WriteClick: Editor's Choice

Editor's Note: This is the first issue of Write*e*Click™: Editor's Choice, where we print selected Write*e*Click submissions previously posted online. Here, we feature Michael Swash's comments on Michael Brooke's farewell as Editor of the Humanities section and an exchange related to dermal nerve morphometry. We were gratified by the rapid use of Write*e*Click: over 28 responses in 6 days. Please keep the comments coming: submit a question, a musing, or a case of your own. For quick access, click on the Write*e*Click link on the home page of www.neurology.org or, if using the *Neurology*® *iPad*® app, tap the "Write*e*Click! Post comments now" button on any *Neurology* article.

—Robert C. Griggs, Section Editor

We also call your attention to important comments posted only online by Papadimas et al. and Puwanant concerning Pompe disease (Making diagnosis of Pompe disease at a presymptomatic stage: To treat or not to treat? Neurology 2011;77:594–595) and Dr. Hess on the article by Strupp et al. (Strupp M, Kalla R, Claassen J, et al. A randomized trial of 4-aminopyridine in EA2 and related familial episodic ataxias. Neurology 2011;77:269–275). The authors' responses also merit your review.

LOVE LIES BLEEDING—THOSE WHO ARE LEFT BEHIND SALUTE YOU

Michael Swash, London: When a last communication appears, a valediction is tempting; but can it really be the last?[1] Writers never stop; they just keep thinking of something else to say. So the lies component of Mike Brooke's "last column" is easily understood. As for his affair with the English language, well, that is readily understood. Some of us brought up with British English, rather than some form of the language subtly altered by other cultures—for example, India, Africa, Asia, and the West Indies—find prose composition in the modern idiom difficult. The latter might loosely be described as Alastair Cooke land—that is, somewhere in the shipping lanes of the north Atlantic east of New York and west of Bristol. For British English speakers, the true form of the language peaked with Jane Austen; beautiful syntax, lots of commas, complex tense structures, and absolutely never an adjectival noun, and also not the overcomplexity of Henry James or his Harvard philosopher brother. The founding fathers of the American republic themselves wrote in a spare and beautiful eighteenth-century English that was the then universal style for all English speakers, before the culture was unexpectedly enriched by diversity. But still it is hard to write in that short-sentenced style that is the current norm. And the best and most mellifluous English is still that spoken and written by the southern Irish. So I suspect, Mike, you will keep on trying. We don't wish to be left bleeding.

1. Brooke M. Love, lies, bleeding. Neurology 2011;76:2046–2047.

MORPHOMETRY OF DERMAL NERVE FIBERS IN HUMAN SKIN

Herbert Schaumburg, Joseph Arezzo, New York, NY: "Morphometry of dermal nerve fibers in human skin"[1] is the first comprehensive analysis of nerve fibers in both the dermal and the intraepidermal portions of 3-mm punch biopsies using widely available laboratory techniques. Expanding the analysis of skin biopsies to include dermal as well as intraepidermal regions might allow 1) examination of longer segments of axons in addition to measures of fiber density, 2) expansion of the range of axon types measured, including larger diameter fibers and axons that innervate mechanoreceptors and sweat glands, and 3) comparison of changes in the distal limb extreme axon terminals with those in more proximal regions.

The report provides clear evidence that the assessment of dermal nerve fibers is feasible; it uses 3 quantitative measures: length of dermal nerve fibers, the fibers per mm of epidermis, and fibers per area of dermis. The values obtained from the dermal tissue highly correlate with measures of intraepidermal fiber density. Although these findings demonstrate the feasibility of the assessment of dermal nerve fibers, the authors neither provide nor claim any direct evidence that dermal measures currently add to the

diagnostic value of the established epidermal endpoints. Their data suggest that approximately 1 in 4 subjects with epidermal measures below the 5th percentile for age had normal dermal assessment, and the 1 in 5 subjects with no history or evidence of neurologic disease, with normal nerve conduction velocity and with normal epidermal fiber density, had significant deficits in their dermal measures. Using the epidermal values as a gold standard is potentially problematic, as it is possible that the dermal measures are in fact more accurate. What the article does not explore is the possibility that there would be significant deficits in the dermal measures in the subjects with less severe changes in the epidermal assessments (e.g., less than 25th percentile).

Commendably, the authors do not overstate the significance of their findings. The final sentence states "We provide a reliable method to quantify the innervations density of dermal nerves that might improve the diagnostic yield of skin biopsy." This meticulous study has established normative data for dermal fiber numbers and provided guidance on the proper zones for analysis; it should serve as a catalyst for further studies to expand the diagnostic yield of this simple biopsy technique.

Author Response: Giuseppe Lauria, Catharina G. Faber, Ingemar S.J. Merkies, Milan, Italy: We thank Drs. Schaumburg and Arezzo for their comments on our article. Skin biopsy has become a widely available tool to investigate small nerve fiber degeneration in peripheral neuropathies. After its introduction in clinical practice (about 15 years ago), most studies in this field focused on the quantification of intraepidermal nerve fiber density (IENFD), providing normative reference values[2] and evidence of excellent diagnostic yield in small fiber neuropathy (SFN).[3,4] Previous studies suggested that dermal nerve fiber quantification might increase the diagnostic spectrum. Our results showed significant correlation between dermal nerve morphometry and IENFD, high performance in distinguishing SFN from healthy individuals, and mainly emphasizing the methodologic background of this new approach. Indeed, we did not test whether the combination between IENFD and dermal nerve morphometry, or this latter alone, would increase the diagnostic value in patients with possible/probable SFN (e.g., with less severe changes in IENFD). The reliability of our method could be analyzed only in a homogeneous group of patients with definite SFN (having abnormal IENFD). IENFD remains the gold standard in defining SFN, as recently demonstrated in patients carrying novel sodium channel mutations.[5] We hope that our findings will prompt new studies on dermal nerve morphometry to define its role in peripheral neuropathies.

1. Lauria G, Cazzato D, Porretta-Serapiglia C, et al. Morphology of dermal nerve fibers in human skin. Neurology 2011; 77:242–249.
2. Lauria G, Bakkers M, Schmitz C, et al. Intraepidermal nerve fiber density at the distal leg: a worldwide normative reference study. J Peripher Nerv Syst 2010;15:202–207.
3. Lauria G, Hsieh ST, Johansson O, et al. European Federation of Neurological Societies/Peripheral Nerve Society guideline on the use of skin biopsy in the diagnosis of small fiber neuropathy. J Periph Nerv Syst 2010;15:79–92.
4. Tesfaye S, Boulton AJ, Dyck PJ, et al. Diabetic neuropathies: update on definitions, diagnostic criteria, estimation of severity, and treatments. Diabetes Care 2010;33: 2285–2293.
5. Faber CG, Hoeijmakers JGJ, Cheng X, et al. Gain-of-function NaV1.7 mutations in idiopathic small nerve fiber neuropathy. Ann Neurol Epub 2011 May 20.

Author disclosures are available upon request (journal@neurology.org).