Researchers discover how 'cryptic' connections in disease transmission influence epidemics

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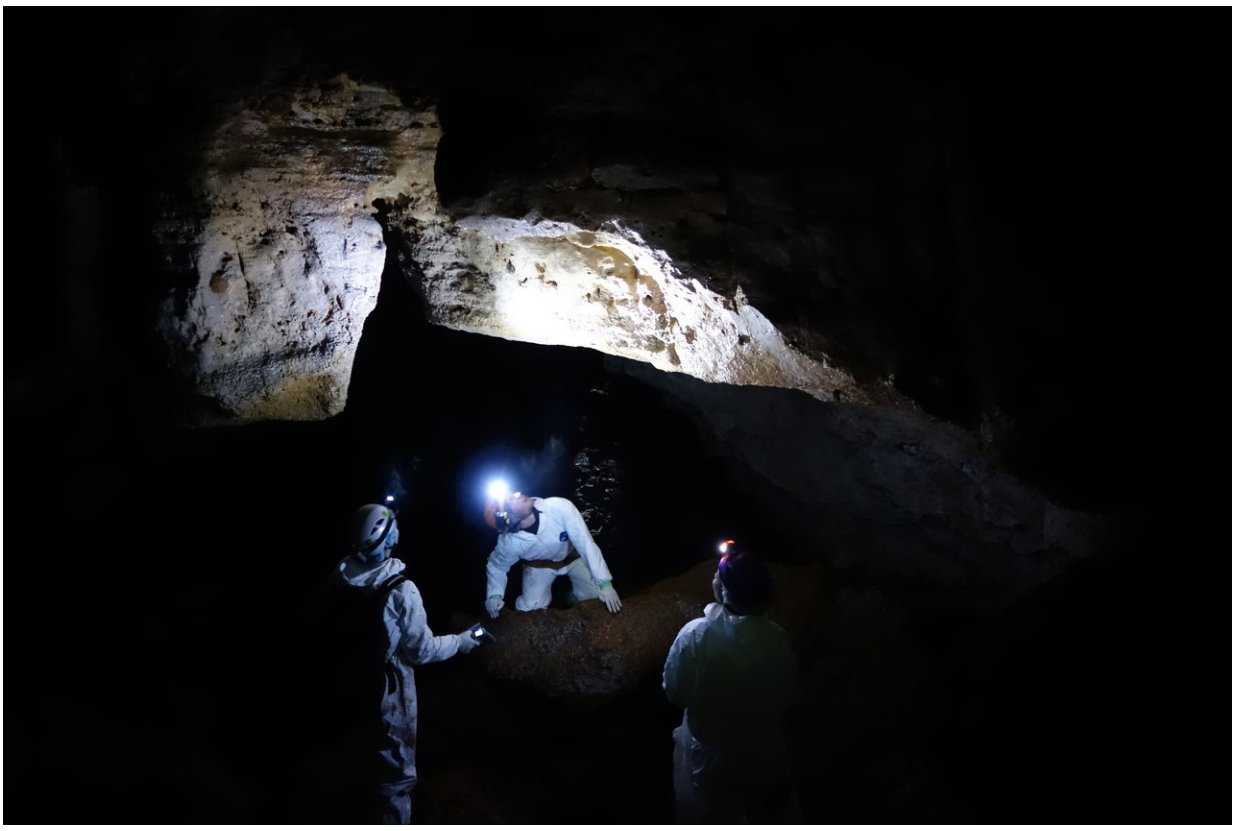


Researchers Kate Langwig, Joseph Hoyt, and Jennifer Redell tagged bats with fluorescent dust and observed their movements to track hidden connections that can spread disease within and between bat species. Credit: Virginia Tech

Diseases have repeatedly spilled over from wildlife to humans, causing local to global epidemics, such as HIV/AIDS, Ebola, SARS, and Nipah.

A new study by researchers of disease transmission in bats has broad implications for understanding hidden or "cryptic" connections that can spread diseases between species and lead to large-scale outbreaks.

By dusting bats with a fluorescent powder that glows under ultraviolet light, Virginia Tech researchers Joseph Hoyt and Kate Langwig were able to trace the dynamics of disease transmission in bat species that have been devastated by white-nose syndrome, a deadly fungal disease that has killed 6.7 million bats in North America since 2006.

Their findings were recently published in the journal *Nature*.

"These results uncovered and quantified connections, both within and among species, that we never knew about before," said first author Joseph Hoyt, who led the study as a UC Santa Cruz graduate student and completed the analyses at Virginia Tech as a research scientist in the Department of Biological Sciences in the College of Science.

