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SUPPRESSION OF THE THYROTROPHIN CIRCADIAN RHYTHM BY GLUCOCORTICOIDS

Y. C. PATEL, H. W. G. BAKER,* H. G. BURGER, M. W. JOHNS† AND JOANNE E. LEDINEK†

*Medical Research Centre and *Monash University Department of Medicine, Prince Henry's Hospital and †Monash University Department of Surgery, Alfred Hospital, Melbourne, Victoria 3004, Australia*

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Pharmacological doses of glucocorticoids inhibit thyroid function in man and laboratory animals due to suppression of thyrotrophin (TSH) secretion (Wilber & Utiger, 1969). Administration of prednisolone or dexamethasone for 1–2 days results in a suppression of basal serum TSH levels in normal subjects and in patients with primary hypothyroidism, whilst the pituitary TSH reserve capacity, as assessed by the response to synthetic thyrotrophin releasing hormone (TRH), remains unaltered (Wilber & Utiger, 1969; Besser, Ratcliffe, Kilborn, Ormston & Hall, 1971; Haigler, Pittman & Hershman, 1971). However, impairment of serum TSH response to administered TRH does occur in patients treated with glucocorticoids for 1 or more months (Otsuki, Dakoda & Baba, 1973). These studies suggest that glucocorticoids may inhibit TSH secretion at both hypothalamic and pituitary levels but the main effect of the short-term treatment is suppression of TRH production.

Nicoloff, Fisher & Appleman (1970) found that the circadian rhythm of thyroidal iodine release was inversely related to the circadian rhythm of cortisol levels and that it was suppressed by glucocorticoid therapy. They suggested that cortisol may be involved in the control of the circadian rhythm of TSH secretion. To investigate this possibility, a preliminary study was undertaken to examine the effects of infusion with pharmacological doses of cortisol on the levels of immunoassayable TSH in the blood.

A man and a woman both aged 22 years volunteered for the study after being informed of its nature. On 2 days, 2 months apart, a continuous venous blood sampling technique (Patel, Alford & Burger, 1972) was used to collect consecutive plasma samples every 10 or 20 min over 24-h periods, for the measurement of integrated plasma concentrations of TSH. The first day served as a control and on the second, cortisol sodium succinate (Intracort, Boots), 500 mg in the male and 200 mg in the female, dissolved in 50 ml physiological saline was infused i.v. at a constant rate over the 24 h period. Plasma TSH was measured by a sensitive radioimmunoassay (Patel, Burger & Hudson, 1971) capable of detecting $0{\cdot}2 \pm 0{\cdot}05$ (S.D.) μu./ml. Mean intra-assay precision was within $\pm 5\%$ over the range 1·0 to 5·0 μu./ml. All samples from the one subject were included in the same assay.

Figure 1 shows the 24 h plasma TSH profile for the female subject before and during cortisol infusion. In the control studies both subjects showed a circadian rhythm of TSH levels as previously described (Patel, Alford & Burger, 1972). In addition to the

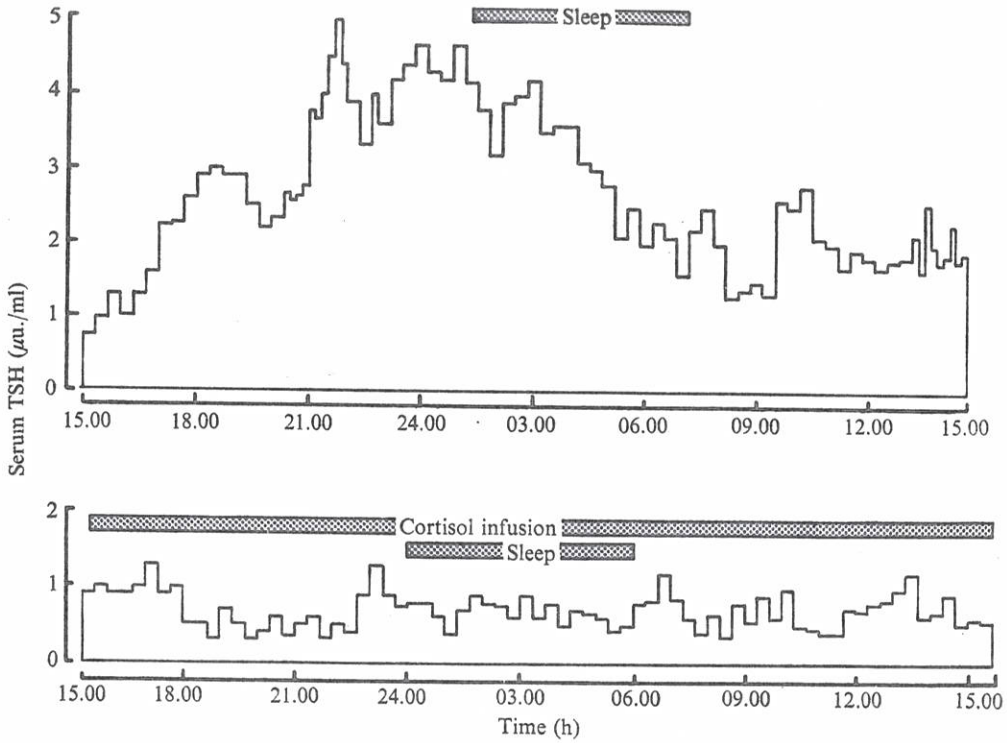

Fig. 1. Twenty-four hour thyrotrophin (TSH) profile for the female subject before and during cortisol infusion (200 mg/24 h).

circadian variation, smaller fluctuations of TSH levels occurred about every 2–4 h. Infusion of cortisol led to an abolition of the circadian rhythm in both subjects. Suppression of plasma TSH to undetectable levels occurred within 3 h of infusion in the man and persisted for the duration of the study. Less complete suppression of TSH secretion occurred in the woman who maintained a 24 h integrated level of 0·7 μu./ml and showed small fluctuations in the TSH levels.

It is concluded that cortisol has an acute inhibitory effect on thyrotrophin secretion which is probably mediated by suppression of TRH production. Further studies using smaller doses of cortisol are in progress to examine the physiological relationship between cortisol levels in the blood and the normal TSH secretory pattern.

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