

# Adrenal Insufficiency During Prednisolone Treatment

– need for cortisol replacement strategies in patients on long-term low-dose glucocorticoid treatment?

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## BACKGROUND AND OBJECTIVE

### BACKGROUND

- Patients on long-term prednisolone treatment are at risk of adrenal insufficiency during treatment.
- High-dose prednisolone treatment is often sufficient to overcome most stressful situations.
- A low dose of 5 mg prednisolone daily is equivalent to 20 mg hydrocortisone, often used as basal glucocorticoid replacement dose in adrenal insufficiency.
- Contrary to patients in replacement therapy for adrenal insufficiency, patients treated with long-term low-dose prednisolone for various reasons are often not instructed in self-administration of supplemental doses in stressful situations.

### OBJECTIVE

- We aimed to assess the prevalence of glucocorticoid-induced adrenal insufficiency in patients treated with only 5 mg prednisolone daily.

| Patient Handling Today              | Adam<br>- has Addison's Disease     | Robert<br>- has Rheumatoid Arthritis                                 |
|-------------------------------------|-------------------------------------|--|
| Treatment                           | Hydrocortisone<br>10 + 5 + 5 mg/day | Prednisolone<br>5 mg/day<br>(equivalent to hydrocortisone 20 mg/day) |
| Steroid Emergency Card              | +                                   | +/-  |
| Patient education in adrenal crisis | +                                   | -  |
| Stress doses                        | +                                   | -  |
| Synacthen® test                     | At diagnosis                        | -<br>(Maybe at withdrawal)   |

## SUBJECTS AND MEASURES

### SUBJECTS

- Patients with rheumatoid arthritis treated with 5 mg prednisolone/day for at least 6 months, included as part of a larger study.

### MEASURES

- A 250 µg Synacthen® test was performed fasting, in the morning, after a mean prednisolone pause of 47 hours. P-cortisol was measured before and 30 min after Synacthen® injection.
- Cut-off for normal adrenal function was 30 min P-cortisol > 500 nmol/l as this is validated for our local cortisol assay[1].

