Antimicrobial resistance takes another step forward

Background and epidemiology: On July 5, 2002, the US Centers for Diseases Control and Prevention described the first case of vancomycin-resistant *Staphylococcus aureus* (VRSA).[1] In June 2002 VRSA was isolated from the catheter site of a Michigan man receiving chronic renal dialysis.[1] Two months earlier he had been treated for methicillin-resistant *S. aureus* with a regimen that included vancomycin. One week after the VRSA was isolated, the catheter site appeared healed. However, culture of a suspicious foot ulcer also grew VRSA and vancomycin-resistant enterococci (VRE). Although resistant to vancomycin, the *S. aureus* isolate was sensitive to a number of other drugs, including trimethoprim–sulfamethoxasole and linezolid. The patient remained stable and received aggressive outpatient wound care and systemic treatment with trimethoprim–sulfamethoxasole.

S. aureus has thwarted medicine twice before, first twisting itself free of penicillin in the 1940s[2,3] and then challenging methicillin 30 years later.[4] This latest development raises fears of increased therapeutic failures.

Bacteria's ability to change their susceptibility to antibiotics is more than an evolutionary side effect. There are direct dangers to the infected patient. In one study, patients with VRE bacteremia had a 37% higher mortality than matched control patients infected with a vancomycin-sensitive strain.[5]

Resistance can occur at any level along the pathway of antibiotic action and usually happens through genetic mutation or genetic exchange.

Genetic mutations of the bacterial chromosome occur spontaneously and can lead to alterations in cell chemistry or structure that decrease or eliminate an antibiotic's effectiveness. Some examples are changes in penicillin-binding proteins that lead to β-lactam resistance in *Staphylococcus pneumoniae*[6] or development of β-lactamases that hydrolyze broad-spectrum cephalosporins.[7] A mutation can lead to a failure of an entire class of drugs or necessitate a higher dose of a previously effective antibiotic.

Bacteria can exchange genetic information. Gram-positive bacteria do this through transformation and transduction, gram-negative ones through conjugation. Exchange between gram-positive and gram-negative organisms has also been reported.[8] The transmission of vancomycin resistance from *Enterococcus* to *Staphylococcus* was accomplished in the laboratory in 1992[9] but had not been seen in humans until now. In the case of the Michigan patient, genetic tests showed that the isolate contained the *vanA* resistance gene from enterococci, which suggests genetic transfer as the mechanism of resistance.

Prevention: Before this incident, there was growing concern that *Staphylococcus* was developing increasing resistance to vancomycin because of reports of *S. aureus* showing intermediate levels of minimum inhibitory concentration. Guidelines were developed to decrease the risk of transmission of this vancomycin-intermediate *S. aureus* and should apply to VRSA.[10] Health care professionals are advised to isolate the patient, use contact precautions (gown, mask, gloves and antibacterial soap) and minimize the number of people coming into contact with the patient, providing one-on-one care if possible. These steps should be taken in full cooperation with experts in infection control and with consultation from Health Canada.

Antibiotic resistance flourishes when antimicrobial drugs are "abused, misused and dispensed at levels lower than treatment guidelines dictate."[11] Increased surveillance and recognition of the problem has led to public campaigns, with physicians being encouraged to limit empiric use, avoid prescribing broad-spectrum antibiotics when possible and use a full therapeutic dose of appropriate duration. Thorough handwashing, appropriate use of barrier precautions and proper cleaning and disinfection are also important.

The developing world's inability to obtain health services and necessary drugs allows infections to flourish. Combine limited public health knowledge of the importance of targeted therapy of appropriate duration with drugs of dubious quality and the problem is compounded. It is in these areas of greatest need that resistance is often highest.

Judicious use of antibiotics, access to essential medicines, public health knowledge and infection control policies are integral in slowing the trend of drug resistance.

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