The key and critical objectives of STUDENTJAMA addressed the emerging emphasis on evidence over opinion. To remove STUDENTJAMA from the journal in the interest of “incorporating high-quality articles” misses the function of the section. Students, of course, will rarely publish research of the type and quality demanded by the pages of JAMA, but what students bring is as important. Students write and speak of the ideals of medicine, of their hope for the best patient care, of their struggles to forge new identities as healers. And in the process of exchanging ideas over the pages of JAMA, we believe that medical students offer our senior colleagues a chance to reflect on their own work as a physician.

For a generation, JAMA saw these attributes as central to its mission. Indeed, they align well with 3 of JAMA’s 9 objectives: to foster responsible and balanced debate on issues that affect medicine and health care, to anticipate important issues and trends in medicine and health care, and to inform readers about nonclinical aspects of medicine and public health, including the political, philosophic, ethical, legal, environmental, economic, historical, and cultural.

Medical students will benefit from JAMA’s development of an elective in medical journalism and enriched manuscript review for student research submissions. These enhancements are appropriate and important, but they in no way speak to the void left by removing a student section from JAMA. We regret this decision.

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In Reply: We appreciate the recognition by Dr Palmer and Ms Martin that our decision to incorporate articles by medical students into JAMA with those of all other authors addresses the “emerging emphasis on evidence over opinion.” However, our encouraging submission of evidence-based manuscripts (as we do evidence-based practice) from all authors does not eliminate our continued interest in publishing well-thought-out opinion articles. We encourage submission of such manuscripts from any JAMA reader, including medical students, and will continue to publish special communications, commentaries, A Piece of My Mind, and poetry.

We believe that, with a little extra assistance, medical students can and will be able to publish all types of articles in JAMA. Since publication of our editorial, we have accepted 2 research papers in which medical students are the first author. In addition, we have had a number of inquiries and submissions from medical students, as well as inquiries about the medical student elective in medical journalism.

We ask Palmer and Martin to have patience and let the evidence prove which is the more beneficial method for medical students to have a forum for their work.

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RESEARCH LETTER

Age-Related Testosterone Depletion and the Development of Alzheimer Disease

To the Editor: Normal male aging is associated with declines in serum levels of the sex steroid hormone testosterone, which contributes to a range of disorders including osteoporosis and sarcopenia.1 Unknown is how this relationship applies to age-related disorders in the brain, an androgen-responsive tissue. We hypothesize that testosterone levels in the brain are depleted as a normal consequence of male aging and that low brain levels of testosterone increase the risk of developing Alzheimer disease (AD). Recent data suggest a correspondence between reduced serum levels of testosterone and the clinical diagnosis of AD.2,3 However, it is unclear whether testosterone depletion contributes to or results from the disease process. To investigate this issue, testosterone and estradiol levels were analyzed in postmortem brain tissue of elderly men and compared with their neuropathological diagnoses.

Methods. Brain tissue from men who had provided informed consent was collected at autopsy by repositories associated with Alzheimer’s Disease Research Centers at University of Southern California; University of California, Irvine; University of California, San Diego; and Duke University. Tissue was collected between 1997 and 2003, with postmortem delay less than 8 hours (mean delay = 4.6 hours). Subjects with conditions associated with altered testosterone levels (eg, end-stage renal disease, liver disease, alcoholism, and diabetes) were excluded from the study. Included subjects satisfied 1 of the following neuropathological diagnoses: (1) neuropathologically normal (controls) (Braak stage 0–1 without evidence of other degenerative changes, and lacking a clinical history of cognitive impairment; n = 17), (2) AD (Braak stage 5–6 with neuropathological diagnosis of AD in the absence of other neuropathology; n = 19), and (3) mild neuropathological changes (Braak stage 2–3 in the absence of discrete neuropathology; n = 9). No subjects were neuropathologically diagnosed with Braak stage...
Men in the 3 groups were of similar age, ranging from 50 to 97 years who were diagnosed as neuropathologically normal, mild neuropathological changes, or moderate to severe AD. For testosterone levels, $P<.05$ is the comparison of age-matched controls vs subjects with MNC and of age-matched controls vs subjects with AD by $t$ test following analysis of covariance with age as a covariate. Error bars indicate SEM.

Comment. Brain levels of testosterone significantly decrease with age in men who lack any evidence of neuropathology, suggesting that neural androgen depletion is a normal consequence of aging. In comparison with the control subjects, men with AD exhibit significantly lower testosterone levels in the brain. In contrast, the data suggest that estrogen levels in the male brain are affected by neither advancing age nor AD diagnosis. Notably, testosterone depletion likely precedes and thus may contribute to rather than result from the development of AD, since low brain testosterone is observed in men with early indications of AD neuropathology. Although it remains possible that low testosterone may reflect an unmeasured correlate of AD rather than be a contributing factor, we controlled for established causes of low testosterone by our exclusion criteria and statistical adjustment. How testosterone depletion may contribute to AD development is unknown. However, we have recently reported that androgen depletion in male rodents increases brain levels of $\beta$-amyloid, the protein implicated as a causal factor in AD pathogenesis, and decreases neuronal survival upon exposure to toxic insult. Collectively, these findings suggest that normal, age-related testosterone depletion in the male brain may impair beneficial neural actions of androgens and thereby act as a risk factor for the development of AD.

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