

# Differentiation of pathologic/neoplastic hypercortisolism (Cushing syndrome) from physiologic/non-neoplastic hypercortisolism (formerly known as Pseudo-Cushing syndrome): response to Letter to the Editor

James W Findling<sup>1</sup> and Hershel Raff<sup>2</sup>

<sup>1</sup>Endocrinology Center and Clinics, Medical College of Wisconsin, Menomonee Falls, Wisconsin, USA and

<sup>2</sup>Departments of Medicine, Surgery, and Physiology, Medical College of Wisconsin and Endocrine Research Laboratory, Aurora St Luke's Medical Center, Aurora Research Institute, Milwaukee, Wisconsin, USA

Correspondence should be addressed to J W Findling  
**Email**  
[james.findling@froedtert.com](mailto:james.findling@froedtert.com)

We apologize for the misleading statement in our article. Plasma corticotropin-releasing hormone-binding protein (CRH-BP) is detectible in pregnant women but declines towards the end of the third trimester (1). To quote from our reference 67 (2), 'We conclude that most of the increased plasma CRH found in pregnant women is bound to CRH-BP, and so is inactive, therefore, plasma ACTH levels do not increase to above the normal range.' Interestingly, as outlined in our reference 69 (3), the lack of a major effect of placental CRH on maternal ACTH secretion during most of pregnancy may also be due to desensitization of the maternal pituitary in addition to binding of CRH to CRH-BP, although others have suggested that placental CRH may be important in the control of the hypothalamic-pituitary-adrenal axis as well as other adaptations in women during pregnancy and parturition (3, 4). It is clear that the role of CRH during pregnancy and parturition is deserving of further research. Thank you for the opportunity to clarify our article.

#### Declaration of interest

The authors declare that there is no conflict of interest that could be perceived as prejudicing the impartiality of this article.

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#### References

- 1 Linton EA, Perkins AV, Woods RJ, Eben F, Wolfe CD, Behan DP, Potter E, Vale WW & Lowry PJ. Corticotropin releasing hormone-binding protein (CRH-BP): plasma levels decrease during the third trimester of normal human pregnancy. *Journal of Clinical Endocrinology and Metabolism* 1993 **76** 260–262. (<https://doi.org/10.1210/jcem.76.1.8421097>)
- 2 Suda T, Iwashita M, Tozawa F, Ushiyama T, Tomori N, Sumitomo T, Nakagami Y, Demura H & Shizume K. Characterization of corticotropin-releasing hormone binding protein in human plasma by chemical cross-linking and its binding during pregnancy. *Journal of Clinical Endocrinology and Metabolism* 1988 **67** 1278–1283. (<https://doi.org/10.1210/jcem-67-6-1278>)
- 3 Thomson M. The physiological roles of placental corticotropin releasing hormone in pregnancy and childbirth. *Journal of Physiology and Biochemistry* 2013 **69** 559–573. (<https://doi.org/10.1007/s13105-012-0227-2>)
- 4 Sasaki A, Shinkawa O & Yoshinaga K. Placental corticotropin-releasing hormone may be a stimulator of maternal pituitary adrenocorticotropic hormone secretion in humans. *Journal of Clinical Investigation* 1989 **84** 1997–2001. (<https://doi.org/10.1172/JCI114390>)

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