Medical Xpress

Key to controlling drug resistant bacteria

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When you check into a hospital, the odds are one in ten that you will become infected with a strain of antibiotic-resistant bacteria as a result of your stay. That is because the problem of drug-resistance has become endemic in today's hospitals despite the best efforts of the medical profession. In the United States alone this currently causes about 100,000 deaths per year.

Now, a sophisticated new mathematical model has identified what may be the key to getting this growing health problem under control: Changing the way that antibiotics are prescribed and administered.

"We have developed the mathematical model in order to identify the key factors that contribute to this problem and to estimate the effectiveness of different types of preventative measures in typical hospital settings," says Vanderbilt mathematician Glenn F. Webb, who described the results at a presentation at the annual meeting of the American Association for the Advancement of Science on Feb. 17 in Boston.

"According to our analysis, the most effective way to combat this growing problem is to minimize the use of antibiotics," he says "It is no secret that antibiotics are overused in hospitals. How to optimize its administration is a difficult issue. But the excessive use of antibiotics, which may benefit individual patients, is creating a serious problem for the general patient community."

For example, the model calculates that in a hospital where antibiotic treatments are begun on average three days after diagnosis and continued for 18 days, the number of cross-infections by resistant bacteria (that is, cases where patients are accidentally infected by health care workers who have been exposed to these bacteria while treating other patients) waxes and wanes but never disappears completely. However, when antibiotic treatments are begun on the day of diagnosis and continued for eight days, the cross-infection rate drops to nearly zero within 250 days.

The model was developed by an interdisciplinary team of researchers. In addition to Webb, the contributors are Erika M.C. D'Agata at Harvard University's Beth Israel Deaconess Medical Center, Pierre Magal and Damien Olivier at the Université du Havre in France and Shigui Ruan at the University of Miami, Coral Gables. It is described in the paper "Modeling antibiotic resistance in hospitals: The impact of minimizing treatment duration" published in the *Journal of Theoretical Biology* in December 2007.

The researchers constructed a two-level model: (1) the bacterial level where non-resistant and resistant strains are produced in the bodies of individual patients and (2) the patient level where susceptible patients are cross-infected by health care workers who have become contaminated by contact with infected patients.

At the bacterial level, the model takes an ecological approach that describes the competition between non-resistant and resistant strains of infectious bacteria. In untreated patients, non-resistant bacteria have a competitive advantage over the resistant strains that keeps the numbers of resistant bacteria extremely low. During treatment, however, the antibiotics kill off the normal bacteria and that allows the resistant strain to take over. As a result, a patient on antibiotics becomes a potential source of infection with resistant bacteria. This continues as long as the treatment lasts. After the treatment is ended, the population of non-resistant bacteria of all types rebounds and the population of resistant bacteria begins to drop until the patient ceases acting as a source.

In the model, what is going on at the bacteria level is linked with the second level which simulates the interactions between patients and hospital care workers who carry the bacteria from patient to patient. In order to account for individual variations in behavior, the researchers developed an "individual based model" that views patients and workers as independent agents. They then used a method called a Monte Carlo simulation to simulate the spread of the different strains of bacteria under various conditions by generating thousands of probable scenarios using random values for uncertain quantities.

The mathematical analysis reveals that the "optimal strategy" for controlling hospital epidemics is to start antibiotic treatments as soon as possible and administer the drugs for the shortest possible time. Beginning treatment as early as possible is the most effective in knocking down the population of the non-resistant bacteria that is causing a patient's initial illness and minimizing the length of treatment shortens the length of time when each patient acts as a source of infection.

Currently, hospitals are concentrating on improving hygiene to combat this problem. The model confirms that improvements in hygiene can substantially reduce the frequency of cross-infections. The model also demonstrates that hygiene alone may not be sufficient and improving the way antibiotics are administered will be necessary to eliminate the problem of resistant bacteria.

"Our results point out an urgent need for more research into the issue of the best timing for the administration of antibiotics and how to reduce its misuse and overuse," says Webb.

Source: Vanderbilt University