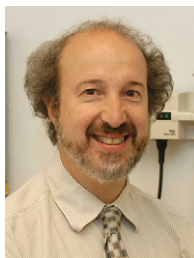


## Preface



Howard S. Smith, MD  
*Guest Editor*

Pain and suffering remain a significant dilemma. Pain continues to be among the most common reasons why patients seek medical attention (commonly for headache and back pain). Providing comfort and alleviation of pain and suffering remains a primary and crucial goal of patient care, as well as a great medical challenge. These issues of *Medical Clinics of North America, Pain Management* (Parts I and II), expose clinicians to a broad spectrum of available evaluation and management strategies.

The subjective nature of pain complaints, not uncommonly coupled with a lack of objective findings, continues to be troublesome for many clinicians who long for specific blood tests or imaging modalities that detect various pathophysiologies, in particular those which may help explain a patient's pain. Many physicians who are comfortable providing medical care to patients with hypertensive or diabetic issues do not have a similar level of comfort providing analgesia to patients with persistent noncancer pain.

In 2004, the American Society of Functional Neuroradiology (ASFNR) was founded to promote clinical applications of brain imaging techniques, such as magnetic resonance imaging (fMRI), positron emission tomography (PET), and an MRI method known as diffusion tensor imaging (DTI). It is hoped that these and other functional neuroradiologic techniques may eventually be clinically useful for patients suffering from pain and other symptoms.

In the Proceedings of the National Academy of Science (December 20, 2005), neuroscientists reported using fMRI to teach people with chronic

pain to monitor and control their own brain activity (in specific regions)—a high-tech version of biofeedback. Patients attempted to extinguish computer-generated flames, and the intensity of the flames reflected MRI neural activity in the patient's right anterior cingulate cortex (ACC)—a region implicated in pain perception. Patients who were best at quelling the flames (neural activity in the ACC), reported the most pain improvement after the session.

Using genetics in the assessment of pain and its treatment has only just begun. Waxman's group at Yale identified the first inherited painful neuropathy from a mutation producing a hyperpolarizing shift in activation and depolarizing shift in steady-state activation. Studies of families with autosomal dominant erythromelalgia (characterized by severe burning pain in the limbs in response to mild thermal stimuli or moderate exercise) have demonstrated mutations in *SCN9A*, the gene that encodes sodium channel Na(v)1.7 and which is selectively expressed within nociceptive dorsal root ganglion and sympathetic ganglion neurons. Other genetic analgesic treatment strategies may involve selectively dampening the expression of undesirable genes using RNA interference technologies. Future work may enable viral vectors to deliver small interfering (siRNA) molecules to reduce or eliminate mRNA with resultant long-term suppression of algia-promoting molecules.

It seems that the analgesic magic bullet is nonexistent, and the list of analgesic targets continues to grow. Future clinical analgesic strategies may include investigator-driven preclinical strategies, such as modulation of bidirectional communications between neurons and glia, ablation or inhibition of NK-1 expressing superficial dorsal horn cells, or intrathecal cytokine therapy or proteasome-induced inhibition of ubiquitination pathways.

Despite the explosion of preclinical research, the art of clinical pain medicine remains in its infancy. Optimally, individually designed mechanistic-based targeted analgesic treatments can be tailored for specific patients, thereby eliminating or reducing pain to minimal levels. Although clinicians remain limited in their ability to identify specific cellular/molecular mechanisms contributing to an individual patient's pain complaints, it is our hope that these volumes will help clinicians approach the evaluation and management of patients with persistent pain.

Howard S. Smith, MD  
*Albany Medical College*  
*Department of Anesthesiology*  
*47 New Scotland Avenue, MC-131*  
*Albany, New York 12208*

*E-mail address:* [SmithH@mail.amc.edu](mailto:SmithH@mail.amc.edu)