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► COVER: 'A to B' by George Marshall, inspired by the Review on p28.

**M**ore than 1,400 bacterial, viral and parasitic species are known to cause human disease. Understanding how these pathogens colonize, survive and inflict disease remains one of the key goals of microbiology. This, the first issue of 2008, features several Reviews that discuss microbial virulence.

On page 79, John Boothroyd and Jean-Francois Dubremetz discuss the specialized rhoptry organelle, which exists in apicomplexan parasites such as *Toxoplasma gondii*. In *T. gondii*, recent findings indicate that these organelles contain the molecular machinery that enables the parasite to affect host gene expression and co-opt host functions.

Dealing with bacteria, Samuel Miller and colleagues discuss the mechanisms that enable Salmonellae to interact with, and manipulate, host cells (page 53). Specifically, they focus on the interplay between various bacterial and host proteins that enables the invasion of epithelial cells, stimulation and repression of signalling cascades, sensing of the intracellular environment and establishment of a niche for intracellular replication.

So, how can we harness our understanding of microbial virulence to stem the continuing rise in infectious-disease-related morbidity and mortality? Antibiotic-based strategies, which typically target bacterial viability, have resulted in widespread resistance — meticillin-resistant *Staphylococcus aureus* infections reached epidemic levels last autumn in some parts of the United States. Perhaps rather than targeting bacteria for eradication, we should focus instead on de-clawing pathogens by inhibiting the virulence mechanisms that promote infection or that cause disease symptoms. On page 17, Scott Hultgren and colleagues highlight various bacterial virulence mechanisms that could be targeted and consider the recent efforts towards, and the remaining challenges that face, antivirulence-based drug discovery.



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