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**Editorial**

In addition to two original research articles this issue of TCRM contains some excellent reviews on diverse clinical areas including control of chronic pain, Parkinson's disease and the use of a novel biologic to treat chronic plaque psoriasis. Nersesyan and Slavin (2007) have provided a comprehensive overview of the problem of providing adequate analgesia for cancer patients. Indeed they point out that in the US alone 70% of people with cancer experience some degree of pain and that this inevitably intensifies as the disease progresses. Regrettably less then half of these patents are given adequate pain relief giving rise to significant suffering; of these around 25% actually die in pain. This is despite of the availability of several practice guidelines for cancer pain management of which the most widely used is the 3-step analgesic ladder developed by the World Health Organization. The authors propose that in a significant number of cancer patients, particularly in those with neuropathic pain or pain associated with bone involvement, a more sophisticated 5-step algorithm might be required. In addition the authors have provided a comprehensive review of cancer pain assessment and its pharmacological or surgery-related management. The authors conclude with the recommendation that the control of cancer-related pain should be individualized for each patient and should include periodical re-evaluation of the medication regimen to ensure adequate analgesia and to minimize exposure to potentially dangerous adverse effects.

In contrast noncancer related chronic pain is most often associated with patients with lower back pain, myofacial pain or osteoarthritis thereby significantly reducing quality of life together with considerable economic costs. In his timely review Bill McCarberg (2007) considers current treatment guidelines for the management of chronic pain and reviews the use of an extended-release formulation of tramadol. Tramadol is a centrally acting oral analgesic that acts through opioid receptor binding and inhibition of norepinephrine and serotonin reuptake. It is currently recommended as an alternative for patients unresponsive to or intolerant of nonselective NSAIDs and COX-2 inhibitors. The review focuses on the pharmacokinetics, safety and efficacy of extended-release tramadol in the control of moderate to moderately severe pain in adults requiring treatment over an extended time period. The author concludes that extended release tramadol has benefits that may merit its earlier use in the treatment of moderate to moderately severe chronic pain.

Parkinson's disease (PD) is a progressive neurodegenerative disorder that affects 1%–2% of adults over the age of 60. However, the number of affected people may be much higher because of the initial asymptomatic progression of the disease—60% of the dopaminergic neuron population in the CNS having already degenerated before the appearance of symptoms. PD is generally regarded as a dopamine deficiency disorder. The available therapeutic strategies mainly elevate the reduced levels of dopamine by utilizing different pharmacological mechanisms. However, none of these agents retards the progressive neurodegeneration associated with PD. Shimon Lecht and colleagues (2007) review the current treatment strategies for PD treatment with an emphasis on rasagiline, a novel selective and irreversible ropargylamine inhibitor of monoamnine oxidase B. It seems that this approach increases endogenous content of dopamine resulting in the reduction of PD symptoms. Unlike the prototypic monoamnine oxidase inhibitor selegiline; rasagiline is not metabolized to potentially toxic amphetamines.

Interestingly there is evidence that rasagiline and other propargylamines derivatives exhibit neuroprotective effects in different neuronal models of PD and this property appears to be independent of monoamnine oxidase B inhibition. The authors finish by emphasizing the need to further elucidate the pharmacological mechanism of action of propargylamines in order to gain better insight into neuroprotective pathways to permit identification of new pharmacological targets for the development of novel anti-PD drugs.

The chronic inflammatory skin disorder psoriasis is a significant problem affecting up to 2% of the global population with approximately 30% of patients suffering from psoriatic arthritis. The condition exhibits a spectrum of symptoms with milder forms controlled by topical skin treatment while therapy for moderate to severe forms consists of treatments associated with significant side effects. Psoriasis is an inflammatory autoimmune disease driven by inappropriate T cell activation. T cell activation requires a dual signal in which antigen presenting cells present antigen in association with the major histocompatibility class complex to the T cell receptor. Activation requires costimulatory signals which can be mediated by bridging of the lymphocyte function antigen (LFA)-3 on antigen presenting cells and CD2 on T cells. Alefacept is a novel dimeric human fusion protein consisting of the extracellular portion of the human LFA-3 fused to the Fc portion of immunoglobulin G. This construct effectively blocks the interaction between LFA-3 and CD2 thereby inhibiting the activation and proliferation of T cells. Jenneck and Novak (2007) have provided an interesting review on alefacep in the treatment of chronic plaque psoriasis. The authors report that alefacept represents a safe alternative therapeutic option for the treatment of patients with moderate to severe chronic plaque psoriasis with contraindications or resistance to traditional systemic therapies. However, they acknowledge limitations for the use of alefacept such as cost and the fact that a significant number of patients do not respond to treatment. The latter problem is compounded by the fact that several months of treatment are required before nonresponders can be identified. Moreover $CD4^+$ T cells are essential for normal immune responses; thus effective therapy requires monitoring of lymphocytes counts in addition to evaluation of potential signs of infections or malignancies during treatment with alefacept.

## References

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