Dear Readers,

Every now and then I have a sleepless night. Not because I am ill or dealing with stress or problems but because I need time for reflection, time to think. During one of these insomniac nights I was thinking about the true meaning of the word Advances... What is it that makes something advanced or that something contributes to an advance? Is it only that it is new and previously unknown; is it because somebody looks at the old issues in a new way and with fresh understanding? And finally, can something belong to the category of advances because old knowledge and experience are finally implemented and accepted? Recently we had a vivid discussion about the introduction of buprenorphine patches in the hospice, the hospital and in the community. In my eyes this drug offers many new things and is a breath of fresh air in pain management. So, for me it is a true Advance. On the other hand, I was confronted with the inertness of the System and of so-called Evidence Based Medicine. Nobody knows how to implement this new and promising treatment. The drug may also, apart from its potential to control intractable pain, show some delayed toxicity. It is also not known how to give breakthrough medication. How much, what, and when? It is true that the evidence is very thin for this and that this is an argument for not implementing it. However, looking at the evidence of the breakthrough medication needed to back up the treatment with fentanyl patches, the situation was, and maybe still is, exactly the same. There is no direct evidence for this. When fentanyl patches were introduced some 15 years ago a patch of 25 mcg/hour was equal to 30–120 mg of oral morphine. An incredible range, you would think. Why? Because fentanyl was a different opioid working in a different (and not always clarified) way from morphine so it was (and it still is!) impossible to say that the 25 mcg/hour fentanyl patch is equal to, let us say, 60 mg of oral morphine. But the System could not absorb this kind of knowledge and translate it into comprehensive teaching that would guarantee safe prescribing. So what happened next? The System told us that we should choose one value instead of the range. Then, everything was simple again. The doses could be calculated and everybody was happy. Everybody? No, some patients were prescribed doses that were not enough to control their pain and some were given too much. I witnessed the deaths of several patients who could not cope with the opioid toxicity of fentanyl. But the system accepted this as true and declared it to be evidence. Oral morphine, to which everything is compared, is not exactly the same as buprenorphine and comparisons need to be done very carefully. Again, we do not know with what to combine buprenorphine and how to calculate the dose. The guidelines give variable doses. Again the system opposes implementation of this drug because things are not clear. We shall never make them clear without trying it. Once again the answer is in the philosophy. The breakthrough doses should be started low and increased if necessary. They should be titrated starting from the lower doses upwards. The doses may be very low, much lower than you would expect from traditionally calculating the equianalgesic dose of morphine and dividing it by 6. So be careful!

So, what is the Advance? The discovery of buprenorphine some 45 years ago? Its extraordinary safety profile or the successful implementation in clinics for the benefit of the patients? For me, advances are not moments in history that change the world but the processes they initiate and maintain. True advances will only be seen after decades and something that looked like an advance 15 years ago may now seem different when seen with new knowledge and experience.

In this edition of Advances, we present articles which, as a perfect mix of the new and old, cannot be taken as advances separately but may initiate processes that might lead to progress. One of the articles, written by my student, is on the discontinuation of opioids and how to do it safely when it is needed. The

guidelines are missing and the case report may be such a momentum that it initiates new thinking. The second article is completely different, on the basic aspects of endogenous opioids and opioid receptors. It paves the way to new thinking. Perhaps we do not yet understand what endogenous opioids have to do with the everyday symptoms we treat but the horizon is slowly becoming clearer. The third article is on gabapentin and pregabalin. Both drugs are now well known in palliative care and used mainly for indications other than those for which they were originally licensed. Analyzing the literature, I discovered that these two drugs, but mainly gabapentin, can be used not only for symptoms such as control of itch, sweating and hot flushes but also for restless legs and nausea. I analyzed and weighed the evidence about these applications and came to some surprising results. The fourth article is on the rare (in palliative care practice) syndrome of Churg-Strauss, which in this case presented like disseminated malignant disease. The last article is on something we know intuitively: that pain negatively influences the patient's quality of life. Extremely interesting is the article by Krajnik et al. on what the family members remember from the last months of their deceased relatives. I always was convinced that what we do for the dying people we do not only for them but even more for their relatives who will live with the memories and traumas acquired during this process. In my arrogance, I thought that this should not be an issue for research, as we have already known this for ages. Those who feel as arrogant as I did should read this article and they will perhaps change their minds. The relationship is not as straightforward as I thought and the article touches several different, previously unknown subjects.

Whether these articles are true Advances in palliative medicine, you should judge for yourself.

Zbigniew Zylicz
Vice Editor