CLINICAL PHARMACOLOGY SECTION

The relationship between leucocyte ascorbic acid and plasma iron

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Similar human circadian rhythms exist for plasma iron (Hamilton, Gubler, Cartwright & Wintrobe, 1950) and for plasma ascorbic acid (AA) (Wilson & Loh, 1969) with maxima and minima in the morning and at midnight, suggesting a dynamic relationship exists between these variables. Leucocyte and plasma AA concentrations and plasma iron concentrations were measured at 4 h intervals 6 times in each of nine young adults during 24 h in February. The existence of rhythms was confirmed for the plasma iron and AA, which reached their maxima at 08.00 h and their lowest levels at midnight. The leucocyte AA also underwent a 24 h rhythm whose maximum and minimum phases occurred at the same times as those for the plasma iron and ascorbic acid. A significant correlation of $+0{\cdot}2663$ was obtained between the leucocyte AA concentrations and plasma iron during the 24 h period. Comparison of the individual regression lines at each 4 h interval showed no significant difference between them. A consistent ratio was therefore maintained throughout the 24 h period between these variables.

Leucocytes take up AA released into the plasma from the erythrocytes, by active and passive processes (Loh & Wilson, 1970). Leucocyte AA uptake has been measured in the presence of ferrous iron by the methods described previously (Loh & Wilson, 1970) (Table 1). In the presence of 500 μg/100 ml Fe^{2+} the leucocyte AA uptake was significantly increased by 39% after 2 h incubation in a medium con-

TABLE 1. *Leucocyte ascorbic acid concentrations ($\mu g/10^8$ cells) after incubation at 37° C in the presence of Fe^{2+} (500 μg/ 100 ml) in different concentrations of ascorbic acid*

No. of observations	Control (Mean+S.E.M.)	Ascorbic acid 3 mg/100 ml (Mean+S.E.M.)	Fe^{2+} with AA 3 mg/100 ml (Mean±S.E.M.)
5	46·12±4·35	70·79±9·01	89·05±9·09
% change	100	154	193
		Ascorbic acid 6 mg/100 ml	FE^{2+} with AA 6 mg/100 ml
5	32·86±2·85	100·77±9·36	121·63±12·75
% change	100	307	370

taining 3 mg/100 ml. In the presence of the same concentration of Fe^{2+}, but when the AA concentration was doubled, its uptake was increased by 63% ($P<0{\cdot}05$). This suggests that Fe^{2+} acts as a metallic catalyst which increases the active uptake of AA when its concentration in the medium is increased.

The interlocking of the circadian phasing of plasma and leucocyte AA values demonstrates the lability of blood ascorbic acid. It can pass rapidly into and out of the leucocytes where it is stored (Loh & Wilson, unpublished). Storage occurs actively in the presence of ferrous iron. The circadian rise in plasma iron may therefore actively promote uptake of ascorbic acid by the leucocytes from the plasma under normal physiological conditions.

REFERENCES

HAMILTON, L. D., GUBLER, C. J., CARTWRIGHT, G. E. & WINTROBE, M. M. (1950). Diurnal variation in the plasma iron level of man. *Proc. Soc. exp. Biol. Med.*, **75**, 65–68.

LOH, H. S. & WILSON, C. W. M. (1970). The origin of ascorbic acid stored in the leucocytes. *Br. J. Pharmac.*, **40**, 169P–170P.

WILSON, C. W. M. & LOH, H. S. (1969). Studies in ascorbic acid taste threshold circadian rhythm in relation to plasma ascorbic acid levels. *Irish J. med. Sci.*, **2**, 396.

Cardiovascular effects of pancuronium in anaesthetized man

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Pancuronium (2β,16β-dipiperidino-5α-androstane-3α,17β-diol diacetate dimethobromide) is a non-depolarizing neuromuscular blocking agent which clinically does not appear to cause the arterial hypotension which may accompany the administration of tubocurarine (McDowell & Clarke, 1969). This communication describes an investigation into the cardiovascular effects of pancuronium bromide given intravenously (0·07 mg/kg body weight) to anaesthetized humans. The subjects were in-patients undergoing routine surgery under general anaesthesia. All had consented to the investigation. Premedication was with hyoscine (0·4 mg) and papaveretum (15–20 mg) given intramuscularly 30 min before induction of anaesthesia with thiopentone (250–400 mg). After tracheal intubation under succinylcholine relaxation, anaesthesia was maintained with 60% nitrous oxide in oxygen, supplemented with phenoperidine (0·065 mg/kg body weight). Artificial ventilation was performed with a Manley ventilator to maintain the end-tidal P_{CO_2} at 30±2 mmHg.

At 18 and 20 min after induction of anaesthesia, control measurements were made of heart rate and rhythm, systolic and diastolic blood pressures, and end-tidal P_{CO_2}; cardiac output was estimated by dye dilution using indocyanine green and a photoelectric earpiece. This technique accurately records changes of output (Gabe, Tuckman & Shillingford, 1962) but does not give absolute values; therefore all results are expressed as a percentage of the control values. The subjects were then given either pancuronium (ten patients) or no drug (five patients), and the measurements repeated 2, 5 and 10 min later. There was a marked increase of heart rate, with lesser increases of mean arterial pressure and cardiac output; total peripheral resistance was unchanged (Table 1).

TABLE 1. *Changes in cardiovascular parameters at various intervals after intravenous injection of pancuronium*

	No drug (n=5)			Pancuronium (n=10)		
	2 min	5 min	10 min	2 min	5 min	10 min
Heart rate	98·8±1·1	97·9±0·6*	97·3±0·9*	122·2±4·6**	125·3±3·0**	125·9±3·4**
Cardiac output	96·0±3·9	98·5±3·1	100·0±4·1	108·6±3·5*	106·7±3·0	105·8±3·1
Stroke volume	97·9±4·7	100·6±3·1	102·8±4·2	89·7±4·2*	85·6±3·6**	84·6±3·6**
Mean arterial pressure	99·2±1·0	99·4±2·8	98·6±1·1	109·3±2·1**	108·6±2·1**	108·3±2·0**
Total peripheral resistance	103·9±3·5	101·3±3·8	99·1±3·3	103·2±4·3	102·9±4·6	102·9±4·5

All results (mean±S.E.M.) are expressed as percentages of values obtained before injection of pancuronium (0·07 mg/kg body weight) or no drug.
* $0·01<P<0·05$. ** $P<0·01$.