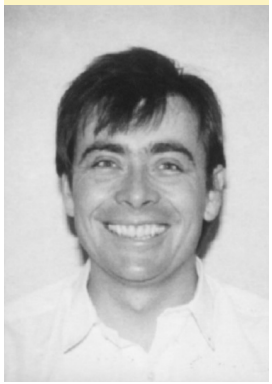
COMMON INFECTIONS — LOCAL AND SYSTEMIC



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The 6th edition of Price's *A Textbook of the Practice of Medicine* was published in 1941, a few years before penicillin came into general clinical use. Common infectious diseases are meticulously described and the characteristics of the infecting organisms are discussed in detail. The only group of antibiotic agents available, however, were the sulphonamides. Sulphanilamide had revolutionised the treatment of bacterial meningitis and infections due to *Streptococcus pyogenes*, and sulphapyridine had been found to be invaluable in the treatment of pneumococcal pneumonia, pyelonephritis and gonorrhoea. However, tuberculosis, typhoid and systemic infections due to *Staphylococcus aureus* carried a grave prognosis, and infective endocarditis was invariably fatal. The treatment of syphilis was prolonged, painful and unpredictable. The only agent available for the treatment of malaria was quinine. More than 60 years later we have a plethora of highly effective antibiotics, and tuberculosis is routinely cured by a standardised course of potent antituberculous drugs. Even the almost invariably lethal human immunodeficiency virus (isolated only 20 years ago) can be tamed by highly active antiretroviral therapy (HAART).

The flip side of the coin however is that pathogenic microbes evolve resistance to our armamentarium with dismaying speed. Penicillin-resistant pneumococcus, methicillin-resistant *S. aureus*, and co-trimoxazole-resistant *Escherichia coli* are everyday features of our medical landscape. Malaria is resistant to many of the more recently developed agents, and worries over the development of HIV resistance to HAART temper the optimism surrounding the antiretroviral rollout.

Resistance occurs when random mutations in an infecting microbe's genome confer a survival advantage to the strain carrying the mutation when the infection is treated with a given agent. Resistance is more likely to occur when the treatment is taken irregularly (causing sub-therapeutic levels) or if the treatment is used frequently. Examples of common mechanisms that microbes use to protect themselves against anti-infective drugs are summarised in Table I. Genetic material coding for antibiotic resistance spreads rapidly among Gram-negative organisms by means of plasmid exchange — the multidrug-resistant organisms frequently isolated in our intensive care units are thought to acquire resistance in this way. Last year, a gene coding for vancomycin resistance was shown to have been transferred from an enterococcus to a *S. aureus* infecting the same diabetic patient.

Table I. **Common mechanisms of resistance to antimicrobials**

Mechanism	Examples
Decreased intracellular drug concentration	
Decreased drug penetration	Beta-lactams (decreased bacterial membrane permeability)
Increased drug efflux	Tetracyclines (up-regulation of trans membranous pumps)
Intracellular drug inactivation	Beta-lactams (destruction by beta-lactamase enzymes), aminoglycosides
Drug target modification	Beta-lactams (alterations in penicillin-binding proteins), quinolones (DNA gyrase modifications), macrolides (ribosomal RNA changes), HIV reverse transcriptase inhibitors and protease inhibitors
Drug target bypass	Vancomycin (alterations to terminal amino acids of peptidoglycan)

The theme of this month's *CME* is appropriate use of anti-infective drugs to optimise therapeutic benefit while trying to minimise the development of drug resistance. Dr Anne von Gottberg sets the scene by giving the most recent data on antibiotic resistance among commonly isolated organisms in South Africa. She emphasises the fragmented nature of the data, and the need for more structured surveillance programmes. Clinicians working in primary care settings and in emergency units frequently see patients with fever, and need to rapidly decide if the fever is due to a benign viral infection or to a potentially serious infection requiring antibiotic treatment. Dr Kevin Rebe and Dr Graeme Meintjes give a practical approach to the causes of fever with a view to rapidly and effectively diagnosing serious infections. Dr Kriyanand Naidoo discusses the controversial issue of the use of antibiotics in acute respiratory tract infections, while Dr Elizna Coetzer and Professor B Singh give systematic overviews of infections of the urinary tract and ear. In the 'More About' section Dr Karen Barnes gives the reasoning behind the use of combination therapy in the treatment of malaria. In the developed world, where antiretroviral therapy is widely available, more than 10% of new HIV infections are with a drug-resistant virus, and Dr Catherine Orrell discusses the highly relevant topic of adherence to antiretroviral therapy as a strategy to limit the development of resistant HIV. We hope the readers of this month's *CME* will find the articles as interesting and thought provoking as we did, and we would like to thank the contributors for generously giving of their time and expertise.

Recommended reading

Hooton TM, Levy SB. Antimicrobial resistance: a plan of action for community practice. *Am Fam Physician* 2001; **63:** 1087-1098.
Little SJ, Holte S, Routy JP, *et al.* Antiretroviral drug resistance among patients recently infected with HIV. *N Engl J Med* 2002; **347:** 385-394.
Soju Chang, Sievert DM, Jeffrey C, *et al.* Infection with vancomycin-resistant *Staphylococcus aureus* containing the *vanA* resistance gene. *N Engl J Med* 2003; **348:** 1342-1347.