MECHANISM OF CHANGE IN BLOOD VOLUME AND SERUM PROTEIN IN PREGNANCY

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There are during pregnancy considerable changes in endocrine control which determine metabolic and structural changes in mother and fetus. There is a sharp increase in estrogen production during this period. In the last 3 months of pregnancy the estradiol content of the plasma rises to 9.7% and estriol increases to 8.8%. The 24 h urinary excretion of estriol in normal pregnancy is 12-22 mg [15, 16].

There is evidence that both natural and synthetic estrogens cause retention of water with increase of blood volume [8, 18, 19], stimulate protein synthesis and thus produce metabolic changes characteristic of pregnancy [12].

The effects of injected estrogen (diethylstilbestrol) on volume of blood and plasma and on individual serum protein fractions were now investigated and results were compared with corresponding changes observed in the course of normal pregnancy.

METHOD

Blood volume and serum proteins were estimated before and after the injection of diethylstilbestrol to 12 rabbits. The diethylstilbestrol was injected intramuscularly in doses of 1 mg in 0.1% oily solution every 2nd day for a month. The total dose administered to each animal was thus 15 mg. The same estimations were made between the 20th and 22nd days of pregnancy in the case of 10 rabbits.

Plasma volume was estimated by injecting Evans' stain, 1 ml/kg of an 0.03% solution, into an ear vein. Blood was collected for estimation of the stain after 10 min. The stain was not estimated in plasma, as many recommend [9, 21], but in the blood serum, as the author, like others [4], had satisfied herself that the results are virtually the same. The stain concentration in the serum was determined by means of a photoelectric colorimeter from a calibration curve. Hematocrit indices (with whole body corrections [14, 17]) were also determined and the volume of the blood was calculated from the plasma volume.

Total serum protein was estimated by the refraction method and protein fractions by paper electrophoresis [1, 10]. The results were processed statistically [3, 7].

RESULTS

Blood volume and serum protein values for the control rabbits before injection of estrogen were much the same as values already reported [4, 11].

The diethylstilbestrol injections were followed by considerable increases in total blood volume, red cell volume and volume of plasma (Table 1). The increase in circulating blood volume was almost the same as after the injection of 10 mg estradiol monobenzoate which, according to Michnikovskii [19], produces an increase of 15% in the volume of the circulating blood in rabbits. The increase in plasma volume was, however, 12% in our experiments, as compared with 36% in Michnikovskii's experiments. The inference is that diethylstilbestrol leads to less retention of water in the body than a natural estrogen, estradiol (ovocyclin).

TABLE 1. Changes in Blood Volume, Red Cell Volume and Plasma Volume after Diethylstilbestrol Injections and in Pregnancy

Group of animals	Number of animals	Weight (kg)	Blood volume	Red cell volume		Hb (g/100 ml)	Plasma volume	
				ml	ml/kg		ml	ml/kg
					$M \pm m$			
Controls (C)	12	3,5±0,23	129±7	29±2,9	8,3±0,62	8,9±0,47	100±5	29,8±1,98
Given estrogen (E)	12	3,5±0,25	161±7	39±2,2	10.6±1,05	9,0±0.26	124±6	36,6±1,84
P_{C-E}		—	<0,001	<0.01	0,1	0,9	<0,01	<0,02
Pregnant (Pr)	10	3,4±1,58	186±4	53±4	15,6±1,37	11,3±0,33	133±9	39,3±1,81
P_{C-Pr}		0,9	<0,001	0,001	<0,001	<0,001	<0,001	<0,001
P_{Pr-E}		0,9	<0,01	0,001	<0.001	<0.001	0,5	0,3

TABLE 2. Changes in Serum Protein Contents After Diethylstilbestrol Injections and in Pregnancy

Group of animals	No. of animals	Total Protein			Protein fractions							
					Relative content (%)				Absolute quantity (g)			
		g	g/kg	g/100 ml	Albumin	Globulins			Albumin	Globulins		
							β	γ		α	β	γ
Controls (C)	12	8,2±0,48	2,4±0,15	6,4±0,11	63,4±0,80	11,2±0,75	11,8±0,86	13,6±0,91	5,05±0,32	0,86±0,06	0,85±0,10	1,05±0,10
Given estrogen (E)	12	9,0±0,47	2,6±0,28	5,6±0,45	75,3±1,26	9,2±0,53	5,9±0,69	9,7±0,89	6,75±0.41	0,83±0,10	0,51±0,05	0,84±0,07
P_{E-C}		0,3	0,5	0,2	<0,001	<0,05	<0,001	<0,001	<0,001	0,7	<0,01	0,1
Pregnant (Pr)	10	9,3±0,72	2,8±0,19	5,0±0,13	72,0±1,44	9,0±0,45	8,8±0,62	10,1±0,82	6,66±0,47	0,84±0,08	0,85±0,11	0,96±0,13
P_{pr-C}		0,2	0,2	<0 001	<0,001	<0,02	<0,01	<0,01	<0,001	0,8	—	0,6
P_{Pr-E}		0.8	0.4	0,3	0,5	0,8	<0,01	0.8	0,9	0,9	<0,01	0,5

The increase in total blood volume in the pregnant rabbits was greater and this was due mainly to increase in red cell volume ($P<0.001$). The increase in the volume of the plasma in the pregnant rabbits was the same as in the animals given injections of synthetic oestrogen.

Total serum protein concentration was reduced both by the estrogen injections and in pregnancy, but the reduction was greater in the latter case (Table 2). Yet, despite the reduction in concentration, the absolute protein content of the serum was not reduced and might even show some tendency to increase.

These series of experiments revealed an inverse relationship between plasma volume and protein concentration in the serum (correlation coefficient -1). On the other hand, there was a close direct relationship between plasma volume and absolute protein content of the serum (correlation coefficient +1).

Both the injection of diethylstilbestrol and pregnancy led to changes in the protein formula and absolute contents of individual protein fractions in the serum. There was a marked shift in the protein formula indicative of increase of albumin. The absolute increases of serum albumin after estrogen injections and in pregnancy were of the same magnitude.

Examination of globulins, however, revealed certain differences. Diethylstilbestrol produced a reduction in the absolute β-globulin content of the serum which was quite unusual in pregnancy (Table 2).

These changes in the protein composition of the blood serum in rabbits have not been observed in other animal species or in man [5, 6, 13, 20, 23].

A point of considerable weight, however, is that, in these experiments, the changes in plasma volume and in the protein composition of the blood produced by the injection of synthetic estrogen were similar to the changes occurring in pregnancy in animals of the same species.

It is suggested that the retention of water produced by estrogens is effected through mineralocorticosteroids as injection of estrogens is followed by significant hypertrophy of the adrenal cortex [2, 22].

SUMMARY

A study was made of the diethylstibestrol injections (15 mg per course) on the plasma volume and the serum protein fractions in rabbits. The results were compared with the changes of these 2 indices in pregnant rabbits. Estrogen caused changes analogous to those seen in pregnancy, i.e., an increase of the plasma volume and of the total albumin content.

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All abbreviations of periodicals in the above bibliography are letter-by-letter transliterations of the abbreviations as given in the original Russian journal. *Some or all of this periodical literature may well be available in English translation.* A complete list of the cover-to-cover English translations appears at the back of this issue.
