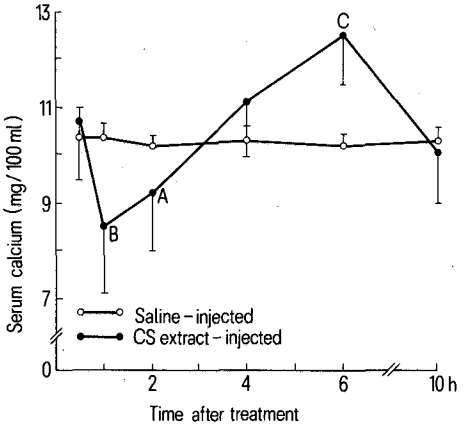
the injection, the calcium level exhibits a significant decrease ($p < 0.01$). Thereafter, it gradually increases resulting in a significant hypercalcemia at 6 h ($p < 0.001$). At 10 h, the calcium level has returned to control values (fig.). The present observation clearly indicates that the extract from the CS removed from *A. cuchia* contained a calcium-lowering factor (s). The hypocalcemic effect of CS extract has been reported earlier in eels[3], *Fundulus heteroclitus*[8] and rats[10]. The results reported from rats are surprising as one would not normally expect a hormone, extracted from an organ present only in bony fishes, to be effective in mammals. Leung and Fenwick's[10] report and also the present study lead to the inference that the hypocalcemic factor (s) present in CS is universally effective in vertebrates. This is further strengthened by the hypocalcemic effect of CS extracts in anurans (*Rana cyanophylctis* and *Bufo andersonii*, unpublished data of our laboratory).

In the present study the hypercalcemia at 6 h may be due to the activity of the parathyroid glands in response to the CS extract-induced hypocalcemia.



Changes in the serum calcium level after administration of saline and CS extract. The blood samples were collected at 0.5, 1, 2, 4, 6 and 10 h following the injection. Each point indicates mean ± SD of 6 determinations. A, B and C represent significant responses, $p < 0.05$, $p < 0.01$ and $p < 0.001$, respectively.

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Thyroid gland influences the period of hamster circadian oscillations[1]

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Summary. The locomotor activity of ovariectomized, adult golden hamsters was monitored under constant dim illumination. Thiourea treatment lengthened the period (τ) of locomotor activity of thyroidectomized hamsters in comparison to pre-operative τs and in comparison to the τs of control hamsters. The results confirm hormonal modulation of the circadian system.

The free-running period (τ) of mammalian circadian oscillations is remarkably stable and unresponsive to all but a few chemical manipulations[2]. Removal of various endocrine organs (gonads, pituitary, thyroid, pancreas, pineal and adrenals) of rats does not eliminate free-running activity rhythms, thereby demonstrating that the driving circadian oscillator for this rhythm is not localized in any of these glands[3]. However endocrinological manipulation (castration of male mice[4] and female hamsters[5,6], hypophysectomy[7]) lengthens τ; replacement testosterone[4] and estradiol[5,6] shortens τ. In the canary[8], radiothyroidectomy shortens τ and replacement thyroid hormone lengthens τ. These studies suggest that hormones can modulate the frequency of circadian oscillations.

The present experiment extended this analysis to an assessment of the influence of the thyroid gland on circadian activity rhythms of hamsters. Specifically, we tested the hypothesis that reduction of thyroid activity (accomplished via surgical thyroidectomy plus administration of a thyroid suppressing agent) would lengthen the period of circadian oscillations. Lengthening of circadian activity cycles was predicted on the basis of the general hypometabolic state induced by hypothyroidism.

Methods. 20 adult, ovariectomized golden hamsters bred in our laboratory from stock animals (LVG-LAK) obtained from Lakeview Hamster Colony (Newfield, NJ) were used. Prior to the study, animals were group housed and exposed to 14 h of light per day (LD 14:10; lights on between 08.00 and 22.00 h PST); food and water were available ad libitum. During the experiment all hamsters were exposed to constant dim illumination (average light intensity at cage

Group	n	Period (h) Pre-thiourea		During thiourea
Control	7	24.17 ± 0.03*	vs	24.15 ± 0.03*
Thyroidectomized	9	24.10 ± 0.04	vs	24.30 ± 0.06**

Mean and SEM of the period of the activity rhythm of control and thyroidectomized hamsters before and during thiourea treatment. *t-test nonsignificant; **t-test $p < 0.01$.

level < 10 lux) and were housed individually in plastic cages (45 × 24 × 20 cm) equipped with activity wheels. Each revolution of the wheel tripped a micro-switch that caused the deflection of a pen on moving chart paper (chart speed = 45.7 cm/24 h). The chart paper was cut into 24-h strips; each strip was pasted beneath the one from the previous day.

