Medical Xpress

# Hidden infections crucial to understanding, controlling disease outbreaks

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(PhysOrg.com) -- Scientists and news organizations typically focus on the number of dead and gravely ill during epidemics, but research at the University of Michigan suggests that less dramatic, mild infections lurking in large numbers of people are the key to understanding cycles of at least one potentially fatal infectious disease: cholera.

Using a model developed with new statistical methods, U-M researchers and their collaborators came up with results that challenge longstanding assumptions about the disease and strategies for preventing it.

Their findings appear in the Aug. 14 issue of the journal *Nature.*

The goal of the study was to develop a model that would explain puzzling patterns seen in 50 years of cholera death records from 26 districts in Bengal, cholera's "native habitat."

"In that region, we see two cholera seasons per year, with peaks in spring and fall," said assistant professor of ecology and evolutionary biology Aaron King, the study's lead author. In addition, longer-term ups and downs can be seen over periods of three to five years, with many cholera cases reported during some periods and few during others.

Explanations have been proposed for both the seasonal and multi-year cycles, and King and coworkers wanted to test the validity of those and other possible scenarios. In particular, they wanted to explore the impact of infection-induced immunity on the dynamics of cholera outbreaks.

It's surprisingly hard to get really sick with cholera, an intestinal infection that causes diarrhea, vomiting, and leg cramps. The bacterium that causes the illness, Vibrio cholerae, lives in surface waters, and in areas where sanitation is poor, food and water are commonly contaminated with the bug. But it takes 100 billion bacteria to cause severe illness when ingested with water; 100 million when taken in with food (which protects the bugs from stomach acid). As a result, in areas like Bengal where exposure is high, lots of people are walking around infected, but not ill.

"The consequences of that have not been clear," King said. "Are those mild cases infecting other people? What are the immunological consequences—how long are people with mild infections protected against re-infection?"

To answer these and other questions, King and coworkers developed a series of models that incorporated known or suspected mechanisms of disease transmission and immunity and then looked to see which model best fit the actual data.

"What we found was a real surprise," said King, who has joint appointments in the Department of Mathematics and the Center for the Study of Complex Systems. "Our analysis showed that the best explanation for the patterns seen in the data is that many more people are being exposed to the bacteria than are getting serious infections or dying, and that individuals with mild infections are losing their immunity quite quickly, in a matter of weeks or months."

The model revealed that as an epidemic spreads, many people develop this short-term immunity. Once large numbers of people are immune, the epidemic comes to a halt. "But before the year is out, they're susceptible again," and the cycle starts all over, King said.

The quick waning of immunity found in this study contrasts with the widely-held belief—based only on studies of people with severe cholera, not on those with mild cases—that immunity to reinfection lasts at least three and possibly as long as ten years. The most effective cholera vaccines, by contrast, produce an immunity that lasts only a few months. The new model raises the possibility that current vaccines could be given at the beginning of cholera season to squelch an incipient epidemic.

"In order to understand how to control this disease, we really need to understand what's going on in the bulk of cases, not just what's happening in the most severe," King said.

The researchers are using similar models to explore patterns seen in other infectious diseases, such as malaria and whooping cough.

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