

DNA sequencers stymie superbug spread

Whole-genome analysis helps identify source of MRSA outbreak on infant ward.

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A superbug outbreak that plagued a special-care neonatal unit in Cambridge, UK, for several months last year was brought to an end by insights gained from genome sequencing. The case, reported today in *Lancet Infectious Disease*, marks the first time that scientists have sequenced pathogen genomes to actively control an ongoing outbreak¹.

Sharon Peacock, a clinical microbiologist at the University of Cambridge, and her team became involved in the outbreak after three infants at nearby Rosie Hospital's 24-cot special-care baby unit tested positive for methicillin-resistant *Staphylococcus aureus* (MRSA) within a couple days of each other.

Bacteria isolated from the three infants were resistant to a nearly identical spectrum of antibiotics, pointing to a common source, says Peacock. The unit was scrubbed clean, and officials hoped that the outbreak was over.

Out of scientific curiosity, though, Peacock's team went on to investigate whether the three cases were linked to a string of MRSA infections at Rosie over the previous six months. Lab tests suggested that at least 8 other children had been infected by MRSA strains with similar antibiotic-resistance profiles in that time. But weeks would go by without an infection, suggesting that the bacteria were not simply spreading from baby to baby in the unit.

Joining the dots

In the hope of connecting the dots, Peacock's team began sequencing the genomes of MRSA strains from the unit, as well as similar strains collected from adult patients at other hospitals and doctor's surgeries. They suspected that adult carriers explained the long gaps between infections in the baby unit.

But the latest outbreak wasn't over. Days after the unit was sterilized, another baby there tested positive for MRSA. Genome sequencing confirmed that the strain matched the other suspected cases.

Confronted with an ongoing outbreak, Peacock and the hospital epidemiologists cast their net wider, searching for the outbreak strain among the 154 workers on the baby unit. One tested positive for a matching MRSA strain, despite showing no symptoms. "We thought it was likely that this individual had been involved in bridging the gaps," Peacock says. "We could take that individual out of circulation and effectively stop the outbreak from continuing."

Further surveillance turned up additional infections among adults in the community, including parents who had contracted MRSA from their babies. Fourteen patients in total — six infants and eight adults — developed serious infections requiring treatment. The final case, a father who had acquired MRSA from his spouse, occurred a year after the outbreak began. No one died.

Dispelling the mystery

Genome sequencing provided clarity that could never have been obtained otherwise, says Julian Parkhill, a microbiologist at the Wellcome Trust Sanger Institute near Cambridge, and a co-author on the *Lancet* paper. Genome sequencing can reveal the series of small mutations that occur over the course of an outbreak, allowing epidemiologists to create an evolutionary tree and trace the outbreak back to close to its suspected source. The infected employee had probably picked up their MRSA from an infant on the ward, the evolutionary analysis suggests.



“Much of the mystery is gone, so now we really do know what has happened in this situation and all the links are made. And that's a tremendous opportunity to improve hospital practice,” says Julie Segre, a microbiologist at the National Human Genome Research Institute in Bethesda, Maryland, whose team retrospectively analysed a *Klebsiella pneumoniae* outbreak that killed 11 patients at a nearby research hospital².

Although the sequencing for the Cambridge outbreak took as little as 48 hours and cost £95 (US\$150) for each MRSA isolate, whole-genome sequencing is not likely to become routine in the control of hospital infection in the near future, says Peacock. DNA sequencers are costly to buy and to operate and, more significantly, analysing pathogen genomes requires considerable expertise.

However, Parkhill and others are developing software that could turn genome analysis into a 'black box' that simply provides hospital epidemiologists with the information needed to guide an investigation into an outbreak. “I think it's inevitable that sequencing will find its place in infection control in the future,” Peacock says.

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References

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