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This issue of *Therapeutics and Clinical Risk Management* contains original articles that address two very different but important clinical issues namely improving diagnostic imaging in carcinoma of the bladder and an observational study that evaluated the association between metabolic syndrome and high homocysteinemia (HHcy) in relation to cardiovascular disease. Atopic dermatitis (AD) is a distressing and common chronic relapsing cutaneous disease that has significant impact on the quality of life of those affected. It is seen more frequently in children and the symptoms of AD include dry and scaly skin and intense itching. The latter symptom leads to an itching-scratching cycle that exacerbates the condition, particularly in young children. Triggers for the condition include allergens, microbial infections and a disrupted skin barrier function. Corticosteroids represent the treatment of choice for AD as they target the T-cell driven inflammatory response that underlies the pathogenesis of AD. Emollients are also important treatments as they provide relief for the dry and flaky skin characteristic of AD. It is of interest therefore that Lee and colleagues (2007) have provided a comprehensive review in the current issue on pimecrolimus, an ascomycin macrolactam derivative developed specifically for the treatment of inflammatory skin diseases. Currently, pimecrolimus has been approved as second line therapy for the treatment of mild to moderate AD in non-immunocompromized children over 2 years old and in adult patients. Pimecrolimus has high affinity for macrophilin-12, a cytosolic T-cell receptor, and this interaction blocks the activity of the calcium dependent phosphatase calcineurin. This in turn prevents the transcription factor NF-AT activating genes that encode the TH2-type cytokines IL-4, IL-10 and the TH1-type cytokines IL-2 and IFN-γ. Pimecrolimus also decreases cytokine production and the release of preformed mediators from mast cells. These beneficial effects in modulating the inflammatory processes in the skin of AD patients must be tempered with the potential side effects of this treatment – issues compressively addressed in this article. The authors highlight several clinical trials demonstrating the long-term safety and efficacy of pimecrolimus in pediatric and adult patients suffering from mild to moderate AD. The article also discusses data from the recent ISOLATE trial (Zuberbier et al 2006) which assessed the impact of AD on patients' quality of life including the social and emotional consequences of the condition. Moreover, topical anti-inflammatory therapy with pimecrolimus was associated with significant improvement in quality of life over the 6 month study period together with a significant steroid sparing effect. The authors concluded that topical anti-inflammatory therapy has an important place in long term AD treatment.

The skin theme continues with a review by Townsend and colleagues (2007) on complicated skin and skin structure infections (cSSSIs) and complicated intra-abdominal infections (cIAIs) with a focus on tigecycline. These are the two most prominent sites for bacterial infections often after surgical procedures; many of which are caused by antibiotic resistant strains. Effective management of cSSSIs or cIAIs require timely instigation of appropriate antimicrobital therapy while in some select cases surgical intervention may also be required. Tigecycline is related to the tetracycline antibiotic class and is the first of a new class of antimicrobials termed glycylcyclines. The authors give a clear and detailed description of how tigecycline overcomes the resistance mechanisms developed by several types of bacteria to

tetracyclines that most frequently involves protection of the ribosome and/or efflux pumps. The microbiological, pharmacokinetics and pharmacodynamics of tigecycline are detailed in the review together with clinical efficacy and safety issues. The authors conclude tigecycline to be a new effective treatment option for both cSSSIs and cIAIs with favourable in vitro activity against a wide variety of aerobic Gram-positive, Gram-negative and anaerobic organisms. The available clinical trials suggest similar efficacy by tigecycline to comparator treatments for a variety of cSSSIs and cIAIs. The main adverse effect appears to be nausea and vomiting in some patients.

The arthritic diseases are prevalent and distressing conditions that are associated with significant morbidity typified by reductions in functional capacity and quality of life with attendant substantial healthcare expenditure. Development of specifically targeted biologic agents in recent years has greatly enhanced the therapeutic options for the treatment of the arthritic diseases rheumatoid arthritis, psoriatic arthritis, and ankylosing spondylitis (AS). AS is a inflammatory joint disorder affecting the axial skeleton, peripheral large joints, some areas of tendon and ligaments attachment to bone and extra-articular sites such as the anterior uvea. Current treatment approaches to AS are reviewed in the current issue by Walter Maksymowych (2007). These include the use of non-steroidal anti-inflammatory agents and the anti-TNFα class of drugs. TNF is an attractive biologic target as it has been implicated as a major pro-inflammatory player in a wide range of chronic inflammatory conditions including AS. Three TNF antagonists are currently available infliximab, a chimeric anti-TNF mAb, adalimumab, a fully human anti-TNF mAb and etanercept, a recombinant soluble p75 TNF-receptor-Fc fusion protein. These have been assessed in clinical trials in AS patients and it appears that all three available anti-TNFα agents appear to have similar efficacy in improving the articular manifestations of AS with positive clinical responses being observed in 60% of patients. However, the author points out that several issues are outstanding including whether anti-TNF therapies are disease modifying in that they prevent structural damage progression together with the issue of the efficacy or otherwise of methotrexate therapy for AS in combination with anti-TNFα therapies.

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