Surgical thyroidectomies were performed on 11 of the animals, 3 were subjected to sham-thyroidectomies and the remaining 6 animals served as unoperated controls. 60 days post-operatively, all animals were offered a 1% thiourea solution (Sigma Chemical Co.) dissolved in a 1% saccharine solution in place of tap water. Saccharine was used to increase consumption of the unpalatable solution of thiourea[9].

The free-running period of locomotor activity was estimated by fitting a straight line through onset times of at least 10 days of running activity. The 2 experimenters independently calculated τs; only those values that were in agreement within 0.05 h were included in the data analyses. A τ was calculated before the time of surgery (τ^1) (approximately 10–20 days pre-operatively), after surgical manipulation (τ^2) (approximately 25–35 days post-operatively) and during thiourea treatment (τ^3) (approximately 30–40 days after thiourea treatment was initiated). The change in period ($\Delta\tau$) was computed and differences between the groups evaluated by a Student's 2-tailed t-test for independent samples.

Hamsters subsequently were injected i.p. with 1 mC_i of radioactive iodide (^{131}I (NaI) (New England Nuclear)). 24 h later, animals were sacrificed and a section of the trachea ($\bar{x} = 377.25$ mg) and an approximately equal weight ($\bar{x} = 340.07$ mg) of leg muscle were removed. Relative radiation present in each tissue was measured in a Packard gamma radiation spectrometer. A correlation coefficient was calculated between the counts/min/mg of tissue weight and $\Delta\tau$.

Results and discussion. The data from the sham-operated and the unoperated animals were combined for purposes of statistical analyses. There were no pre-operative differences between the τs of the activity rhythms of thyroidectomized and control animals ($p > 0.05$). During thiourea treatment (table) the τs of the thyroidectomized hamsters were lengthened in comparison to those of control animals ($p < 0.01$). The counts/min/mg of leg muscle were not correlated with $\Delta\tau$ (τ^3-τ^1) ($p > 0.05$). However, the counts/min/mg of trachea were negatively correlated with $\Delta\tau$ ($p < 0.05$); that is, decreased thyroid activity, as indicated by a reduction in the number of counts/min/mg of trachea was associated with a lengthening in τ of the activity rhythm. Surgical thyroidectomy in combination with thiourea treatment increased the period of the circadian activity cycle by 0.20 h. The magnitude of this change is consistent with other reported manipulations of τ in mammals[3-5].

Thyroidectomy did not by itself affect τ ($p > 0.05$); however, there was a transitory change in the τ of the activity cycle of control animals during this interval ($p < 0.05$). A combination of surgical thryoidectomy and chemical treatment with thiourea was necessary to produce effects on the circadian system. Surgical thyroidectomy only eliminated approximately 90% of thyroid tissue. It is possible that a more complete suppression of the thyroid gland is necessary to affect the circadian activity rhythm.

The activity rhythm of a hypothyroid man free-ran with a $\bar{\tau}$ of 25.0 h during 5 months of observation. After treatment with thyroid hormone, τ was shortened to 24.5 h[11]. This change in τ is consistent with changes observed in the present study. The consequences of thyroidectomy are comparable to those of hypophysectomy with respect to circadian locomotor rhythms. Either hypophysectomy[7] or thyroidectomy results in an increase in the free-running period of locomotor activity. Some, if not all, of the effect previously attributed to hypophysectomy may be due to resultant hypothyroidism.

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Effects of a bovine pineal peptidic fraction (E_5) on plasma and pituitary levels of LH, FSH and prolactin[1]

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Summary. Pituitary levels of prolactin were significantly diminished after 5 s.c. injections spaced 12 h apart of 5 µg of a partially purified bovine pineal peptide fraction (E_5) in both intact and castrated rats. E_5 treatment did not significantly affect the castration-induced changes in plasma luteinizing hormone (LH), follicle-stimulating hormone (FSH) or pituitary LH but did partially block the pituitary fall in FSH in castrated animals.

In 1972, Neacsu[5] described the isolation and amino acid analysis of a partially purified antigonadotrophic polypeptide (E_5) from bovine pineal glands. In that study, E_5 blocked spermatogenesis in frogs and inhibited the LH-induced rise in uterine weights in immature mice. The present study further characterizes the hormonal effects of this peptide fraction in intact and castrated animals using sensitive radioimmunological assays for LH, FSH and prolactin.

Materials and methods. Adult male Sprague-Dawley rats