Klebsiella pneumoniae 'superbug' is being studied

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University at Buffalo researchers are expressing concern about a new, under-recognized, much more potent variant of a common bacterium that has surfaced in the U.S.

"Historically, in Western countries, classical strains of Klebsiella pneumoniae have caused infections mostly in sick, hospitalized patients whose host defense systems are compromised," says Thomas Russo, MD, professor in the Department of Medicine at the UB School of Medicine and Biomedical Sciences and head of its Infectious Disease Division.

"But in the last 10 to 15 years, a new variant of it has begun causing community-acquired infection in young, healthy individuals," he says. "This variant causes serious, life-threatening, invasive infections and is able to spread to other organs from the initial site of infection."

Perhaps most important, says Russo, these hypervirulent strains of *Klebsiella pneumoniae* have the potential to become highly resistant to antibiotics, similar to *Escherichia coli* and classical *Klebsiella pneumoniae*.

"These hypervirulent strains are the next 'superbugs' - in-waiting," he says. "If they become resistant to antibiotics, they will become difficult, if not impossible to treat."

With recent funding from the National Institutes of Health under a

program to fund high-risk, high-reward research, Russo and his UB colleagues are studying the microbiology of the new variant of *Klebsiella pneumoniae* in an effort to identify the genes that make it hypervirulent so they can figure out how to stop it in its tracks.

"Infections due to highly resistant bacteria are becoming increasingly problematic," says Russo. "We are continually threatened by a 'post-antibiotic' era. The combination of a bacterium that is both highly virulent and resistant to antimicrobials is double-trouble."

The researchers' concern stems from the fact that classical *Klebsiella pneumoniae* is one of the bacterial species that can easily acquire mobile genetic units, called plasmids, that contain multiple genes that confer high levels of antimicrobial resistance.

"That's in part why we're concerned," says Russo. "We know that this bacterium has the potential to acquire these plasmids and it almost certainly will."

He notes that most bacteria that have proven to be resistant to most or all of the drugs currently available do not usually infect healthy members of the community.

"What is alarming about the hypervirulent *Klebsiella pneumoniae* is that they do possess the potential to infect healthy people," says Russo. "If this hypervirulent bacterium also becomes highly resistant to antimicrobials, we will have a significant problem to manage. We hope that our research and that of others can prevent this possibility."

While the new hypervirulent variant was first seen exclusively in in the Pacific Rim, it has now been found in several cities in North America, including Buffalo, and in Europe, Canada, Israel and South Africa as well. The UB researchers characterize it as "under-recognized" both by

physicians and microbiology laboratories.

The disease most commonly presents as a liver abscess, which is not typical for otherwise healthy patients.

"This new variant presents with unique and scary features: first is its tendency to infect young, healthy people in the community and the second is its unique propensity for metastatic spread to other parts of the body," says Russo. "It spreads to sites beyond the initial source of the infection, such as the lungs, the central nervous system and the eye, potentially causing loss of vision. If infection spreads to the brain, there can be brain damage as well. Between 10 and 30 percent of cases are fatal."

In Buffalo, this hypervirulent variant of *Klebsiella pneumoniae* was identified in an otherwise healthy, young person several years ago. The patient, who was in his 20s, was hospitalized for several months before making a full recovery. Similar cases are causing concern throughout the international infectious disease community.

At the moment, most cases of hypervirulent *Klebsiella pneumoniae* resolve if treated aggressively with antibiotics and drainage of abscesses; however, some infections, despite optimal treatment, result in a persistent morbidity or death, Russo says.

He notes that the potential for the bug to acquire drug resistance is adding a sense of urgency to the research.

Russo says that microbiology labs should be aware that an important characteristic of these hypervirulent strains (also known as hypermucoviscous strains) is that when bacterial colonies grown on a solid surface in the laboratory are stretched by a common microbiology tool, called an inoculation loop, they form a viscous "string" greater than

5 millimeters in length.

Russo's team at UB is now beginning to develop a clearer picture of this formidable bacterial opponent.

In November, he and his colleagues published a *PLoS ONE* paper that showed that hypervirulent *Klebsiella pneumoniae* acquires iron more efficiently than the usual strains of K. pneumoniae.

"With the NIH grant, we hope to further elucidate the precise details of the bacterial factors that are responsible for hypervirulent *Klebsiella pneumoniae* acquiring iron so much more efficiently," he says. "The goal of this line of research is that these iron-acquisition factors possessed by hypervirulent *Klebsiella pneumoniae* will then lend themselves as therapeutic or vaccine targets so that we can better treat or prevent infection."

Provided by University at Buffalo