Results of treatment in the two groups subdivided according to endoscopic diagnosis

Lesion	Cimetidine (n = 33)		Placebo (n = 36)	
	Rebleed	No rebleed	Rebleed	No rebleed
Duodenal ulcer	7	6	6	9
Gastric ulcer	1	3	2	6
Oesophagitis	3	4	2	3
Mallory-Weiss	1	5		2
Gastric erosions		1		3
Stomal ulcer		1		
Gastric volvulus		1		
Unknown				3
Total	12	21	10	26

bleed, and of these two rebled. Twenty-three patients in the placebo group had had a mild initial bleed, and of these five rebled. The table gives the results according to endoscopic diagnosis. No effect from cimetidine was apparent in any subgroup.

Comment

Our results do not support a policy of routinely treating with cimetidine all patients admitted to hospital with acute upper gastrointestinal bleeding. Nevertheless, we cannot exclude the possibility of benefit in selected patients, since the diagnostic subgroups were small.

We thank the clinical research department of Smith Kline and French Laboratories Limited for supplies of cimetidine and matching placebo.

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(*Accepted 22 January 1979*)

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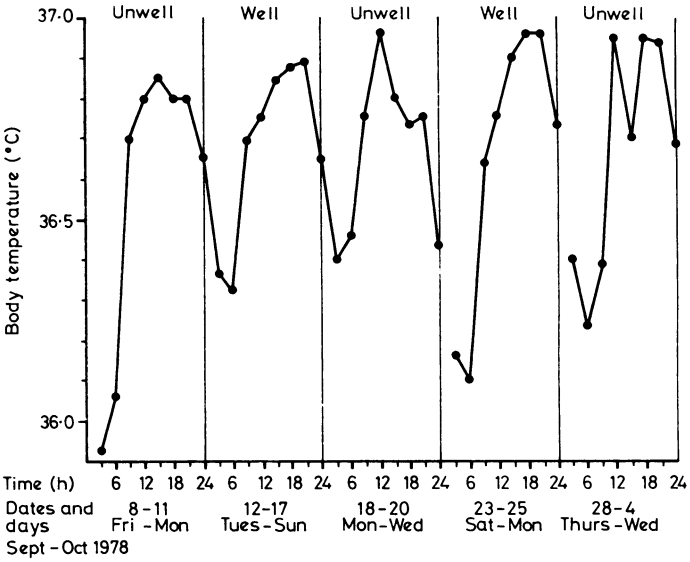
Endogenous anxiety and circadian rhythms

Nikitopoulou and Crammer[1] showed that diurnal body temperature curves change in manic-depressive illness, and suggested that this change in circadian rhythm might be related to the diurnal variation in depth of mood that is also associated with early morning waking in depression. They thought that these findings suggested a disturbance in brain centres or neurological organ function rather than in scattered synapses or cellular function. In 1977[2] I drew attention to the possibility that some anxiety states might fall into the same endogenous category of mood change, since they exhibited increasing intensity of emotion towards evening associated with difficulty in getting to sleep at night. I recognised, however, the difficulties of carrying out suitable body temperature studies to support this hypothesis. Recently a patient with an anxiety state co-operated in such a study.

Case report

In 1978 a 25-year-old, happily married man who was employed as a computer scientist was referred to me. He had had a chronic intermittent anxiety for six years, which had worsened considerably in the last six months. A maternal aunt and possibly his mother had a history of similar severe nervousness, though three sisters and two brothers were well. Psychological environmental stress did not account for his anxiety. Serum thyroxine concentration, triiodothyronine uptake, and free thyroxine index were within normal limits, as were the results of screening for excess catecholamines. He



Three-hourly body temperature curves over 24 hours. Vertical lines separate average curves of each period of several consecutive days during which the patient was well or unwell.

was taking lorazepam (Ativan), 2·5 mg twice daily, prescribed by his family doctor, and felt comparatively well on waking in the mornings, his symptoms becoming more obtrusive in the late afternoon and continuing until he fell asleep in the early hours of the morning. Lorazepam helped to reduce his symptoms but did not clear them, even when I suggested that he should take both his daily doses towards evening.

His symptoms were of nameless dread, apprehensive tension, loss of appetite, nausea, diarrhoea, and difficulty in getting to sleep. He was interested in their possible relation to body circadian rhythms, and agreed to chart each symptom on a three-point scale as "absent," "moderate," or "marked," while taking his body temperature by mouth three-hourly, which he did daily from 26 August to 6 October. He continued to take both his daily 2·5-mg doses of lorazepam towards evening. An attempt after 6 October to do without medication failed because his symptoms immediately worsened.

Comment

The records that he kept for six weeks unexpectedly showed that even during such a relatively short time his condition fluctuated every few days, in a way unaccounted for by weekends. After he had settled into his recording routine five separate periods, each of several consecutive days, could be identified, during which he was either continuously symptom free or moderately to severely anxious every evening. Following the method of Nikitopoulou and Crammer, the daily body temperature recordings for each of these five periods were averaged to give 24-hour temperature curves (see figure). The curves during the two periods when he was well were smoother and peaked at between 6 and 9 pm, whereas in the three periods when he was unwell they were more disorganised and tended to peak some 6-9 hours earlier.

These findings do not conclusively show a relation between endogenous anxiety and a change in diurnal body temperature rhythm, but may provide a basis for extending studies on untreated or otherwise suitable patients. Though I have seen other patients with the same evening patterns, none have yet been suitable for this purpose. If an endogenous basis can thus be conclusively shown for some anxiety states, however, and the central nervous site[3] for this firmly established, it might provide a stimulus to research on anxiolytic preparations that could be more effective than those we have at present.

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(*Accepted 25 January 1979*)

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