# Lab-on-a-chip could speed up treatment of drug-resistant pneumonia

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The emergency treatment of drug-resistant infections with targeted antibiotics is often delayed by the need to identify bacterial strains by growing them in culture first. At this week's AVS 53rd International Symposium & Exhibition in San Francisco, Michael Lochhead, a bioengineer at the Denver biotechnology company Accelr8, described a new lab-on-a-chip that can identify single bacterial cells for the most common cases of drug-resistant pneumonia, cutting down the wait from days to hours. The technology could also help in the development of new drugs.

The constant bombardment by antibiotics and disinfectants has bred strains of super-bugs that only respond to very specific drugs. These super-bugs often lurk in hospitals, where patients with weakened immune systems can pick up obstinate, life-threatening infections such as pneumonia. "When you get pneumonia in the hospital, you're much more likely to get a resistant strain," Lochhead said. "It's an emerging public-health disaster."

The most acute cases are admitted into intensive care units, where doctors have just days, if not hours, to save the patients' lives, Lochhead said. But reliably identifying the bacterial strain that's causing the infection traditionally requires growing the bugs in culture first, a procedure that can take two to three days. Meanwhile, doctors often have no other option than to start stopgap treatments with broad-spectrum antibiotics.

The Accelr8 technology is a "microfluidic" lab-on-a-chip designed to manipulate and analyze bacteria without growing them first. Samples are first washed out of the patient's lungs with saline solution in a procedure called bronchoalveolar lavage. The organisms are then separated, suspended in a specially designed fluid, and pumped into the chip.

Inside the chip, the bacteria flow into several different compartments -- eight in the current version of the chip -- and are made to stick to a bacteria-friendly surface using an electric current. Antibodies then flow in. The antibodies bind specifically to certain strains of bacteria, and mark them with fluorescent dyes of different colors. The dyes color-code cells from known strains. A microscope monitors the viable cells -- those that are still reproducing -- and the rate at which they duplicate helps to identify their species.

In the next step, different antibiotics are pumped into the chambers. If the cells in a chamber stop reproducing, that indicates that a certain drug is likely to be effective at fighting the infection. The death of the bugs is confirmed by checking with a special dye.

Once the bacteria-carrying fluid is injected into the chip, the entire procedure is automatic-- including the counting of fluorescent-marked cells, which is done by a computer -- and takes less than eight hours.

One of the most difficult steps was to design a surface that would be hospitable to the bacteria but that would at the same time keep the antibodies and antibiotics from sticking to it, Lochhead said. While Accelr8 is working on finding a "universal" material that will allow virtually all pathogenic bacteria to stick to it, the company has so far focused on nine bacterial species that cause most of the cases of drug-resistant pneumonia, including Staphylococcus aureus (staph), Pseudomonas aeruginosa, Klebsiella pneumoniae, and Escherichia coli (E. coli). "If we can characterize the nine panel organisms, we'll cover 80

to 90 percent of hospital-acquired pneumonia cases," Lochhead said.

The company also hopes to apply the technology not just to identifying known strains but also to testing the efficacy of new drugs, or of existing drugs on unknown strains. "Even if you don't know the identity of an organism, if you know which drug works, it's still useful," Lochhead says.

Accelr8, a former software company that refashioned itself into a biotechnology company, plans to place development instruments in collaborating clinical laboratories within a year.

Paper: "Microfluidic Devices That Capture Bacteria for Growth and Kill Analysis," Tuesday, November 14, 2006, 9:40am, Room 2001, AVS 53rd International Symposium & Exhibition, San Francisco, CA, abstract at www.avssymposium.org/paper.asp?abstractID=199

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