

**Garry Walsh**

Asthmatic and Allergic Inflammation  
Group, School of Medicine,  
University of Aberdeen, UK

Issue one of the second volume of *Therapeutics and Clinical Risk Management* presents a range of review articles from internationally recognised authors, each of whom addresses an important and apposite topic in the therapeutic management of clinical risk.

Overactive bladder (OAB) and urinary incontinence are prevalent and distressing conditions with significant associated direct and indirect economic costs. Moreover, the majority of OAB patients do not present for treatment in spite of a considerable reduction in mental health and health-related quality of life. Antimuscarinic agents have been at the forefront of therapy for OAB for 30 years; however, patient compliance rates are extremely poor as a result of drug expenses, suboptimal dosage regimens, a commonly incomplete improvement in symptoms, and intolerable systemic side-effects. McCrery and Appell review the latest alternative drug delivery systems for the antimuscarinic agent, oxybutynin chloride (OXY), including OXY-ER, an extended-release formulation, and OXY-TDS, a transdermal system, together with a range of other antimuscarinic agents.

The worldwide prevalence of asthma has increased to approximately 300 million and represents a major socioeconomic and healthcare load. The established efficacy of inhaled corticosteroids (ICS) has resulted in their being promoted as the cornerstone of asthma therapy. However, local and systemic adverse effects can limit their use and result in significantly reduced compliance. Ronald Dahl presents a comprehensive review of ciclesonide, a nonhalogenated corticosteroid that demonstrates potent anti-inflammatory activity with similar efficacy to other ICS in asthma and did not elicit unfavorable side effects at dosages used in clinical trials. This knowledge may enhance the management of this prevalent condition in which poor compliance to prescribed medication is common.

The number of liver transplants secondary to hepatitis viruses has risen substantially over the past 20 years in Europe and the US. Approximately 50% are due to infection with hepatitis C virus (HCV) and projections suggest that the impact on public health will continue to increase. Picciotto reviews the natural history of HCV patients following transplant and the available therapeutic options, for which there is as yet no consensus. Post-transplant clinical sequelae are characterized in most patients by HCV reinfection and development of chronic hepatitis. Therapeutic strategies for the management of HCV during the peri-transplant phase include pretransplant prophylaxis to prevent the transplanted organ becoming infected; post-transplant prophylaxis to attenuate risk of acute hepatitis; and management of the stabilized chronic disease state.

Musculoskeletal conditions, including rheumatoid arthritis (RA) and osteoarthritis (OA) amongst others, represent a significant burden in terms of socioeconomic cost and morbidity. Although nonsteroidal antiinflammatory drugs (NSAIDs) play an important role in the management of RA and OA, their longer-term use is associated with considerable upper gastrointestinal symptoms that contribute to poor compliance and inadequate control of inflammation and pain. Etoricoxib is a selective COX-2 inhibitor, a subclass of NSAIDs that demonstrate comparable clinical efficacy to traditional NSAIDs together with significantly reduced gastrointestinal toxicity. The timely evaluation from Brooks and Kubler reviews the pharmacology of etoricoxib

and summarizes the current clinical data on its efficacy, tolerability, and patient acceptability.

Zhanel and colleagues examine the role of telithromycin, the first ketolide antibiotic to gain US Food and Drug Administration (FDA)-approval for the treatment of acute bacterial sinusitis, acute exacerbations of chronic bronchitis, and community-acquired pneumonia in adult outpatients. Collectively, these three conditions are responsible for significant morbidity and substantial socioeconomic costs. The authors present a review of the mechanisms by which telithromycin exerts its antibacterial activity and also assess the pharmacokinetic and pharmacodynamic properties, clinical efficacy, and tolerability-safety profiles.

The increasing prevalence of osteoporosis worldwide contributes significantly to morbidity and mortality amongst our aging populations with considerable attendant health and financial implications. In the first of two complementary reviews examining the primary role of the bisphosphonates in the management of osteoporosis, Bauss and Schimmer comprehensively review the efficacy and safety of ibandronate, a highly potent N-containing bisphosphonate that combines the known efficacy of this drug class with enhanced safety and tolerability profiles. Grey and Reid use the limited available data to critically evaluate the differences between agents of this expanding class of drugs in terms of potency, administration route, duration of action, and efficacy. Bisphosphonates demonstrate a high antiresorptive potency that allows lower doses and extended dosing intervals and has recently been approved as the first once-monthly oral drug for the treatment and prevention of postmenopausal osteoporosis in the US.

Larkin and Eisen report that incidence of renal cell carcinoma (RCC) in the UK increased by almost 20% between 1991 and 2000. In cases of metastatic RCC, whilst immunotherapy may offer a small overall increase in survival, it does not benefit the majority of patients and there is thus a need to elucidate new therapeutic approaches. Sorafenib is an orally administered, novel member of the kinase inhibitor class of drugs. In phase 2 studies amongst patients with RCC pretreated with immunotherapy, it has demonstrated significant activity with manageable toxicity while a phase 3 study has shown prolonged progression-free survival when compared with placebo.

In the second of our two complementary reviews, Tadicherla and Berman examine the role of noninvasive percutaneous drug delivery systems used in the local control of pain. They outline the mechanisms of percutaneous absorption of these products and address their composition, duration of onset of anesthetic effect, and uses and side effects. The authors also discuss novel advances in the use of heat to enhance anesthetic penetration, as provided by the Synera<sup>TM</sup> patch, and use of a peel method to deliver anesthesia, such as that provided by S-Caine patch, a product that is currently awaiting FDA approval. The opioid class of analgesics has proven efficacy and a long history of use in the management of both acute and chronic pain; however, concerns over their safety, tolerability and longer-term acceptance to patients have prevented them from realising their therapeutic promise. Rudolf Likar presents a review of the safety aspects of the transdermal semisynthetic opioid buprenorphine and highlights the results of two decades' work that indicates its superior therapeutic benefits and safety profile.