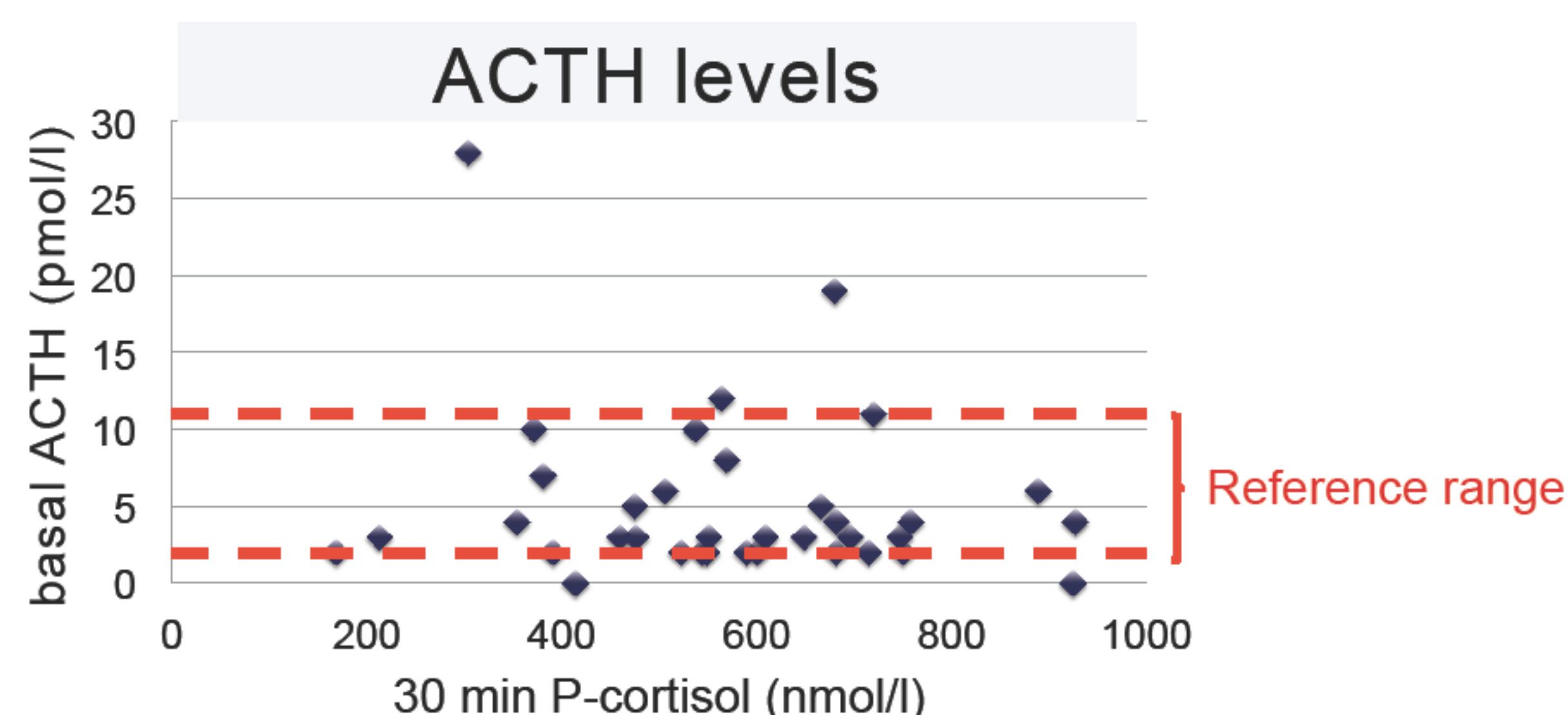
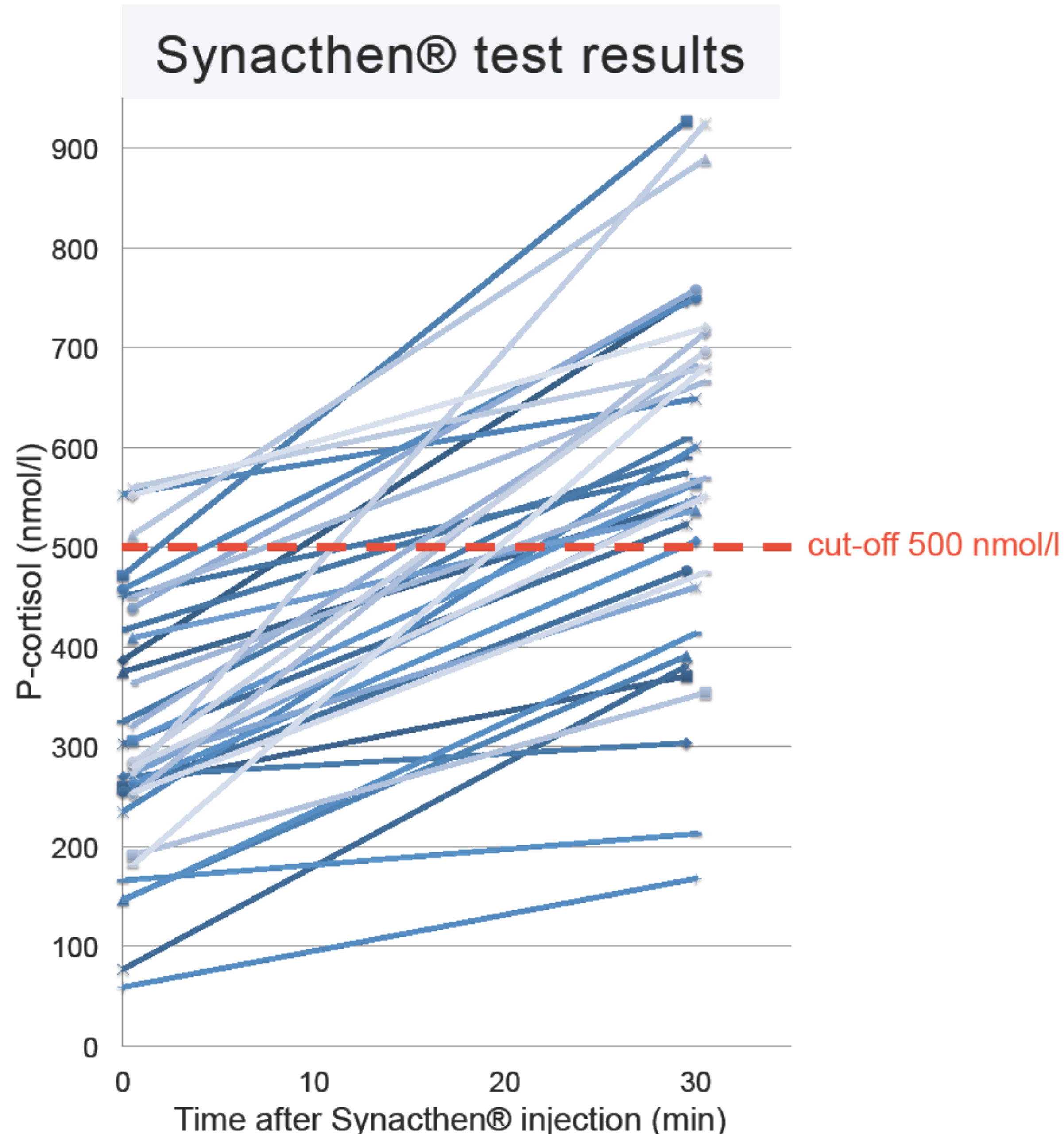
### Patient Characteristics

