

Garry Walsh

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

The third issue of volume two of *Therapeutics and Clinical Risk Management* presents review articles and original research papers on a wide range of topics.

World Health Organisation guidelines indicate morphine use for control of moderate-to-severe pain in chronic cancer based on factors such as accessibility, effectiveness, ease of administration, and cost as opposed to its being therapeutically superior. Survey data from the Research Network of the European Association for Palliative Care indicate that opioid rotation may achieve more effective pain control with fewer side effects than single usage alone. Oxycodone is a member of the opioid class with high oral-to-parenteral bioavailability with no threshold in its analgesic effect. Giuseppe Biancofiore examines the pharmacokinetics and pharmacodynamics of oxycodone and reviews a selection of studies examining its efficacy and safety profile in the treatment of cancer pain.

Considerable evidence exists to support the use of the bisphosphonate alendronate sodium in the management of osteoporosis. Prinsloo and Hosking comprehensively discuss the fracture intervention trial (FIT), a major grouping of four pivotal studies that demonstrated alendronate's efficacy and provided the foundation for subsequent clinical trials and a range of post-hoc analyses. The two studies of the vertebral fracture arm, the clinical fracture arm and the osteoporotic cohort are all critically evaluated in depth and the results expanded upon in the discussion of the prevention of multiple fractures, prediction of responses to treatment, and aspects of primary prevention. In addition, the authors present data relating to the role of alendronate in the management of male osteoporosis and in corticosteroid-induced osteoporosis.

Mucositis-related pain is one of the primary side effects of cancer treatment with approximately 40% of chemotherapy patients and most patients undergoing bone marrow transplant affected. Despite the plethora of current therapies, none is especially specific to or effective in mucositis. Debra Harris reviews recent advances in our knowledge of pain management in mucositis including its pathophysiology, clinical manifestations and the strengths and weaknesses of the respective assessment tools including the Harris mucositis-related pain assessment tool that is specific to mucosal pain and contains dimensions of pain; functional ability; and effectiveness of interventions. Although the tool is as yet unvalidated it contains numerous validated elements from other assessment methods. The author concludes with a range of key recommendations aimed at standardising assessment, classification and patient treatment in a mucositis-specific manner.

Cervical cancer is the second most common malignancy amongst females worldwide. In their overview Winters et al examine the role of vaccination against human papilloma virus by highlighting a range of recent studies considered to be of greatest relevance to cervical cancer. Their approach includes discussion of pathology, epidemiology and current prevention strategies and treatment. Furthermore the authors examine studies of vaccines in development, prophylactic vaccines and some relevant associated contentious issues.

Bortezomib is a novel proteasome inhibitor whose introduction heralds a major advance in the management of multiple myeloma and as first-line therapy prior to stem cell transplantation. Bortezomib is notable for its positive response in the previously refractory patient and enhanced survival rates in the relapsed patient, data that led to its approval by regulators in the US in 2003 and in Europe in 2005. In this review, Antonia Field-Smith and colleagues present a comprehensive overview of findings from Phase II/Phase III clinical trials and address its clinical use, including

side effects and toxicity; management of associated peripheral neuropathy (which affects 30% to 40% of patients) and thrombocytopenia. Finally, the authors give a comprehensive overview of bortezomib in combination with other chemotherapeutic agents and conclude that it is effective when administered in the outpatient setting.

A range of management strategies exists which can attenuate the sequelae of age-related osteoporosis. MacLaughlin et al review the background to the topic and discuss epidemiology and economic impact, diagnosis and classification together with an analysis of the intrinsic and extrinsic risk factors for fall-related fractures. In addition, they provide information on the respective roles of many pharmacological therapies including: calcium and vitamin D; the bisphosphonates; calcitonin; estrogen receptor stimulators; strontium ranelate; sodium fluoride; and teriparatide.

Secondary hyperparathyroidism (SHPT) is a serious clinical outcome of chronic renal disease. The renal impairment-associated decline in active vitamin D (calcitriol) is critically linked to the development of SHPT and its allied cardiovascular complications. While intravenous vitamin D analogues such as paricalcitol are routinely used in hemodialysis patients, the US FDA approved a novel oral paricalcitol preparation for use in pre-chronic kidney disease in 2005. Cheng and Coyne review the data underpinning oral paricalcitol and consider its potential long-term benefits for reduced hospitalizations and enhanced survival and include a brief discussion of its emerging role in the attenuation of vascular calcification, atherosclerosis and renal fibrosis.

Migraine is a prevalent condition predominantly affecting females with approximately half of these being susceptible to menstrual headache onset. This may last longer and demonstrate greater resistance to treatment than other forms of migraine. Frovatriptan, a 5-HT receptor agonist, is a second-generation triptan with a pharmacokinetic profile of proven benefit in the management of menstrual migraine. Ebrahim Balbisi reviews its pharmacology and pharmacokinetics and discusses the clinical efficacy, safety and tolerability of frovatriptan in the treatment of this common and distressing condition.

Non-standard prescribing practices have been found to play a significant role in the under-utilisation of anticoagulant drugs. The technique of academic detailing aims to enhance prescribing behavior and has been used successfully in both community and hospital environments. Roberts and Adams examined the effects of introducing guidelines based on academic detailing on initiation of

warfarin therapy, reversal of warfarin over anticoagulation, and uptake of deep vein thrombosis prophylaxis in four teaching hospitals. The authors report that use of academic detailing enhanced guideline roll-out, produced positive results in the majority of areas studied and was well-received by prescribing practitioners.

Small-cell lung cancer (SCLC) has a poor prognosis associated with significant morbidity, mortality and economic cost. Although several novel, third-generation chemotherapeutic drugs are available for SCLC treatment, their cost effectiveness have yet to be fully determined. Uylde Groot and colleagues have developed a Markov chain model for the projection of patient outcome parameters and associated costs in SCLC for patients treated with either etoposide–cisplatin combination therapy or a hypothetical new drug. They conclude that increased future costs for SCLC treatment will result in only a relatively minor extension of survival time. However, both palliation and quality of life parameters should also be enhanced and the authors predict enhanced outcome and cost-effectiveness with emerging treatment regimens.

Psoriasis therapy represents a substantial healthcare expenditure that was previously estimated at \$1.6bn–3.2bn in the US alone; the recent emergence of 3 novel biologic response modifiers has significantly increased this projection. Cost-utility analysis (CUA) utilises quality-adjusted life years (QALYs) as an effectiveness endpoint and between US\$50–100 000 is considered an affordable therapeutic intervention. Weiss et al used Euro-Qol 5 Dimension (EQ5D), an instrument that has been standardized for the description and evaluation of health states, in order to formulate a preliminary CUA of psoriasis therapy. The authors conclude that current psoriasis therapeutics confer comparable utilities relative to those in other medical specialties.

Gastroesophageal reflux disease (GERD) is a highly prevalent, unpleasant and debilitating condition characterized by heartburn and regurgitation of food, the latter being associated with Barrett's esophagus and adenocarcinoma of the esophagus and gastric cardia. Nowak and colleagues conducted a retrospective case series study of 23 adult patients who attended a dietetic clinic for lifestyle intervention in the management of GERD. The authors report that 22 patients reported an improvement in their symptoms and noted a reduction in medication usage amongst 11 of the 18 patients who had been taking GERD medication at time of presentation. In spite of the small number of patients studied, their results indicate further evaluation of the role of lifestyle modification in GERD is warranted.