

## Remembering Dr. Wilder Penfield

I enjoyed reading in the *CMAJ* about Dr. Blum's encounter with Dr. Wilder Penfield.<sup>1</sup> I recall first seeing Dr. Penfield in the cafeteria at the Royal Victoria Hospital when I was a medical student (probably around 1970) and being somewhat awed by his presence. I had read *The Second Career* a few years before, and I also knew him by reputation, through the media.

The memory that stands out most vividly is of attending grand rounds in the amphitheatre of the Montreal Neurological Institute sometime during 1975–1976, when I was a final-year radiology resident. I arrived late, just as the “patient,” an elderly man with a protuberant abdomen distending his dressing gown, got up from his wheelchair and began to describe the histology slides of his own untreatable abdominal sarcoma. When I realized that the patient was Dr. Penfield, the enormity of the moment struck me.

I admire Dr. Blum's maturity and self-confidence as an intern, in having been able to sit down and carry out a personal conversation with Dr. Penfield. Only after several years of medical practice did I reach the point where I became at ease when dealing with famous people and was able to see the common humanity that we all share.

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### Reference

1. Blum A. A bedside conversation with Wilder Penfield. *CMAJ* 2011;183:745-6.

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I wish to thank Dr. Blum for the delightful *CMAJ* article about a visit with Dr. Wilder Penfield.<sup>1</sup>

Now 87, I was a medical student at McGill University and graduated in 1949. I never met Dr. Penfield, but I occasionally watched him operate from behind the glass in the Montreal Neurological Institute, and of course I attended his seminars

there as well. I have only one story about the great man and it is this:

It often happened that there was some “visiting fireman” in town who would be asked to join the seminar and to speak to the students. On this occasion the guest was droning on about some topic when he suddenly said, “Isn't that so, Dr. Penfield?” All eyes turned to Dr. Penfield, and there he was, asleep.

I went on to become a general surgeon and well know what a late night in the operating room can do to one's concentration the next day, so I have every sympathy for what may have been a late night for him, too.

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### Reference

1. Blum A. A bedside conversation with Wilder Penfield. *CMAJ* 2011;183:745-6.

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## Recommendations for stroke: 2010

The inclusion of dabigatran in the 2010 Canadian guidelines for stroke care,<sup>1</sup> and more recently in the updated practice guidelines from the American College of Cardiology Foundation, American Heart Association and Heart Rhythm Association,<sup>2</sup> is important because of the need for an alternative to warfarin for anticoagulation in patients with atrial fibrillation.

In his interesting commentary in *CMAJ*, Rudd emphasizes that dabigatran is recommended for patients meeting the inclusion criteria of the RE-LY (Randomized Evaluation of Long term anticoagulant therapy) trial.<sup>3</sup> Rudd notices that this recommendation is made “despite a lack of data on the long-term safety and efficacy of this drug.” The guidelines appear to support the use of dabigatran as an alternative to warfarin without any restrictions. However, we expected a more critical update from the guideline developers on the RE-LY study that would have included some reservations about the use of this molecule.

First, Connolly and colleagues analyze their data under the intention-to-treat principle.<sup>4,5</sup> In this specific case, because the analysis does not take into account the number of dropouts in the patient groups, it overestimates the effects of dabigatran by 4% to 11% for embolic or hemorrhagic cerebrovascular or transient ischemic attack. This observation is important given that dropout rates are higher in the groups receiving dabigatran (21%) than in those receiving warfarin (16%). On the contrary, analysis based on the number of patients who completed the study shows some modification of these results: the result for non-specific ischemia, dabigatran 150 mg v. warfarin, becomes nonsignificant (rate ratio [RR] 0.82, 95% confidence interval [CI] 0.64–1.05); the result for myocardial infarction becomes significant in favour of warfarin in comparisons of dabigatran 110 mg v. warfarin (RR 1.44, 95% CI 1.04–1.99) and dabigatran 150 mg v. warfarin (RR 1.49, 95% CI 1.07–2.49); and the result for hospital admissions becomes nonsignificant when comparing dabigatran 110 mg v. warfarin (RR 0.99, 95% CI 0.95–1.03).

Second, the RE-LY study shows that dabigatran requires an acid environment for absorption; hence, the addition of an acidifying agent is required to allow absorption, and this is what seems to cause dyspepsia and eventually hemorrhage with that molecule. Yet Connolly and colleagues present the results in patients with and without a proton pump inhibitor (PPI).<sup>5</sup> Analysis of these results shows a marked reduction in the effectiveness of dabigatran 150 mg when taken with a PPI (RR 0.94, 95% CI 0.56–1.58). This is a predictable result, given the mechanism of action of PPIs. Thus, a warning should be issued about the use of dabigatran in patients taking a PPI until there are controlled studies that show its effectiveness under this condition. The use of PPIs and any antacids to prevent dyspepsia secondary to dabigatran should also be discouraged.

Out of concern for scientific rigour and to protect patients, we believe a warning about the use of dabigatran should be included in the recommenda-