

# In vivo analysis of the 11-beta-hydroxysteroid dehydrogenase activity during critical illness using isotopically labeled cortisol and cortisone

<b>Submission date</b> 30/10/2009	<b>Recruitment status</b> No longer recruiting	<input checked="" type="checkbox"/> Prospectively registered <input type="checkbox"/> Protocol
<b>Registration date</b> 23/11/2009	<b>Overall study status</b> Completed	<input type="checkbox"/> Statistical analysis plan <input checked="" type="checkbox"/> Results
<b>Last Edited</b> 07/05/2013	<b>Condition category</b> Other	<input type="checkbox"/> Individual participant data

**Plain English summary of protocol**  
Not provided at time of registration

## Contact information

**Type(s)**  
Scientific

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## Additional identifiers

**Protocol serial number**  
S51644

## Study information

**Scientific Title**

In vivo analysis of the 11-beta-hydroxysteroid dehydrogenase activity during acute and prolonged critical illness using isotopically labeled cortisol and cortisone: an observational study

### **Study objectives**

Current hypothesis as of 15/02/2012

Cortisol levels remain high in critically ill patients, in spite of low adrenocorticotrophic hormone (ACTH) levels. We hypothesize that hypercortisolism during critical illness is driven mainly by a reduced cortisol metabolism.

Previous hypothesis

Cortisol levels remain high in prolonged critically ill patients, in spite of low adrenocorticotrophic hormone (ACTH) levels. We hypothesize that hypercortisolism during acute critical illness is driven mainly by the hypothalamic-pituitary-adrenal (HPA) axis, whereas during prolonged critical illness regeneration of cortisol in the peripheral tissues in an ACTH-independent way via 11beta-hydroxysteroid dehydrogenase (HSD) becomes predominant.

As of 15/02/2012, the following changes were made to the record.

Public title: Updated from In vivo analysis of the 11-beta-hydroxysteroid dehydrogenase activity during acute and prolonged critical illness using isotopically labeled cortisol and cortisone to In vivo analysis of the 11-beta-hydroxysteroid dehydrogenase activity during critical illness using isotopically labeled cortisol and cortisone

Anticipated start date was updated from 01/01/2010 to 13/02/2012.

Anticipated end date was updated from 31/12/2010 to 01/06/2012.

### **Ethics approval required**

Old ethics approval format

### **Ethics approval(s)**

Institutional Review Board of the Catholic University Leuven School of Medicine approved on the 21st September 2009 (ref: B32220096943)

Adaptations to the original protocol are approved on the 27th of January 2012.

### **Study design**

Observational case-control study

### **Primary study design**

Observational

### **Study type(s)**

Screening

### **Health condition(s) or problem(s) studied**

Critical illness

### **Interventions**

Current interventions as of 15/02/2012

After admission to the SICU, patients will be evaluated on their appropriateness for the study and written informed consent will be obtained from the patient or the closest family member or legal guardian.

11-beta-reductase activity will be assessed by infusion of a deuterated cortisol tracer (D4-cortisol). This is a non-radioactive labelled form of cortisol, the body's own natural steroid hormone. In addition, a deuterated cortisone tracer (D2-cortisone) will be infused at the same time to obtain information on the directionality of the 11-beta-hydroxysteroid dehydrogenase activity.

Infusion of D4-cortisol/D2-cortisone will occur according to the following schedule:

- 9,11,12-D4-cortisol as a bolus of 0.7 mg followed by infusion of 0.35 mg/hour; blood samples are taken at t = -5, +60, +120, +160, +165, +170, +175 min.
- 1,2-D2-cortisone as a bolus of 0.076 mg at t = +100 followed by infusion of 0.1053 mg/hour; an additional blood sample is taken at t = -5 min, +120min,+140 min.
- urine samples are collected at t =0, +60, +120, +180.
- A complete 24h urine collection will be collected started at the moment of study.

