arrhythmic properties were recognised. Its effects include bradycardia, augmentation of coronary blood flow, and prolongation of the action potential of atrial and ventricular muscle. In 1973 Coumel and Bouvrain² reported that amiodarone was highly effective in treating various arrhythmias including those complicating the WPW syndrome. Rosenbaum *et al*³ later achieved total suppression of arrhythmias in all of 27 cases with this condition. A wide variety of other atrial and ventricular arrhythmias can also be controlled, even in patients with severe congestive failure.³

The beneficial effect of amiodarone in atrial fibrillation and on conduction in anomalous pathways is related to the prolongation of action potential and refractory period of the myocardium. The drug is cumulative with a slow rate of elimination.⁴ The onset of action is slow and persists for weeks after dosage has ended.³ These properties explain the continued success of amiodarone in our case when dosage was reduced to 200 mg on alternate days. Microdeposits occur in the corneae⁵ but, in the dosage used to control arrhythmias, rarely cause symptoms³ and are reversible. The drug has not yet been licensed in Britain by the Medicines Commission.

In this case amiodarone produced a dramatic and life-saving effect, restoring a severely incapacitated man to excellent health after the reversion of previously refractory atrial fibrillation to sinus rhythm.

Dr Dennis Krikler suggested to us in 1973 that the electrophysiological properties of amiodarone seemed appropriate for the management of refractory arrhythmias in WPW syndrome. Amiodarone (Labaz, Brussels) was supplied by Dr R Smith of Reckitt and Colman.

¹ Wellens, H J, and Durrer, D, *Circulation*, 1973, **47**, 1229.
² Coumel, P, and Bouvrain, Y, *Le Journal des Agrégés*, 1973, **6**, 69.
³ Rosenbaum, M B, *et al*, *American Journal of Cardiology*, 1976, **38**, 934.
⁴ Broekhuysen, J, Laruel, R, and Sion, R, *Archives internationales de pharmacodynamie et de thérapie*, 1969, **177**, 340.
⁵ Verin, Ph, *et al*, *Archives d'ophtalmologie et revue générale d'ophtalmologie*, 1971, **31**, 581.

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Diurnal variation of serum urate in pregnancy

The degree of hyperuricaemia is widely used as a prognostic index in pre-eclampsia.¹ Nevertheless, the reliability of the random blood sample conventionally used for this has not been adequately assessed during pregnancy, despite evidence in non-pregnant women of considerable variation from day to day and within any given day.²⁻⁴ We therefore decided to examine changes in serum urate concentration in normal pregnant women throughout a 24-hour period.

Serum urate concentrations ($\mu\text{mol/l}$) throughout 24 hours in 14 pregnant women

Case No	0600	1000	1400	1800	2200	0600	Mean $\pm$ SD
1	178	170	163	158	162	170	166.8 $\pm$ 7.2
2	184	180	174	158	155	162	168.8 $\pm$ 12.1
3	351	344	353	316	320	318	333.7 $\pm$ 17.5
4	304	310	298	281	265	265	287.2 $\pm$ 19.7
5	193	207	199	187	175	196	192.8 $\pm$ 11.0
6	343	336	347	327	320	308	330.2 $\pm$ 14.7
7	184	169	144	137	128	132	149.0 $\pm$ 22.5
8	235	244	210	208	211	224	222.0 $\pm$ 15.0
9	193	184	168	174	187	186	182.0 $\pm$ 9.2
10	242	261	253	240	227	254	246.2 $\pm$ 12.3
11	330	323	291	277	269	288	296.3 $\pm$ 24.8
12	287	281	271	268	254	273	272.3 $\pm$ 11.4
13	231	233	219	198	191	203	212.5 $\pm$ 17.7
14	233	235	210	191	188	215	212.0 $\pm$ 20.0
Mean $\pm$ SD	249.1 $\pm$ 62.5	248.4 $\pm$ 62.5	235.7 $\pm$ 67.7	222.9 $\pm$ 61.7	218.0 $\pm$ 59.9	228.1 $\pm$ 57.3	233.7 $\pm$ 16.1

Patients, methods, and results

Fourteen normotensive inpatients were studied without restriction of diet or activity throughout 24 hours during the third trimester of pregnancy. One patient (case 3) was carrying twins. No patient was taking medication known to affect the serum urate concentration. Venous blood samples were withdrawn at 0600, 1000, 1400, 1800, and 2200 on day 1 and at 0600 the next morning. Serum was analysed on the day of collection, or snap-frozen in liquid nitrogen and stored at -20°C for not more than three weeks. This procedure had been validated,⁵ and its reliability was confirmed in our laboratory. Duplicate samples were analysed manually by an enzymatic method based on a commercial reagent pack (Uricquant). The mean error of the method was $\pm 1.5\%$.

The interpatient variability was much greater than the intersample variability in any patient (see table). The overall mean and the standard deviation within samples within patients showed that the variability among random samples was small, but a range of up to 30% was found in some women. No consistent pattern of variation emerged, but there were significant differences between certain of the time points. A longer study, however, would be needed to validate these differences.

Comment

The results suggest that pregnant women have considerable fluctuations of serum urate during the day. Despite a tendency towards lower concentrations during daylight hours, no single reading would be representative for any individual. These results agree with published data in non-pregnant women.

Furthermore, serum urate concentration does not appear to remain stable from day to day; comparison of samples taken 24 hours apart again shows considerable variation within individuals. In the data presented the second of the results is lower than the first in most cases. This unexpected pattern has not been confirmed in subsequent studies.

Intersample variability is itself of different magnitude from patient to patient, so that it would not be reasonable to predict the accuracy of a given result on the basis of the concentration of urate reported. Thus a single blood sample in the individual case may not truly represent the mean value for that patient throughout the day. This is particularly relevant to the popular practice of screening pregnant women for hyperuricaemia at a routine antenatal visit.

The cause of this diurnal variation remains unexplained. The overall pattern does not suggest a relation between urate and purine ingestion at meals. One factor may be an alteration in urate excretion, and this is being investigated.

¹ Redman, C W G, *et al*, *Lancet*, 1976, **1**, 1370.
² Bröchner-Mortensen, K, *Acta Medica Scandinavica*, 1937, Supp, **84**, 13.
³ Zachau-Christiansen, B, *Scandinavian Journal of Clinical and Laboratory Investigation*, 1957, **9**, 244.
⁴ Rubin, R T, *et al*, *Journal of the American Medical Association*, 1969, **208**, 1184.
⁵ Liddle, L, Seegmiller, J E, and Lester, L, *Journal of Laboratory and Clinical Medicine*, 1959, **54**, 903.

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