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## An introduction to the Biennial Review of Pain

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My pat response to queries from friends and colleagues outside of the pain field about life in the field, is to quote from Charles Dickens: “these are the best of times and the worst of times.” This response is generally prompted by my daily experience as a basic scientist reflecting on the contrast between the staggering potential of the sophisticated tools and techniques currently available and the ongoing struggles to secure funding needed to employ them. However, I find myself returning to this quote as I reflect on the broader issues associated with the study and management of pain so strikingly illustrated in the manuscripts in this volume. I had the pleasure of working with Judy Turner, the current President of the IASP, as well as the group of talented and dedicated individuals that made up the Scientific Program Committee who were charged with putting together a panel of experts who could speak to these broader issues in a manner that was at least close to representing the depth and breadth of the interests and passion of the members of the association. While this would have been a challenge had we even doubled the number of plenary and award lectures at the World Congress, as beautifully illustrated in the manuscripts in this volume, and the talks to be presented at the World Congress, I think we came close to meeting it.

With respect to the worst of times, one need look no further than the global burden of pain, as so succinctly documented in the article by Blyth and Schneider [3] who not only present data on the magnitude of the problem but also how this problem is exacerbated by the lack of a coherent global health policy. The deleterious impact of this lack of coherent global policy is further amplified by issues addressed in the articles by Ballantyne [1] and Goh and Lee [9]. That is despite the increased understanding of mechanisms that may contribute to the limited efficacy of opioids for the management of chronic pain in some individuals, if not a number of the more deleterious consequences of these compounds, as summarized by Ballantyne [1], we are reminded by Goh and Lee that of the 298.5 metric tons of morphine-equivalent distributed in the world, only 0.1 metric tons is distributed in low-income countries. Goh and Lee [9] highlight the impact of this disparity at the patient level with data from the Lancet Commission report on access to palliative care and pain relief, where only 5 mg of morphine-equivalent opioids are available per patient in need in Haiti compared to the 55,000 mg available to a patient in the US. In contrast, the response to the opioid crisis in the US not only stigmatizes pain, but is starting to limit access in situations where these drugs have utility.

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No conflicts.

The picture is not a lot brighter in the context of pain education where IASP members have long struggled to address the dearth of training health care professional receive in pain and pain management. As argued by Carr [5], this problem is exacerbated by the rejection of science that typifies the postmodern era, so blatantly on display by leaders around the world. On the other hand, appreciating context in which data were generated and may be implemented not only provides a framework for pain education, but can serve as the basis for strategies to address problem at local level, in particular, in low resource countries as detailed by Brandon and colleagues [4].

Despite the persistent barriers to pain education and management, these are also the best of times for a number of reasons so well illustrated in many of the articles in this volume. Several have detailed ways in which we will be able to, or better yet, already are taking advantage of therapeutic approaches currently available. For example, as Eccleston,7 points out, the number of psychology-based approaches currently available for the management of pain continues to grow, along with evidence for identification of patients who may be most responsive to a given intervention, despite the persistent lack of evidence in support of a variety of approaches. Within the bio-psycho-social view of pain, and the now well-established impact of the placebo effect on the efficacy of interventions, we now understand the mechanisms underlying this effect better than ever. Fields [8] has not only detailed these mechanisms, but summarized approaches being to developed to leverage these mechanisms to maximize the efficacy of the interventions currently available. Similarly, years of detailed analysis of factors that contribute to post-surgical pain, have enabled the identification of factors associated with the development of persistent pain after surgery. And while these data are only now being used in context of enhanced recovery from anesthesia protocols, Kehlet [10] describes how standardization of these protocols is paving the way for implementation of these data into tailored treatment programs.

What is particularly exciting about the current state of pain research is that we are finally starting to see a real pay-off from all the time and effort put into gaining a mechanistic understanding of pain. For example, as illustrated Krock and colleagues [11], our mechanistic understanding of the pain associated with rheumatoid arthritis has led to the generation of novel therapeutics. Interestingly, with a focus on pain mechanisms as opposed to the inflammatory processes per se, it is now possible to account for why some drugs work and others do not. And while it is clear from article by May [12] that there is still much to be resolved with the respect to mechanisms of craniofacial pain with it unique features that highlight the multiplicity of mechanisms contributing to these debilitating pain syndromes, migraine is yet another pain syndrome in which translational research has led to the generation of a new class of what appear to be highly effective drugs for at least a subpopulation of patients. Similarly, it is generally appreciated that exercise is good for a variety of health issues, including pain. However, as summarized by Sluka and colleagues [14] the identification of mechanisms contributing to the exercise-induced exacerbation of chronic pain as well as those underlying its efficacy as treatment, should enable health care professionals to further maximize the efficacy of this important therapeutic modality. Bennett and colleagues [2] have taken a different angle on the question of how to use what we already know to maximize the therapeutic efficacy of the approaches available. That is, they make a compelling case for why we don't have to wait for the implementation of the

future goal of truly personalized medicine, arguing that we can already use our mechanistic understanding of pain to identify and more effectively treat subpopulations of patients. Finally, while long overlooked as a barrier to implementation of effective management approaches, particularly with the focus on translation from pre-clinical models and the limited training health care professionals receive on pain and pain management, it is clear from the article from Chambers [6], the issue of knowledge translation, or the effective dissemination and implementation of new discoveries, may be just as, if not an even greater barrier to improvements in pain management. Importantly, with the variety of approaches now available to reach stakeholders critical for change (patients, health care professionals, administrators, policymakers), it is now easier than ever before to jump this gap.

Finally, as illustrated in several of the manuscripts in this volume, the power of the techniques and tools available for the study of biological processes is enabling us to address questions and establish causal links between processes that would have been considered impossible even 10 years ago. Optogenetics, or the use of light regulated ion channels, receptors, and pumps is one of the techniques that is having one of, if not the most transformative impacts in this context. Mickle and Gereau [13] have succinctly illustrated both the power and potential of this new tool. From a discovery perspective, this technology is enable the identification of the specific cell types responsible for a particular process. Even more excitingly, this technology holds the promise of the selective elimination of pain, enabling the silencing or activation of the cells responsible.

While it is clear that there remains a tremendous amount of work to done to achieve IASP's mission, it is also clear that there are many reasons to be optimistic about the potential for improved pain relief worldwide.

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