For patients, blood and urine samples are taken via the catheters that are present. Control persons will receive two intravenous catheters for the collection of blood samples; for collection of the urine samples they will be asked to urinate at the appropriate time points.

#### Previous interventions

After admission to the SICU, patients will be evaluated on their appropriateness for the study and written informed consent will be obtained from the patient or the closest family member or legal guardian.

11-beta-reductase activity will be assessed by infusion of a deuterated cortisol tracer (D4-cortisol). This is a non-radioactive labelled form of cortisol, the body's own natural steroid hormone. In addition, a deuterated cortisone tracer (D2-cortisone) will be infused at the same time to obtain information on the directionality of the 11-beta-hydroxysteroid dehydrogenase activity.

Infusion of D4-cortisol/D2-cortisone will occur according to the following schedule:

- 9,11,12-D4-cortisol as a bolus of 0.7 mg followed by infusion of 0.35 mg/hour; blood samples are taken at t = -5, +60, +120, +160, +165, +170, +175 min.
- 1,2-D2-cortisone as a bolus of 0.076 mg at t = +120 followed by infusion of 0.1053 mg/hour; an additional blood sample is taken at t = +140 min.
- urine samples are collected at t =0, +60, +120, +180.

For patients, blood and urine samples are taken via the catheters that are present. Control persons will receive an arterial catheter for the collection of blood samples; for collection of the urine samples they will be asked to urinate at the appropriate time points. Both patients and control persons will receive an extra intravenous catheter for infusion of the tracers.

In addition to the tracer injection, daily blood samples (4 ml) will be taken from all included patients for characterisation of the HPA axis during critical illness.

#### Intervention Type

Drug

#### Phase

Not Applicable

#### Drug/device/biological/vaccine name(s)

Cortisol, cortisone

### **Primary outcome(s)**

Current primary outcome(s) as of 15/02/2012

An estimation of the amount of ACTH-driven cortisol production , the amount of cortisol regenerated from cortisone via 11-beta-HSD1 and 2 and the activity of the different metabolizing enzymes based on urinary metabolites.

Previous primary outcome(s)

An estimation of the amount of ACTH-driven cortisol production and the amount of cortisol regenerated from cortisone via 11-beta-HSD1, measured at day 2 and 7 after admission.

### **Key secondary outcome(s)**

No secondary outcome measures

### **Completion date**

01/06/2012

## **Eligibility**

### **Key inclusion criteria**

Current inclusion criteria as of 15/02/2012

For patients:

1. Admitted to the surgical intensive care unit (SICU) of the Leuven University Hospital
2. No age limits, either sex

For healthy control persons:

1. Age- and gender-matched to the included patients

Previous inclusion criteria

For patients:

1. Admitted to the surgical intensive care unit (SICU) of the Leuven University Hospital
2. Estimated duration of illness prior to admission less than 48 hours
3. No age limits, either sex

For healthy control persons:

1. Age- and gender-matched to the included patients

### **Participant type(s)**

Patient

### **Healthy volunteers allowed**

No

### **Age group**

Other

### **Sex**

All

### **Key exclusion criteria**

Steroids received during the last 3 months

**Date of first enrolment**

13/02/2012

**Date of final enrolment**

01/06/2012

## Locations

**Countries of recruitment**

Belgium

**Study participating centre**

**Director of the Department of Intensive Care Medicine**

Leuven

Belgium

3000

## Sponsor information

**Organisation**

Catholic University Leuven (Katholieke Universiteit Leuven) (Belgium)

**ROR**

<https://ror.org/05f950310>

## Funder(s)

**Funder type**

Government

**Funder Name**

Methusalem (Belgium) - long term structural funding by the Flemish Government

## Results and Publications

Individual participant data (IPD) sharing plan

## IPD sharing plan summary

Not provided at time of registration

## Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
<a href="#">Results article</a>	results	18/04/2013		Yes	No