to learn from West Nile virus, even in our own back yard.

The rapid spread of West Nile virus from New York in 1999 to the West Coast of North America by 2003 still presents somewhat of a paradox for disease ecologists. Before

it jumped the Pond, West Nile virus was well known for its sporadic appearances in Europe and the Middle East, with recent notable outbreaks in Romania and Russia (Weaver & Reisen 2010). These localized epidemics made perfect sense in light of the migratory habits of Old World birds, which annually fly northward from such tropical havens as the West Nile District of Uganda, where the virus was first isolated from a febrile woman in 1937 (Smithburn *et al.* 1940). Since West Nile virus is maintained through transmission cycles involving birds and mosquitoes, it stands to reason that the right bird migrating to the right place at the right time could easily have sparked these Old-World epidemics. We thought we had it figured out.

As any amateur ornithologist knows, however, birds in New World, like the Old, tend to migrate along north-south corridors. How, then, did West Nile virus manage to move so rapidly from the east to the west across its new North American range? Herein lies the paradox. The standard solution has been to postulate a fair degree of 'permeability' in North America's avian flyways, and to play up the role of non-migratory birds in spreading West Nile from east to west through a series of random, seasonal, short-distance hops. Indeed, this process undoubtedly occurs and is important locally, but one is left with a sneaking suspicion that other forces might also be at work, especially on larger spatial scales. After all, West Nile virus moved from the Midwest to the Pacific more quickly than Lewis & Clark, and approximately as rapidly from New York to the west coast as it did in the expected southward direction to the Caribbean and Latin America (Komar & Clark 2006).

Venkatesan & Rasgon (2010) offer an intriguing alternative hypothesis for the rapid expansion of West Nile virus across its western range by reminding us that birds are not the only key players in the virus's transmission cycle with wings. Mosquitoes can also fly, and there are an awful lot of them around at certain times of the year. In the Western United States, *Culex tarsalis* is the dominant mosquito vector for West Nile virus (Fig. 1). By genotyping 12 microsatellite loci in *C. tarsalis* from 20 populations spanning the Upper Midwest to California, the investigators infer the population genetic structure of this important West Nile virus vector. Their results provide compelling evidence that the genetically inferred movement patterns of mosquitoes closely parallel the epidemic spread of West Nile virus across the Western United States. Specifically, the virus appears to have moved quickly within genetically defined *C. tarsalis* clusters but haltingly between them.

According to Venkatesan and Rasgon's analyses, three genetically distinguishable but internally genetically homogeneous *C. tarsalis* populations currently exist: one in the

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Fig. 1 The dominant West Nile virus vector in the Western United States, *Culex tarsalis* (photo credit: Douglas Norris).

Midwest and Great Plains, one ranging from the montane West to the West Coast, and one in the Sonoran Desert. The present-day distribution of these populations appears to result from a complex and imperfectly predictive set of historic phylogeographic barriers to dispersal. Importantly, some populations of *C. tarsalis* at the borders of these populations show evidence of genetic introgression, indicating transition zones of substantial present-day gene flow. This combination of intra-population panmixia and inter-population genetic semi-permeability appears more consistent with the westward expansion of West Nile virus than the 'random bird dispersal' hypothesis. In particular, *C. tarsalis* population genetic structure helps explain the virus's unexpectedly rapid movement across the Great Plains in 2002 but its subsequent saltatory movements into the western-most reaches of its range in 2003 and 2004. To provide a mechanistic explanation, the investigators take pains to point out that *C. tarsalis* is more vagile an organism than one might expect, with daily flight ranges up to 4 km in quest of food and mates, and that weather events might also contribute to its long-distance dispersal. The answer to the question of West Nile virus's westward expansion might, therefore, very well be blowing in the wind.

Venkatesan and Rasgon's results are unlikely to put to rest the issue of whether hosts or vectors best explain the spread of West Nile virus, largely due to the 'chicken-and-egg' problem inherent in the study any infection carried

alternately by hematophagous arthropods and their food. However, their study should convince even the most guarded skeptic of the benefits of looking at both sides of the arboviral equation when trying to understand the emergence of this type of pathogen. More generally, Venkatesan and Rasgon's study is a fine example of the application of molecular genetic methods to a thorny real-world problem in epidemiology and disease ecology. It will undoubtedly motivate others to apply similar approaches to different mosquito populations, which should eventually yield a general picture of the vectorial forces that facilitated the expansion of West Nile virus across the entirety of its New World range. What, for example, might the role of mosquito dispersal have been in spreading West Nile virus across the Northeastern USA where *Culex pipiens* dominates? The resulting insights into the comparative phylogeography of mosquito vectors might also make us better prepared for the coming of other arboviral plagues, such as Dengue and Chikungunya, either of which would almost certainly engender a greater degree of lasting public concern than West Nile virus should they become established. Until then, we should take a lesson from these investigators and keep reminding ourselves that in the realm of arboviral disease, little things mean a lot.

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