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Editors' Note: Neurophobia may explain why medical students avoid neurology training, Sethi suggests. Zuzuárregui and Hohler, authors of "Comprehensive Opportunities for Research and Teaching Experience (CORTEX): A mentorship program" agree and believe early exposure to neurology may spark medical students' interest in the field. Lavi critiques the "Prevalence and distribution of VZV in temporal arteries of patients with giant cell arteritis" study. He notes, among other observations, that VZV antibodies bind nonspecifically to smooth muscle and skeletal muscle cells. Gilden et al. disagree with Lavi and rebut his comments.

—Chafic Karam, MD, and Robert C. Griggs, MD

COMPREHENSIVE OPPORTUNITIES FOR RESEARCH AND TEACHING EXPERIENCE (CORTEX): A MENTORSHIP PROGRAM

Nitin K. Sethi, New York: I read with interest about the Comprehensive Opportunities for Research and Teaching Experience (CORTEX) mentorship program and how it helped increase student recruitment into neurology at the authors' institution.[1] Low medical student recruitment into neurology results in inadequacy of the neurology workforce and this has become a worldwide problem.[2] In the United States, neurology residency attracts far fewer medical students compared with dermatology and radiology, which are now the most sought-after and competitive residencies. In India, out of my class of 180 students, only 3 (including myself) joined the neurology family. Commonly cited reasons why medical students opt out of neurology are that they find it difficult to comprehend (neurophobia) and there is a perception that the field has little to offer in the way of active therapeutics as most diseases are degenerative. An active and longitudinal mentorship program that exposes medical students to various aspects of neurology, including acute inpatient management of neurologic emergencies such as stroke, status epilepticus, and traumatic brain injuries, while offering research and teaching opportunities will help the neurology family grow and flourish by attracting talented physicians.

Author Response: Jose Rafael P. Zuzuárregui, Anna D. Hohler, Boston: We thank Dr. Sethi for his comments on our article.[1] We agree that neurophobia is a barrier to recruitment of medical students into neurology. A study focusing on medical student attitude towards and comfort with neurologic disease and examination demonstrated that these shortcomings were, in part, due to insufficient exposure.[3] By exposing students to the field of neurology early in their careers, we offer students early and frequent exposure to the field, allowing them opportunity to wrestle with and overcome these perceived shortcomings through interaction with faculty.[1] We hope that our program can be implemented at other institutions with similar success.

1. Zuzuárregui JR, Hohler AD. Comprehensive Opportunities for Research and Teaching Experience (CORTEX): a mentorship program. Neurology 2015;84:2372–2376.
2. Larsen DP, Santini VE. Increasing student recruitment into neurology: joining the family. Neurology 2015;84:2302–2303.
3. Zinchuk AV, Flanagan EP, Tubridy NJ, et al. Attitudes of US medical trainees towards neurology education: "neurophobia": a global issue. BMC Med Educ 2010;10:49.

PREVALENCE AND DISTRIBUTION OF VZV IN TEMPORAL ARTERIES OF PATIENTS WITH GIANT CELL ARTERITIS

Ehud Lavi, New York: I read with interest the article by Gilden et al.,[1] but found myself questioning the reported findings and conclusions.

The immunohistochemistry describing the presence of varicella-zoster virus (VZV) protein in the majority of temporal artery biopsies of patients with giant cell arteritis (GCA) is intriguing. However, the findings of VZV antigen staining in the vessel wall, mostly in smooth muscle cells, was not addressed by the authors in other arteries or in other smooth muscle cells.

In my experience, the VZV antibodies bind nonspecifically to smooth muscle and skeletal muscle cells, and therefore can be detected in similar frequencies in GCA cases, non-GCA temporal arteries, any other arteries, or even in endometrial leiomyoma. The detection of this staining pattern, similar to the one described,[1] is seen without surrounding inflammatory response, supporting the idea that it is not a true

viral infection. The lack of VZV myositis cases in the literature—other than vasculitis affecting muscle cases—also negates the suggestion that VZV has affinity for skeletal muscle.

The tissue preservation of the electron microscopy described in the article was poor and hinders the interpretability of such a specimen.

The VZV DNA analysis presented, which appears at a lower rate than antigen detection regardless of a higher sensitivity, may be a reflection of latent VZV in peripheral nervous system or endothelial cells and not a reactivated VZV producing proteins.

Thus, the conclusion of a potential cause and effect relationship between VZV and giant cell/temporal arteritis cannot be easily derived from this investigation.

Author Response: Don Gilden, Maria Nagel, Teresa White, Aurora, CO; Charles Grose, Iowa City: Dr. Lavi incorrectly commented that we reported most VZV antigen staining in smooth muscle cells.[1] Our Abstract and Results state that most VZV antigen was found in adventitia of GCA-positive temporal arteries (TAs), followed by media, then intima.

Most importantly, if our VZV antibodies were nonspecifically staining an antigen in smooth muscle cells, then all smooth muscle in every TA and control cadaveric cerebral artery should be positive, which was not the case. Furthermore, in experimentally infected cadaveric arteries, our anti-VZV antibodies react only with VZV in infected adventitia, never with smooth muscles cells in the media. Finally, in 26% of GCA-positive TAs, no viral antigen was detected, and even in most GCA-positive TAs that contained VZV antigen, virus was not found diffusely in the artery, rather in skip areas, and almost always adjacent to pathology.

With further assertion about specificity of VZV antigen staining, 2 different mouse anti-VZV monoclonal antibodies and one rabbit anti-VZV antibody were used for immunodetection. One anti-VZV monoclonal antibody (called 3B3; figure 2, D and E[1]) has been extensively characterized; its epitope and its binding affinity to its epitope have been defined. In studies dating back to 1983, no nonspecific reactivity of this antibody to other viruses or other human tissue, including muscle, was seen.

Dr. Lavi also noted lack of VZV myositis cases in the literature, but failed to recognize the important detection of VZV in skeletal muscle adjacent to GCA-positive TAs. As pointed out in our Discussion, the presence of VZV in skeletal muscle is likely due to the fact that the mammalian superficial TA is richly innervated and nociception in connective tissue of the temporalis muscle is relayed by afferent fibers with cell bodies in the trigeminal ganglia from which VZV reactivates. Interestingly, approximately 40% of patients with GCA have a history of polymyalgia rheumatica. Since muscle biopsy is not usually performed in these patients, the frequency of VZV infection is unclear.

Although formalin-fixed, paraffin-embedded TAs were studied, both transmission and scanning EM revealed well-delineated herpesvirus particles in the same area that stained with anti-VZV antibody.

Despite fixation, we found VZV DNA in many slides that contained VZV antigen. Dr. Lavi is wrong that VZV is latent in endothelial cells; it is not. The only place in the peripheral nervous system that contains latent VZV is ganglia, where VZV expression is restricted. Our detection of VZV antigen, VZV DNA, and varicella-zoster virions in TAs indicate productive infection.

1. Gilden D, White T, Khmeleva N, et al. Prevalence and distribution of VZV in temporal arteries of patients with giant cell arteritis. Neurology 2015;84:1948–1955.

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