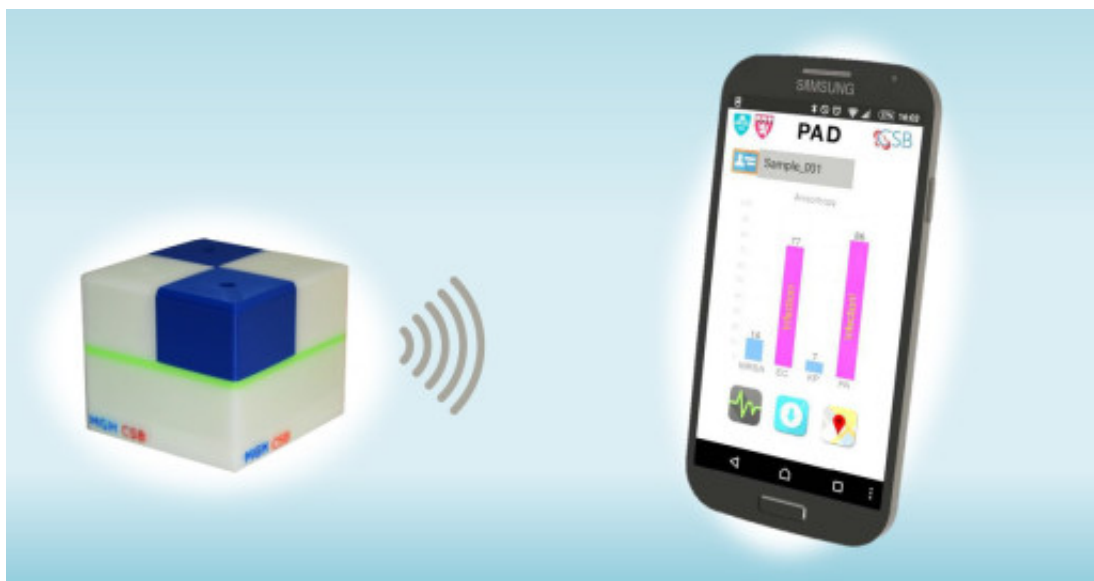


Portable System Uses Light to Diagnose Bacterial Infections Faster



Caption: PAD system. Left, four optical testing cubes (blue and white) stacked on the electronic base station (white with initials); right, a smartphone with a special app to receive test results transmitted by the electronic base station.

Credit: Park et al. *Sci. Adv.* 2016

Every year, hundreds of thousands of Americans acquire potentially life-threatening bacterial infections while in the hospital, nursing home, or other health-care settings [1]. Such infections can be caused by a variety of bacteria, which may respond quite differently to different antibiotics. To match a patient with the most appropriate antibiotic therapy, it's crucial to determine as quickly as possible what type of bacteria is causing his or her infection. In an effort to improve that process, an NIH-funded team is working to develop a point-of-care system and smartphone app aimed at diagnosing bacterial infections in a faster, more cost-effective manner.

The portable new system, described recently in the journal *Science Advances*, uses a novel light-based method for detecting telltale genetic sequences from bacteria in bodily fluids, such as blood, urine, or drainage from a skin abscess. Testing takes place within small, optical cubes that, when placed on an electronic base station, deliver test results within a couple of hours via a simple readout sent directly to a smartphone [2]. When the system was tested on clinical samples from a small number of hospitalized patients, researchers found that not only did it diagnose bacterial infections about as accurately and more swiftly than current methods, but it was also cheaper. This new system can potentially also be used to test for the presence of antibiotic-resistant bacteria and contamination of medical devices.

The traditional method for diagnosing bacterial infections involves spreading patient

samples on nutrient agar in Petri dishes and waiting for up to several days to see what grows. Genetic approaches have also become more popular in the last decade, since every organism has a unique DNA and RNA code. But genetic tests tend to cost more than culture-based tests, and are generally only available in specialized hospital laboratories. In the new study, the team—led by Hakho Lee and Ralph Weissleder at Massachusetts General Hospital and Harvard Medical School, Boston—set out to design a more mobile system for rapid and accurate genetic identification of bacterial infections in patient samples.

The result of their efforts is a prototype system called PAD (short for Polarization Anisotropy Diagnostics). It's based on detecting light signals, not growing anything. Here's how it works: A sample, such as fluid from an infection, is obtained, and genetic material (usually RNA) from the bacteria in the sample is extracted into a small, disposable plastic cartridge and amplified.

The genetic material is then loaded into one of the plastic cubes, measuring about two-by-two centimeters. Also loaded into the cube is an all-in-one "master mix." It contains DNA probes designed to detect genetic sequences that uniquely define a disease-causing bacterium, as well as a reporter probe attached to a fluorescent tag to generate the light signal. When a sample with copies of a target bacterial sequence is detected, the light signal is measured and sent to the electronic base station, where it gets digitized and transmitted to a smartphone with a special PAD app. The app converts the data into an easy-to-read report, complete with a time stamp and global positional coordinates! Total testing time: Under two hours.

The PAD test is inexpensive at about \$2 per test. (For comparison, other genetic methods for identifying bacteria cost about \$10 per test.) It's also sensitive enough to detect a single bacterium in a sample. Importantly, since PAD is based on detection of specific RNA sequences, it can potentially be used to determine not only what kind of bacteria are in a sample, but also whether those bacteria carry genes that would allow them to resist antibiotic treatment.

Their current PAD prototype includes an electronic base station that holds up to four optical cubes, to enable testing of four patient samples at once. Lee says they plan to expand this system for simultaneous testing of up to 16 samples. The researchers expect with further optimization that the testing time can be reduced to under an hour.

While they've demonstrated their device for identifying five types of bacteria, the Harvard team has already developed a library of probes to detect 35 different species along with genetic factors that relate to the bacteria's virulence and antibiotic resistance. In addition to its diagnostic application, the researchers also foresee uses for PAD in detecting bacterial contamination of medical devices, hospital rooms, and labs.

The rise of antibiotic resistant bacteria is a particularly urgent public health concern. There's a critical need for new and better tools for detecting bacterial infections and their resistance to particular antibiotic treatments early. This new technology, and others like it, provide hope that we can win this important battle.

References:

[1] [Health care associated infections](#). Centers for Disease Control and Prevention. 2 March 2016.

[2] [Rapid identification of health care-associated infections with an integrated fluorescence anisotropy system](#). Park KS, Huang C-H, Lee K, Yoo Y-E, Castro CM, Weissleder R, Lee H. Sci. Adv. 2016 May 6;2(5)

Links:

[National Strategy for Combating Antibiotic-Resistant Bacteria](#) (The White House)

[Hakho Lee Lab](#) (Harvard Medical School, Boston, MA)

[Ralph Weissleder Lab](#) (Harvard Medical School, Boston, MA)

NIH Support: National Heart, Lung, and Blood Institute; National Institute of Biomedical Imaging and Bioengineering; National Cancer Institute