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This issue of *Therapeutics and Clinical Risk Management* contains four comprehensive review articles which focus on disorders of the skin. Psoriasis vulgaris represents the most common form of psoriasis. Symptoms include red, raised, scaly lesions that usually occur symmetrically in areas subjected to trauma such as the elbows and knees. Although not considered life-threatening, this is an unpleasant, distressing condition that impacts on quality of life and patient well-being. The chronic nature of the condition requires long-term therapy thereby raising compliance and safety issues. The pathogenesis of psoriasis vulgaris is not well understood but is thought to involve a complex interaction between genetic and environmental factors that impact on innate and acquired immunity. This results in an inflammatory cutaneous response in which T cells, dendritic cells and pro-inflammatory chemokines play particularly important roles. Most treatments are topical with corticosteroids and vitamin D3 analogues being the treatment of choice. Efstratios Vakirlis and colleagues (2008) provide a comprehensive review of the efficacy of treating psoriasis vulgaris with a topical treatment that combines calcipotriol, a vitamin D analog with the corticosteroid betamethasone dipropionate. The authors review the mechanisms by which the two compound ointments (Dovobet®, Daivobet®, Taclonex®) attenuate the inflammatory cascade that results in the symptoms of psoriasis. The combination of the two therapies has a positive additive effect with lesions clearing more quickly compared with separate application of corticosteroids and calcipotriol. The authors also highlight the technical demands of creating the dual formulation due to the tendency of calcipotriol and topical steroids to inactivate each other when mixed in a single formulation. The available randomized clinical trials with the combination medication are comprehensively reviewed together with safety and tolerability for the treatment. It appears that the requirement for a once daily application and a rapid onset of action improves patient compliance. Overall the authors' opinion is that dual formulation of calcipotriol and topical steroids is a safe and effective treatment for psoriasis vulgaris either as initial therapy or as adjunct therapy in patients who also require systemic treatment or phototherapy.

The second review of treatment of dermatological disorders is focused on the immune-response modifying agent imiquimod (Lacarrubba et al 2008). This is a synthetic imidazoquinoline amine that enhances, through cytokine induction, both the innate and acquired immune pathways, resulting in antiviral and antitumor effects. Imiquimod stimulates the immune system in several ways but the main pathway appears to be through the toll-like receptor (TLR)-7, activation of which induces release of pro-inflammatory cytokines from Langerhans cells, monocytes/macrophages and dendritic cells. This in turn results in T cell activation and subsequent killing of virus-infected cells and tumors. The authors review the randomized clinical trials with imiquimod that show it to be an effective treatment for genital and perianal warts, actinic keratoses, basal cell carcinomas, Bowen's disease, and molluscum contagiosum. However, imiquimod treatment is not without side-effects with some patients experiencing mild to severe local skin reactions that may extend beyond the treatment area.

The current issue also contains two reviews on the treatment of complicated skin and tissue infections. These sites are particularly vulnerable to bacterial infections, often after surgical procedures, and many of these are caused by antibiotic-resistant strains making treatment difficult. Effective management of complicated skin and

tissue infections requires timely instigation of appropriate antimicrobial therapy. There is particular concern over the extent of infections caused by resistant strains of *Staphylococcus aureus*, one of the most common and virulent Gram-positive bacteria encountered clinically. *S. aureus* is responsible for both Methicillin-resistant *S. aureus* (MRSA) and the more serious hospital-acquired MRSA that exhibits multidrug resistance, including resistance to all the lactam antibiotics, penems, and carbapenems. The review by Lala Dunbar and colleagues (2008) defines the role of Telavancin, a once-daily intravenous lipoglycopeptide antibiotic that exhibits bactericidal activity via a dual mechanism currently under regulatory review in both the United States and Europe for the treatment of complicated skin and tissue infections. The authors present findings from phase II and III multinational, randomized, double-blinded studies that show Telavancin to be an effective therapy. The authors conclude that current evidence on telavancin supports its safety and effectiveness in the treatment of complicated skin infections and following regulatory approval it should provide an important new option in the treatment of serious infections caused by resistant Gram-positive bacteria. Another potentially important novel treatment for complicated skin and tissue infections is dalbavancin, a parenterally administered semi-synthetic lipoglycopeptide antibiotic similar to the naturally produced glycopeptides vancomycin and teicoplanin. The review by Bennet and colleagues (2008) in the current issue provides comprehensive information on the phacokinetics, pharmacodynamics, and antimicrobial activity of dalbavancin together with available evidence of efficacy from phase II and III clinical trials in patients with complicated skin and tissue infections. Like telavancin, dalbavancin is awaiting regulatory approval but both should prove to be useful additions to the treatment of infections caused by multiple drug-resistant bacterial strains.

References

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