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<http://dx.doi.org/10.1016/j.mayocp.2012.07.012>

In reply: We thank Dr Redegeld and colleagues for their thoughtful letter in response to our original article on the use of nonclonal serum immunoglobulin free light chains (FLCs) to predict overall survival in the general population.¹ The authors introduce several interesting hypothesis-generating concepts regarding potential mechanisms and associations between excess serum immunoglobulin FLCs and inflammation. Works such as theirs may bring further meaning to our observation that excess FLC is associated with poorer survival outcomes in the general population, clarifying whether FLCs are merely markers for more ominous events or whether they actually contribute to pathology.

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1. Dispenzieri A, Katzmann JA, Kyle RA, et al. Use of nonclonal serum immunoglobulin free light chains to predict overall survival in the general population. *Mayo Clin Proc*. 2012;87(6):517-523.

<http://dx.doi.org/10.1016/j.mayocp.2012.07.011>

Changes in Serum Prostate-Specific Antigen Levels

To the Editor: I would like to comment on the study by Jacobsen et al¹ published in the January 2012 issue of *Mayo Clinic Proceedings* that documented the changes in

serum prostate-specific antigen (PSA) values in a large group of men. The authors determined that the median annual change in PSA was about 4.8%, while the 95th percentile for PSA increase was about 50%. Interestingly, while the baseline PSA values and the absolute increases in PSA values increased with age, the increases in PSA were relatively constant across all ages when expressed as a percentage of the baseline value. They propose that PSA velocity, expressed as a percentage increase over the baseline PSA, may have more utility as an indication for biopsy than using a fixed annual increase in PSA. For example, men in their 50s had a median baseline PSA of 0.9 ng/mL, so the 95th percentile increase would be about 0.45. For men in their 70s, with a median baseline PSA of 2.1, the 95th percentile increase would be about 1.05. These examples show how using a percent increase in PSA as a biopsy threshold might prove more adaptive to age-related variations than using a fixed absolute annual increase of 0.75 points, as has been proposed in the past.

Much work needs to be done in this area to validate these findings. Many physicians will choose to follow the reasonable recommendation of the US Public Health Service not to screen for PSA in any category of healthy men until stronger evidence of benefit emerges.² But for those who believe that there is a useful signal buried in all the noise of PSA measurements, perhaps this study is the first step in developing a prostate cancer screening algorithm that will prove robustly beneficial for men across a range of ages and baseline PSA values. As a primary care physician who is stubbornly biased in favor of PSA testing, I would be interested to see further research into the utility of adaptive algorithms when testing PSA.

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2. US Preventive Task Force. Screening for prostate cancer. <http://www.uspreventiveservicestaskforce.org/prostatecancerscreening.htm>. Accessed August 28, 2012.

<http://dx.doi.org/10.1016/j.mayocp.2012.07.014>

In reply: We thank Dr Keller for his comments regarding our study of longitudinal changes in serum PSA levels published in the January 2012 issue of *Mayo Clinic Proceedings*.¹ As Dr Keller notes, our article shows that using changes in serum PSA levels expressed as percent change per year yields more stable findings across different ages and also provides a nomogram to aid clinicians in interpreting changes in serum PSA levels observed in a normal clinical practice. Much controversy currently surrounds the use of serum PSA measurements, and while PSA is not a perfect test, at this time it is still the only widely available option for screening for prostate cancer. Using a single cut point for serum PSA level or changes in serum PSA level irrespective of age or baseline PSA level has often been noted as a drawback of using serum PSA testing.^{2,3} In order to prevent PSA history from repeating itself, either in the continued use of serum PSA measurements or in the development of future prostate cancer biomarkers, it is important to focus on an algorithm that is robust across different ages and baseline levels.

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1. Jacobsen SJ, Jacobson DJ, McGree ME, et al. Sixteen-year longitudinal changes in serum prostate-specific antigen levels: the Olmsted County study. *Mayo Clin Proc*. 2012;87(1):34-40.
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<http://dx.doi.org/10.1016/j.mayocp.2012.07.013>

Levamisole Toxicity

To the Editor: The review of levamisole toxicity by Lee et al¹ published in the June 2012 issue of *Mayo Clinic Proceedings* does not mention leukoencephalopathy as a well-