Next-generation genetics offer new way to combat hospital infections

Hospital infections are a huge public health problem. For the United States in 2011, about 722,000 infections occurred that were brought on during a hospital stay, according to the Centers for Disease Control and Prevention (CDC). These infections are often severe, even fatal, and include pneumonia, surgery site infections, urinary tract infections, and gastrointestinal illness. But lately the situation has gotten worse, as more and more infections are caused by bacteria that have become very good at resisting antibiotics.

The number of these “HAIs” (short for “hospital acquired infection”) has been decreasing, as more screening efforts detect more bacteria, and the use of antibiotics has become more controlled. But 722,000 infections is still a lot, and, it turns out, newer genetics techniques have shown how much more we have to learn about how these infections arise, what causes them, and what the best methods are to combat them.

Usually, when such outbreaks occur and they get public notice, news coverage (and even health remedies) follows a pretty simple pattern: Somebody gets sick, somebody else gets sick, a sample is taken and a bacterium (assuming it’s that) is isolated. Then, hospital staff tries to identify and decontaminate the possible source. Too often, though, the isolation procedure doesn’t cover all bacteria, and a single source isn’t the sole cause of the outbreak.

Headlines declare an epidemic

When antibiotic-resistance and HAIs first started getting attention, early news headlines pointed to alleged shoddy hygiene practices behind the growth of one particular resistant microbe, the bacterium MRSA, or methicillin resistant *Staphylococus aureus*. In 2008, the *Seattle Times* crunched some numbers and found high rates of infection from MRSA. This and other stories introduced the idea of the “superbug” in hospitals to the public:

> Many people first learned about the germ last fall when the federal Centers for Disease Control and Prevention set off a media frenzy with its announcement that invasive MRSA infections claim at least 18,000 lives a year, more than AIDS. But MRSA has been quietly killing for decades. And all along, there has been a simple diagnostic test that could have saved countless lives.

More recent coverage tends to follow a formula, similar to an Associated Press/Fox News story about a mold “outbreak” of four people at the University of Pittsburgh Medical Center (UPMC). The formula usually shows a number of similar infections, at least one death (or a lot of sickness), and the search for a single pathogen in a section of the hospital:

> Four organ transplant patients who developed a mold infection at UPMC likely got it from time spent in a “negative pressure” room normally reserved for those who already had

> infections…DuVall and his wife, Karen, had filed a lawsuit in Allegheny County last month against UPMC Presbyterian, alleging that the hospital recklessly housed him in a room that made him more susceptible to such an infection…UPMC…has maintained that the deaths cannot be directly attributed to mold because transplant patients with weakened immune systems are at risk of picking up infections that otherwise healthy people routinely fight off.

Urine-quan-BA-2_wb

Image not found or type unknown

Bacteria on a culture plate. Each ‘colony’ arose from a single bacteria.

But screening methods available then were mostly the same techniques that had been used for about a century. These involve taking a clinical sample from a patient, culturing that sample, and identifying bacterial strains. Traditionally, identifying bacteria was based on phenotypic characteristics, such as its appearance in culture, its ability to accept or reject a stain, and shape and size under a microscope.

Since, pathology labs and hospitals have started to embrace next-generation genetic techniques, including the polymerase chain reaction and, most important, massively parallel sequencing. These newer techniques have been able to identify exact identities of bacteria (and any other microbe, including viruses), discover brand new types of infectious bugs, and may create a very different picture of how a hospital outbreak happens.

While HAIs have been decreasing, new disease transmissions have been blamed on “breakdowns in infection prevention and control practices, unrecognized transmission in the community, and important new strains of antimicrobial-resistant pathogens,” wrote Canadian researchers Patrick Tang and Jennifer Gardy. However, Tang and Gardy also wrote, new genetics methods are becoming cheap enough to become part of a hospital pathology lab, and a “new” science of genomic epidemiology (using genetics to trace the progress of a disease in populations) “has been instrumental for resolving hospital outbreaks, sometimes disproving previous assumptions regarding nosocomial pathogen transmission.”

The authors point to a case in 2010 in Birmingham, England, which was the first to use whole-genome

sequencing to study a hospital outbreak. In this case, a protracted outbreak of *Acinetobacter baumannii* that resists multiple antibiotics was reported and first analyzed using traditional culture and molecular biology techniques. After 40 weeks, the health care team started using WGS, which could more rapidly rule out certain isolates, winnowing the list down from 102 to 32 genotypes. Genomics epidemiology then showed that transmission occurred in patient wards, but also an operating and treatment room for burn victims. But the cases continued after 70 weeks, and genomic analysis led the team to a contaminated bed, and patients returning to the burn unit. Specific cleaning of the bed halted the outbreak, after 80 weeks.

More recently, new genomics techniques have helped hone in on similar infectious outbreaks, helping determine new isolates and giving a more complete picture of what arises during the outbreaks.

At the University of Washington, researchers spent a year using whole genome sequencing in intensive care units at the university's hospital in Seattle. Looking at 1,229 bacterial genomes from 391 patients, the researchers found that 12 percent of the clinical isolates were distinct, novel species (even though conventional microbiology methods didn't uncover this distinction). Often, patients had overlapping bacterial infections (that is, more than one bug), and different strains of infectious bacteria could arise during the course of the outbreak. These discoveries helped establish new targets for eliminating the bacteria behind the outbreak, and underscored the need to understand the identification and behavior of every infectious strain involved in an HAI.

Modern next-generation sequencing techniques are becoming cheaper, just at a time when antibiotics are facing more dangerous resistance from bacterial pathogens. Newer techniques have the advantage of more granularity compared to traditional methods (including PCR), and could identify brand new pathogens that need to be identified, sooner rather than later.

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