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## **Clinical consequences of endogenous and exogenous glucocorticoid excess**

Broersen, L.H.A.

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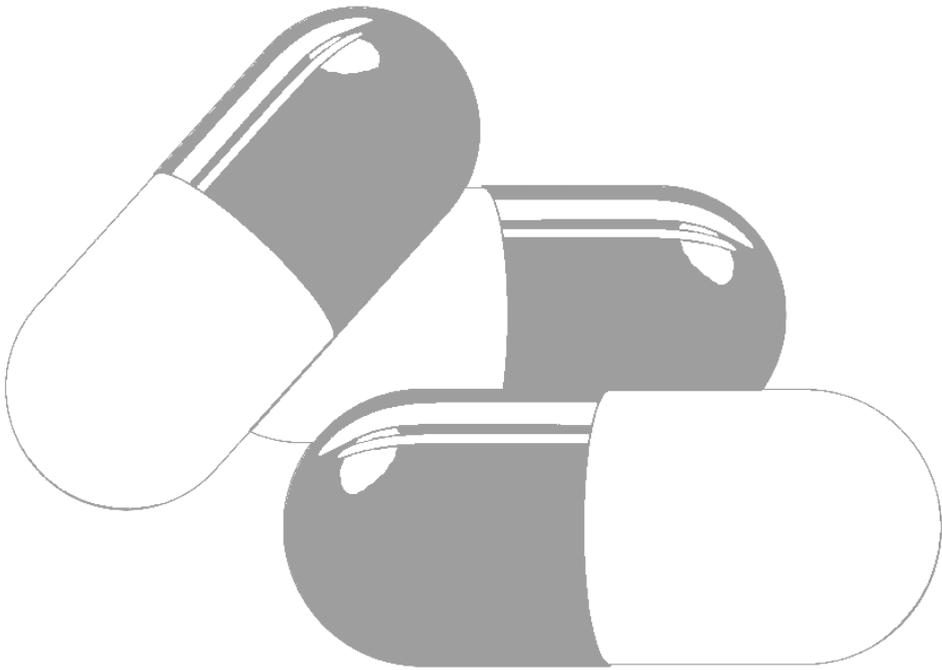
**Author:** Broersen, L.H.A.

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# Appendix II

Response to the Letter by Lindholm, *et al.*



Leonie H. A. Broersen, Alberto M. Pereira, Jens Otto L. Jørgensen,  
and Olaf M. Dekkers

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We thank Dr. Lindholm for his interest in our paper and for drawing attention to two important issues: first, the definition of adrenal insufficiency; and second, the association between the result of a biochemical test for adrenal insufficiency and the need for hormone replacement.

Adrenal insufficiency could be defined as insufficient cortisol secretion in response to stress, of which medical emergencies clearly pose the highest risk. At present we can only assess adrenal function through biochemical measurements and dynamic tests. It is well known that no test – including the ACTH test – is infallible. It might also be that tests perform differently according to the specific condition (pituitary or adrenal disease, glucocorticoid users, patients on intensive care, etc.). Also, cutoff values can be debated (1). When performing a systematic review, one has to be pragmatic, and it is an empirical fact that the ACTH test is the most frequently used; for that simple reason, our study relies largely on the ACTH test.

We fully agree that an inadequate response to the ACTH test does not automatically demand glucocorticoid replacement. For good reasons, there are limited data on the risk of glucocorticoid not being replaced, and pharmaco-epidemiological studies should therefore be undertaken to address this important clinical issue. For the time being, the decision about glucocorticoid replacement is therefore at the discretion of the physician in charge.

The main clinical message from our study is that some degree of secondary adrenocortical failure is detectable in many former glucocorticoid users (2). This is the reason that in glucocorticoid users admitted to the intensive care unit, high-dose glucocorticoid replacement is started immediately (3). But we argue that knowledge of this risk is also of relevance apart from the medical emergencies because adrenal insufficiency is directly related to a decreased quality of life, which will improve after substitution. Awareness of this risk in glucocorticoid users is important, given the high prevalence of such users and the nonspecificity of symptoms of adrenal insufficiency that can be difficult to disentangle from symptoms of underlying diseases or treatment. Physicians should therefore utilize a low threshold to test for adrenal insufficiency in glucocorticoid users, although these tests are not perfect.

## References

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