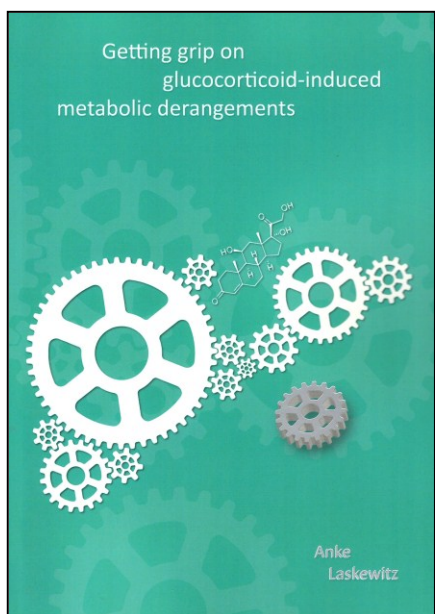




Nederlandse  
Vereniging voor  
Hepatology



## Samenvatting proefschrift Aske Laskewitz

**'Getting grip on glucocorticoid-induced metabolic derangements'**

**Promotiedatum: 8 februari 2012  
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### **Promotores:**

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Synthetic glucocorticoids such as prednisolone have potent anti-inflammatory actions and are widely prescribed for treatment of chronic inflammatory diseases. Unfortunately, these drugs can elicit severe adverse effects, many of which resemble features of the metabolic syndrome such as hyperglycemia, insulin resistance and dyslipidemia. The work described in this thesis focused on the metabolic adverse effects of prednisolone treatment in mice and aimed to unravel (molecular) mechanism that underlie these adverse effects in appropriate mouse models using stable isotope methodologies. A series of novel stable isotope methods to evaluate glucose metabolism in a fasted state have been developed and applied in conventional chow-fed C57BL/6J mice, in C57BLK/6J mice fed a high fat diet to compromise insulin sensitivity and in DBA mice with collagen-induced arthritis, all treated with vehicle or with prednisolone. Surprisingly, in neither model a 'classical insulin resistance' could be detected, although these mice did display distinct metabolic derangements upon prednisolone treatment. In addition, a novel nonsteroidal glucocorticoid receptor agonist was evaluated in these mouse models and found to show less side effects. Finally, the origin of prednisolone-induced dyslipidemia was examined in mice with a dimerization-defective glucocorticoid receptor. The *in vivo* studies described in this thesis provide in-depth analysis of the effects of glucocorticoids on glucose and lipid metabolism and on insulin sensitivity in mice and contribute to an improved understanding of glucocorticoid-induced side effects. The studies described in this thesis provide an important step forward in the recognition of the value of mouse models to evaluate glucocorticoid-related adverse effects. ◀

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