"We had been seeing explosive epidemics where an entire bat population would become infected with white-nose syndrome within a month or two, and it was a mystery as to how that was happening. We are now able to more accurately explain and track the spread of white-nose syndrome, and our study has strong implications for predicting other epidemics," Hoyt said.

When we think about who we might get sick from, we tend to think of our social groups: family, friends, and co-workers. But, we forget about that brief interaction with an employee at the DMV, a barista at a coffee shop, or shared airspace on public transportation. People are aware of these interactions, but not how important they are to the spread of

epidemics. In the past, these types of hidden interactions have been poorly understood because they are so difficult to quantify.

Second author on the study, Kate Langwig, an assistant professor in the Department of Biological Sciences at Virginia Tech, said this study shows that infrequent and indirect connections, also called "cryptic" connections, among individuals play a far larger role in the transmission of disease than was previously understood.

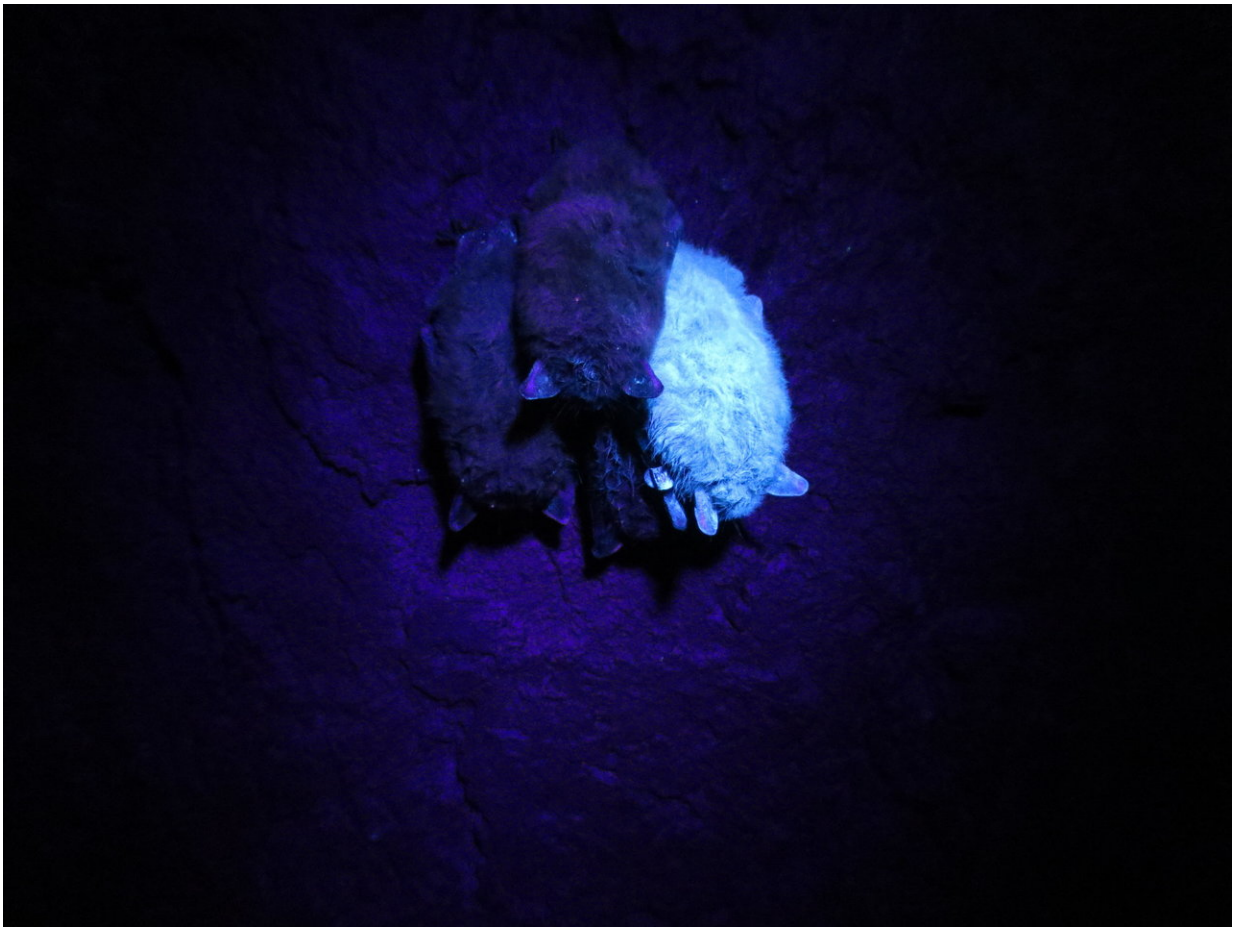
"Cryptic connections are essentially pathways or connections between individuals that we wouldn't normally be able to estimate or observe. They have largely been ignored by researchers in the past, but this study quantifies their importance. Our study creates an integrated model of social group connections and cryptic connections," said Langwig, an affiliated faculty member of the Global Change Center, an arm of the Fralin Life Science Institute.

