

## C1 Inhibitor Therapy and Hereditary Angioedema

*To the Editor:*

We read with interest the recent report by Bork and Hardt<sup>1</sup> and would like to pose our thoughts to the authors. Certainly, a finding of increased attack frequency in hereditary angioedema patients being treated with C1 inhibitor (C1 INH) therapy is interesting and merits further study. However, a 3-subject review that preselects those patients with severe disease requiring C1 INH therapy on demand versus a retrospective historical control group that has never required any prophylactic therapy may not be the most ideal comparison. Many authors have noted that the disease has a tendency to wax and wane, and this selection may have chosen 3 patients whose conditions became somewhat more severe. Given the inherent variability in this disease, we believe a study to prospectively compare treated and untreated individuals over decades would require a large, stratified sample and validated study instruments. Perhaps there is another explanation to these patients' outcomes.

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**Conflict of Interest:** Ira Kalfus was Vice President of Medical Affairs for Lev Pharmaceuticals and is a consultant for ViroPharma Incorporated and an advisor to the US Hereditary Angioedema Association. Michael Frank has served as a consultant to LEV Pharmaceuticals (now ViroPharma Incorporated), CSL Behring, Jerini AG, and Dyax Corp, has chaired the data safety monitoring board for Dyax Corp, and received research funding from LEV Pharmaceuticals.

**Authorship:** Both authors had access to the data and had a role in writing the manuscript.

The authors state that C1 inhibitor treatment was “always effective” and that patients treated with C1 INH were reported to experience considerably shorter attacks, almost no further severe attacks, and no loss of treatment efficacy while treated with the C1 INH concentrate. The dose given to these women was 500 Units per attack (except for 1 patient who received 1000 Units for 5 individual attacks over a 3-year period). We would postulate that these 3 patients' disease states evolved as they aged—experiencing more frequent attacks and requiring additional therapy to stabilize their disease. Perhaps these patients are candidates for routine prophylaxis with C1 INH 1000 U every 3-4 days, which was recently approved in the United States. This regimen might serve to alleviate their symptoms and best control their hereditary angioedema, preventing further attacks.

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## Reference

1. Bork K, Hardt J. Hereditary angioedema: increased number of attacks after frequent treatments with C1 inhibitor concentrate. *Am J Med.* 2009;122:780-783.