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# Analysis and validation of a new extended method for estimating plasma free cortisol including neutrophil elastase and competition from other steroids

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## Abstract

A non-linear mechanistic model for the distribution of cortisol in plasma on free and bound forms is proposed. The influence of progesterone, testosterone and neutrophil elastase on the cortisol distribution in the blood is investigated.

The activity of neutrophil elastase is directly included in the model with the concentration of elastase and the kinetic constants describing the activity of elastase collected in one single input variable. The model is very sensitive towards this input variable and fits data excellently, when it is allowed to be subject specific.

The analysis shows that steroids such as testosterone with low affinity for corticosteroid-binding globulin (CBG) do not significantly influence the concentration of free cortisol. Progesterone has a high affinity for CBG, but low plasma concentrations compared to cortisol. Contrary to expectations, progesterone is shown to impact the distribution of cortisol in plasma both under circumstances with high levels as seen in pregnancy and during the normal menstrual cycle of women.

Comparing the predictions of our model with predictions made with the equilibrium models by Coolens et al. [1], Dorin et al. [2] and Nguyen et al. [3] shows that the models differ considerably not only in their predictions for free cortisol, but also for cortisol on bound forms; i.e. bound to albumin, intact CBG and elastase-cleaved CBG.

Disregarding some of the smallest terms of the model equations a reduced version of the model in form of a fourth order polynomial equation is

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