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Significance of circadian variations of uric acid elimination

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To investigate the significance of inverse circadian variations of renal excretion of uric acid[1] and enteral uricolysis[2 3] it is necessary to demonstrate that they are affected by sleep and that there is a tendency for serum urate to change, even though this may be masked by effective homoeostasis. If during sleep the rate of urate production exceeds elimination by increased enteral uricolysis and reduced renal excretion there should be a detectable increase in serum urate under controlled metabolic conditions.

A three day study comprising two six-hour periods of sleep separated by 42 hours' 'normal' activity was undertaken. During the awake periods the subject was on a low-purine mixed liquid diet of 0·69 MJ (165 k cal) four hourly with a water intake of 200 ml hourly.

Blood samples for estimation of urate concentration were taken every four hours at the midpoint of four hourly pooled urine collections for uric acid (apart from the first sleep period). Urate was measured in one batch by autoanalyser and urine pH by radiometer.

Normal diurnal variation of urate excretion was lost during the 42 hours without sleep and was associated with a fall in serum urate of 0·036 mmol/l (0·6 mg/100 ml). There were two peaks of increased excretion after 22 and 34 hours during this period.

After both periods of sleep there was an increase in serum urate of 0·024 mmol/l (0·4 mg/100 ml), and 0·03 mmol/l (0·5 mg/100 ml). Initially there was fluctation of urine pH, which then stabilised and fell dramatically during the second period of sleep from pH 6·1 ((H+) 794 nmol/l) to pH 5·35 ((H+) 4467 nmol/l) and increased with feeding to pH 6·5 ((H+) 224 nmol/l). Weight loss during the study was 1·5 kg and modest negative fluid balance occurred during sleep and on two occasions during the 42 hours.

As reduced urate clearance should be regarded 'as normal response of the kidneys to the endogenous hyperuricaemia (of primary gout)'[4 5] a combination of reduced urinary excretion and increased enteral uricolysis suggests that there is increased urate production at night as shown by a rise in serum urate.

Enteral uricolysis is increased at night whether fasting or not, yet the normal daily variation of urine urate excretion is lost during fasting.[6] This indicates that circadian elimination via the gut is independent of renal function and food intake. As uricolysis is increased at night it is suggested that complex metabolic changes occur as a result of sleep that causes nucleoproteolysis and increased urate production with secondary renal effects of increased tubular reabsorption and reduced secretion of urate.

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Familial gout, hyperuricaemia, and renal impairment

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We report the case of a woman who suffered recurrent attacks of acute gout from the age of 15. When first seen at this unit 10 years later she gave a family history of gout and was found to be mildly hypertensive. Investigations showed hyperuricaemia uncontrolled by the dose of allopurinol she was receiving and a glomerular filtration rate (GFR) of 15 ml/min. On intravenous pyelography a small right kidney suggestive of damage by ureteric reflux was seen, though this was not confirmed by micturating cystography. Gamma camera