Coauthor A. Marm Kilpatrick, associate professor of ecology and evolutionary biology at UC Santa Cruz, noted that spillover events, when pathogens spread from wild animals to human populations, tend to occur through these kinds of cryptic connections. "We don't normally appreciate how important they are except retrospectively, when we investigate outbreaks of diseases like Ebola or SARS," he said.

"Our study has compelling implications that will allow researchers to track seemingly random or indirect connections in wildlife that may spill over to human populations," said Langwig.

The fluorescent dust used in this study proved to be highly effective at revealing cryptic connections among the bats. The researchers conducted the study at eight hibernation sites, mostly abandoned mine tunnels, in the upper Midwest. Each site had as many as four species of bats using it. At the start of the study, the pathogen causing white-nose syndrome

had not yet reached these populations.



Little brown bat covered in UVF dust roosting in a group with other little brown bats. Credit: Joe Hoyt and Kate Langwig

The researchers first surveyed the bats and characterized their social networks, measuring direct physical contacts among bats hibernating together in groups, as well as additional connections made by bats moving between groups. Then, they applied the fluorescent dust to several bats in early winter, using a different color for each individual bat. In late winter, the researchers returned to see where each color of

fluorescent dust ended up.

"We amassed huge data sets for every single bat in each population. We characterized the bats' social groups, and also used the fluorescent dust to track their movements and contacts," said Langwig.

The researchers found that "the spread of the dust mirrors how the fungal pathogen spreads, so we can see if a bat deposits dust somewhere in the environment and another bat passes through and picks it up. It also reveals infrequent direct contacts that we would not normally observe," said Hoyt.

Researchers were able to track cryptic connections between bats by coating individual bats, such as this tri-colored bat, with a dust that is fluorescent under ultraviolet light ("UVF dust"). Credit: Joseph Hoyt

The fungal pathogen that causes white-nose syndrome arrived in the area after the fluorescent dust studies were conducted, and the researchers also tracked its spread at each site. They found that the actual transmission dynamics of the disease were better explained by the sum of all the connections revealed in the dust studies than by just using the hibernation social groups.

"We were able to explain the actual invasion of the pathogen much better by including those cryptic connections, and they were even more important for explaining transmission between species than for transmission within species," Hoyt said.

One of the puzzling features of white-nose syndrome is its ability to spread through a community of bats during the winter, when the animals are hibernating 99.5 percent of the time. They rouse from hibernation only very briefly every two to three weeks. Yet the dust studies showed that they move around enough to have many more connections than can be observed in their hibernation groups.

Most striking were the cryptic connections revealed for one species, the northern long-eared bat, which roosts by itself, not in groups. Although classical theory would predict low infection rates for this solitary species, it has been hard hit by white-nose syndrome.

"When we put fluorescent dust on the northern long-eared bat, it would show up on other species that we had never seen them interact with. We

would never have predicted that the infection could spread by that route," Hoyt said.

The researchers discovered that a different solitary species, the tri-colored bat, has a lower infection rate and showed less evidence of cryptic connections with other bats, but did transfer dust to surfaces in the sites where it roosts. "We found that the tri-colored bat is much more spatially segregated. It's not that it doesn't rouse and crawl around, it just does so in a range that has less overlap with other bats—it appears to be more territorial in its use of space," Hoyt said.

Unfortunately for bats, the spores of the fungal pathogen that causes white-nose syndrome stay in the environment and remain infectious for years. Once the walls and ceiling of a cave have been contaminated with the spores, bats using the site for hibernation will be exposed to infections year after year.

White-nose syndrome is considered one of the worst wildlife diseases in modern times, having killed millions of bats across North America.

But white-nose syndrome does not appear to pose a risk to human health. It is caused by the fungus Pseudogymnoascus destructans, which grows optimally at low temperatures. The United States Geological Survey said, "Thousands of people have visited affected caves and mines since white-nose syndrome was first observed, and there have been no reported human illnesses attributable to white-nose syndrome. We are still learning about the disease, but we know of no risk to humans from contact with white nose-affected bats."

More information: Joseph R. Hoyt et al, Cryptic connections illuminate pathogen transmission within community networks, *Nature* (2018). DOI: 10.1038/s41586-018-0720-z

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