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## Vitamin C Requirements and Oral Contraceptives

ANIMAL experiments<sup>1-4</sup> indicate that oestrogens increase the rate of ascorbic acid breakdown and lower tissue levels. Vitamin C is poorly stored by humans and widespread sub-clinical deficiencies occur. We have investigated levels of ascorbic acid in blood cells from healthy women, some of whom were taking oral contraceptives. We have also studied pregnant women and others receiving an injected contraceptive. None was receiving supplementary vitamins.

Several brands of "combined-type" oral contraceptives were in use, while the injected product was 'Depo-Provera' (150 mg medroxyprogesterone acetate every 3 months).

Blood was collected by venepuncture and 3.0 ml. added to a special diluting agent<sup>5</sup>, any remainder being added to plastic tubes containing EDTA. A combined leucocyte-platelet button was prepared from the former, and a relatively pure platelet button from the latter. Ascorbic acid was determined by 2,4-dinitrophenylhydrazine<sup>5</sup> and expressed as  $\mu\text{g}/10^8$  cells for the leucocytes and as mg/g for the platelets. Mean values for each group are set out in Tables 1 and 2. We also measured ascorbic acid in blood cells from small groups of young women before and after beginning treatment with steroid contraceptives, and in others receiving no treatment. These results are shown in Table 3.

85 women took part in the main study; 31 were untreated non-pregnant controls (mean age 27 yr), 18 were pregnant (mean 24 yr), while 39 were receiving steroid contraceptives (mean 27 yr). Each group contained European, African and Asian women. For those in the contraceptive group, 21 had been under treatment for under 6 months, 4 for between 6 and 12 months, and 14 for over 1 year.

Our results show that ascorbic acid in both leucocytes and

**Table 1** Leucocyte Ascorbic Acid Content

Group	No.	Ascorbic acid: ( $\mu\text{g}/10^8$ : mean $\pm$ s.d.)	P value* (t-test)
All controls	31	39 $\pm$ 28	—
African controls	12	40 $\pm$ 24	NS
All contraceptives	39	26 $\pm$ 22	<0.01
Norgestrel products	15	27 $\pm$ 21	<0.02
Ethinodiol diacetate products	6	23 $\pm$ 19	<0.02
Lynestranel products	4	25 $\pm$ 10	<0.05
Norethisterone acetate products	7	26 $\pm$ 17	<0.02
Other products	3	25 $\pm$ 19	<0.02
Depot contraceptive	4	38 $\pm$ 17	NS
All pregnant	18	34 $\pm$ 21	NS
First trimester	1	19	—
Second trimester	9	33 $\pm$ 23	NS
Third trimester	8	37 $\pm$ 21	NS

\* Each group is compared with the complete control group: P values greater than 0.05 are listed as NS (not significant).

**Table 2** Platelet Ascorbic Acid Content

Group	No.	Ascorbic acid: (mg/g wet weight) mean $\pm$ s.d.	P value
All controls	10	0.26 $\pm$ 0.11	—
Oral contraceptives*	10	0.19 $\pm$ 0.13	<0.01
Depot contraceptive	5	0.28 $\pm$ 0.14	NS
Pregnant	5	0.24 $\pm$ 0.10	NS

\* As the group is small, it has not been subdivided by product: it contained 3 patients taking 'Gynovlar', 5 taking 'Ovral' or 'Eugynon' (equivalent) and 2 taking 'Ovulen' 50.

**Table 3** Leucocyte and Platelet Ascorbic Acid before and after Treatment with Oral Contraceptives

Group	Age of subject	Product	Interval (months)	Ascorbic acid			
				Leucocyte		Platelet	
				1	2	1	2
Contra- ceptive	31	'Lyndiol' 2.5	2	38	19	0.30	0.25
	22	'Minilyn'	1	65	38	0.27	0.22
	23	'Depo-Provera'*	1	28	29	0.24	0.26
	35	'Neogynon'	1	29	16	0.19	0.15
	23	'Eugynon'	2	32	28	0.23	0.16
Control	20	'Ovulen' 50	2	45	32	0.28	0.20
	28	None	1	31	34	0.24	0.27
	20	None	1	23	28	0.18	0.20
	19	None	1	28	31	0.26	0.28
	21	None	1	38	32	0.28	0.25
18	None	1	42	38	0.24	0.19	

Ascorbic acid concentrations for leucocytes are  $\mu\text{g}/10^8$  cells and for platelets mg/g wet weight. The values shown under column 1 are pre-treatment and under column 2 post-treatment results.

\* Injectable contraceptive.

platelets is significantly lower in women taking steroid contraceptives than in untreated controls or in pregnant women. Only the injected contraceptive appeared not to influence the vitamin C concentration. Cell ascorbic acid was also significantly lower in the 5 women studied before and after beginning oral contraceptives, but not in the woman starting 'Depo-Provera', nor in the untreated group.

It seems likely that oral contraceptive steroids increase the breakdown of ascorbic acid, perhaps by their stimulant action on liver release of ceruloplasmin<sup>6</sup>, a copper-containing protein with ascorbate oxidase activity<sup>7</sup>. It seems clear that many women receiving oral contraceptives may be in an induced hypovitaminotic C condition and require supplementary vitamin. It is possible that some of the reported side-effects of "the pill" may be a consequence of this vitamin lack.

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