Battle of the bugs leaves humans as collateral damage

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Streptococcus meets Saving Private Ryan. Image: Craig Brierley

It's a tragedy of war that innocent bystanders often get caught in the crossfire. But now scientists at the University of Pennsylvania and the University of Oxford have shown how a battle for survival at a microscopic level could leave humans as the unlikely victims.

In work funded by the US Public Health Service and the Wellcome Trust, the researchers have found a possible explanation for why some bacteria turn nasty, even at great risk to their own survival.

The body is home to a wide range of bacteria which in the vast majority of cases exist quietly, causing no harm. Sometimes, a bacterium will evolve properties which are potentially deadly to its human host. But

evolution comes at a cost and this presents a paradox: why should it harm its host when this could result in the demise of the bacteria themselves?

"For many microbes, living in harmony with their host is the best option, so why do some suddenly turn nasty?" asks Dr Sam Brown, a Wellcome Trust Research Career Development Fellow at the University of Oxford. "Sometimes the answer is obvious - for example, the cold virus makes its host sneeze, helping it spread wider. But for other bacteria and viruses, which do not normally cause disease, the reason isn't at all clear."

In a study published today in Current Biology, scientists have modelled in mice how a commonly-found bacterium known as Streptococcus pneumoniae interacts with other bacteria, showing that competition for space between rival bacteria can cause deadlier forms of bacteria to evolve. *S. pneumoniae* usually exists in the nasal passage, where it sits quietly: as many as two in five people in some countries will carry the bug without being aware of it.

When *S. pneumoniae* is forced to share space with Haemophilus influenzae, another common and ordinarily asymptomatic bacterium, the two begin a tussle for space. But *H. influenzae* has an extra trick up its sleeve, calling on our immune system to help get rid of its competitor by recruiting white blood cells called neutrophils, which surround and attack the *S. pneumoniae* bacteria.

"Many bacteria are not a problem to our immune system, so can be left alone," explains Dr. Lysenko. "But the *H. influenzae* bacteria stir up trouble, saying to the body, '*S. pneumoniae* are bad guys - beat them up'. The neutrophils respond, attacking the innocent bacteria and thus helping *H. influenzae* to survive."

Many strains of *S. pneumoniae* exist, each coated with a thick sugar

capsule. In some strains, the capsule is particularly protective, and appears to act as armour against the host's immune response. This allows the bacterium to enter the blood stream where it can go on to replicate and cause serious diseases such as pneumonia, bacteraemia (blood infection), septicaemia and meningitis.

The researchers tested different combinations of three bacteria - two pneumococcal strains (armoured and un-armoured), and *H. influenzae*. They found that when a sufficient amount of *H. influenzae* was present, the more virulent, armoured strain of *S. pneumoniae* began to out-compete its rivals: its thick sugar coating was allowing it to escape attack from the neutrophils, but this property also made it more deadly when it entered the blood stream.

Dr Brown concludes: "Creating a new armour is costly to *S. pneumoniae* in terms of the energy expended to make it, but it means the bacterium wins the battle with *H. influenzae*. However, it also means that if *S. pneumoniae* enters the blood stream, the immune system is unable to stop its rampant progress. Our bodies are unable to cope and the armoured bug could pay the ultimate price: death to its host and death to itself."

According to Dr Jeff Weiser from the University of Pennsylvania School of Medicine, Philadelphia, the results could have implications for the development of new treatments and vaccines against infection.

"Our study demonstrates the complex interactions among the many microbial species that live in our bodies," he says. "Usage of antibiotics and vaccines is increasingly influencing these relationships, potentially tipping the outcome of the battle between competing microbes. Our ongoing war on infectious diseases should consider the effects of microbes on one another."

More information: Paper: www.cell.com/current-biology/abstract/S0960-9822%2810%2900654-8

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