Surprisingly, low-toxin MRSA strains may be the real killer

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The most serious MRSA infections could be those caused by superbugs which produce fewer toxins, as opposed to high toxin strains, according to surprise findings revealed today by scientists from the Department of

Biology & Biochemistry.

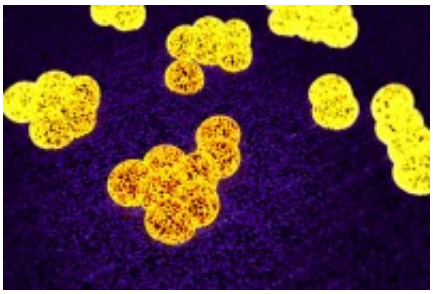
The scientists at Bath have been investigating the complex links between toxicity and virulence for MRSA (methicillin-resistant Staph aureus) infections and publish their findings today in the online access journal *PloS Biology*.

In their new paper, the researchers challenge previous findings, suggesting it's the low-toxin expressing strains we should be looking out for, since they are more likely to establish severe infections.

Previous research had pointed to production of toxins by the Staph aureus as one of the main determinants of the severity of an infection and suggested that those producing high levels of toxins would be the more serious. However, according to the latest study, the opposite might be true which could pave the way for better targeting of treatments.

Around the world MRSA and other superbug infections pose a major problem for public health officials. Once in the blood stream, MRSA mortality rates rise by up to 40 per cent when the disease can also attack heart tissue causing endocarditis. Reports in the US suggest that infections caused by MRSA caused more deaths than HIV/AIDS.

In their paper, 'Evolutionary Trade-Offs Underlie the Multi-Faceted Virulence of Staphylococcus aureas', the authors including Dr Ruth Massey from the Milner Centre for Evolution used two collections of Staph samples to investigate how the infection developed.



Low toxin MRSA strains may be the real killer, according to our latest research.

The first collection included a series of samples taken from a patient as they progressed from carrying the bacteria to developing 'bacteremia' (bacteria in the blood) over a number of months. When the researchers looked at the toxicity of these samples they found that during the 'carriage phase', staph strains secreted more toxins than during the bacteraemia phase.

In the second collection they looked at the same strain of staph – the infamous USA300 strain – taken from multiple patients with varying degrees of infection. They found that carriage and mild infections were far more likely to be caused by high toxin producing strains and, counter-intuitively, that more severe infections were more often established by low toxin producing strains.

Not wasting energy

Dr Massey, explains: "It's generally difficult for bacteria to grow in blood serum, because they have to dodge the defences of the immune system.

"The only difference we found between the low and high toxin strains was their ability to grow in human serum. Given the difficulty for

bacteria in establishing itself in the bloodstream – with the entire immune system present and policing this area – we hypothesised that the cost of producing toxins might be the one thing that disadvantaged these strains in a challenging environment.

"We found the low producing strains grew better in serum than the highly toxic strains. Our findings show that it's the low toxin producing strains that are able to establish blood infections because they do not waste energy producing toxins so have more energy left to defend against antibodies and to grow."

While their findings help explain why low toxin strains are better able to establish severe infections, they also raise another question as to why high toxin producing strains exist at all. To answer this, the researchers devised a mathematical model which they used to better understand transmission rates between the two infections.

Dr Massey adds: "If low toxin-producing strains are better at surviving than high-toxin strains then evolutionary pressure should have purged all high-toxin strains long ago. Yet, while low toxin strains are better at establishing bacteremia, they have much worse transmissibility – a blood infection is very rarely passed between people. It's this lower transmission rate of the less toxic strains which is preventing these from becoming dominant and ensuring the maintenance of highly toxic strains ."

The researchers hope these findings can now be used by the wider research community and medical professions to develop better targeted treatments to help fight MRSA infections.

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More information: "Evolutionary Trade-Offs Underlie the Multi-faceted Virulence of Staphylococcus aureus." *PLoS Biol* 13(9): e1002229. DOI: 10.1371/journal.pbio.1002229

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