|  |                           |
|--|---------------------------|
| Number of participants                         | 37 (26 women)             |
| Mean age (range)                               | 66 years (36-85 years)    |
| Mean duration of therapy (range)               | 108 months (6-336 months) |
| <u>Prednisolone dose above 5 mg</u>            | 5                         |
| • 1 month prior                                | None                      |
| • 2-3 month prior                              | 1 (7.5 mg)                |
| • 4-6 months prior                             | 5 (7.5-15 mg)             |
| Mean time since last prednisolone dose (range) | 47 hours (36-96 hours)    |
| <u>Number also on other glucocorticoids</u>    | 6                         |
| • intra-articular injections                   | 2 (paused 2-6 weeks)      |
| • intra-muscular injections                    | 3 (paused 1-6 weeks)      |
| • steroid cream                                | 1 (paused several weeks)  |

## RESULTS

- Of the 37 patients 11 (30%) had an insufficient adrenal response to the Synacthen® test.
- Adrenocorticotrophic hormone (ACTH) levels were generally low within reference range.

Adrenal Insufficiency: 30%



## CONCLUSION

- We found adrenal insufficiency in approximately one third of patients treated with 5 mg prednisolone daily.
- Since the prednisolone treatment is often sustained for years in these patients, adrenal suppression is likely equally prolonged.
- It raises the question whether patients on long-term low-dose prednisolone treatment need to be handled with some of the same precautions as patients with verified adrenal insufficiency.
- Should Synacthen® tests be routinely performed in these patients?
- Low-dose prednisolone treated patients with adrenal insufficiency should receive supplemental doses during stress.

**More awareness of adrenal insufficiency in long-term low-dose prednisolone treated patients is urgently needed**

| Patient Handling Tomorrow           | Adam<br>- has Addison's Disease     | Robert<br>- has Rheumatoid Arthritis                                 |
|-------------------------------------|-------------------------------------|--|
| Treatment                           | Hydrocortisone<br>10 + 5 + 5 mg/day | Prednisolone<br>5 mg/day<br>(equivalent to hydrocortisone 20 mg/day) |
| Steroid Emergency Card              | +                                   | +  |
| Patient education in adrenal crisis | +                                   | +  |
| Stress doses                        | +                                   | +  |
| Synacthen® test                     | At diagnosis                        | At any suspicion +<br>At routine intervals?                          |

### References:

[1] Klose M et al. J Clin Endocrinol Metab 2007; 92:1326-33

Conflicts of interest: none

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