

THE VARIATIONS IN SERUM CALCIUM, PROTEIN, AND IN-ORGANIC PHOSPHORUS IN EARLY AND LATE PREGNANCY, DURING PARTURITION AND THE PUERPERIUM, AND IN NON-PREGNANT WOMEN

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Marriott and Howland (1), in 1916, showed that in the blood of uremic patients the serum calcium is low but that there is an increased concentration of inorganic phosphorus. That there might be some relation between the rise of phosphate and the fall of calcium was first suggested by Binger (2), who injected solutions of O-phosphates intravenously into dogs and observed an elevation of inorganic phosphorus in the blood accompanied by a reduction of serum calcium, an observation later confirmed by Tisdall (3). Salvesen and Linder (4) noted a parallelism between changes of protein and calcium in sera and transudates from patients with nephritis and heart disease. Among uremic patients with low serum calcium and protein, these observers also noted an enormous retention of phosphates, the decrease in calcium being proportional to the increase in phosphorus.

Peters and Eiserson (5), working mainly on patients with cardiac and renal disease, evaluated statistically their observations and those of Salvesen and Linder (4) and developed a mathematical equation to express the relationship between serum calcium, inorganic phosphorus, and protein, as follows:

$$\text{Ca} = 7 - 0.255 \text{ P} + 0.566 \text{ protein}$$

They concluded that the concentration of calcium in the serum varies directly with the protein content and inversely with the concentration of inorganic phosphorus, and expressed the belief that, in order to interpret serum calcium variations correctly, simultaneous determinations of protein and inorganic phosphorus should be made.

Stearns and Knowlton (6) failed to demonstrate a constant relationship between the level of calcium and protein, or inorganic phosphorus, in the sera of children, from birth to 16 years of age. In their study, no data were included from nephritic or cardiac patients, nor from those with obvious disturbances of calcium metabolism.

The present investigation was designed to extend the study of this relationship to early and late pregnancy, parturition, and the puerperium, as well as to normal non-pregnant women.

METHODS AND MATERIAL

The sera from 98 individuals were examined. Those with renal or cardiac disease were excluded. The blood was collected without (or with minimum) stasis, three to four hours after the previous meal, and immediately centrifuged. The serum was removed promptly from the cells. No anti-coagulants were employed.

TABLE I

Serum calcium and inorganic phosphorus according to total serum protein concentrations

Non-pregnant women			Women in early pregnancy (1 to 3 months)			Women in late pregnancy (8 to 9 months)					
Total protein	Inorganic phosphorus	Calcium	Total protein	Inorganic phosphorus	Calcium	Total protein	Inorganic phosphorus	Calcium			
<i>per cent</i>	<i>mgm. per cent</i>	<i>mgm. per cent</i>	<i>per cent</i>	<i>mgm. per cent</i>	<i>mgm. per cent</i>	<i>per cent</i>	<i>mgm. per cent</i>	<i>mgm. per cent</i>			
6.30	4.0	9.4	6.47	4.2	10.4	4.85	3.2	9.0			
6.40	3.9	10.0	6.48	4.0	10.6	5.63	3.9	9.2			
6.63	4.4	10.9	6.63	4.6	10.5	5.63	3.2	9.4			
6.85	3.9	9.7	6.73	4.0	10.9	5.66	3.9	8.7			
6.98	3.9	10.6	6.74	3.9	10.4	5.79	3.4	9.4			
7.00	3.8	9.9	6.76	3.5	10.4	5.87	3.2	8.8			
7.10	3.9	10.1	6.85	4.7	10.0	5.95	3.0	9.0			
7.12	3.7	11.0	7.46	4.2	10.1	6.00	3.0	9.2			
7.12	4.2	10.3	7.55	4.1	9.8	6.18	4.4	9.7			
7.15	4.5	10.1	7.56	4.2	10.7	6.20	4.1	9.0			
7.48	3.7	10.1	6.92	4.1	10.4	6.21	3.3	9.3			
7.55	4.5	10.7				6.27	4.0	9.2			
7.95	4.6	11.3				6.27	4.0	10.8			
7.95	3.9	10.5				6.43	4.1	9.9			
7.98	4.6	10.9				6.47	3.9	9.1			
8.00	3.2	11.2				6.50	4.2	10.6			
7.22	4.0	10.4				6.50	3.8	9.3			
						6.58	4.4	10.1			
						6.62	4.2	10.0			
						6.63	4.1	9.5			
						6.65	3.8	9.1			
						6.67	3.9	9.3			
						6.75	3.7	9.6			
						6.75	4.1	8.9			
						6.78	4.8	10.4			
						6.78	2.8	9.2			
						6.90	3.4	9.4			
						6.94	3.8	9.9			
						6.96	3.6	9.5			
						7.02	3.4	9.5			
						7.07	3.1	9.2			
						7.10	4.9	9.0			
						7.65	3.6	10.2			
						6.43	3.8	9.5			

TABLE I—*Continued*

Parturient women			Puerperal women (7 to 9 days after delivery)		
Total protein	Inorganic phosphorus	Calcium	Total protein	Inorganic phosphorus	Calcium
<i>per cent</i>	<i>mgm. per cent</i>	<i>mgm. per cent</i>	<i>per cent</i>	<i>mgm. per cent</i>	<i>mgm. per cent</i>
5.10	2.8	9.7	6.66	3.7	9.5
5.70	3.4	8.9	6.77	4.9	9.0
5.71	3.2	9.4	6.84	4.9	9.6
6.00	3.2	9.5	6.96	5.2	9.3
6.07	3.5	10.8	6.97	5.0	9.5
6.07	4.2	11.0	7.01	5.0	9.6
6.10	4.3	9.5	7.04	3.3	9.5
6.16	3.6	9.9	7.11	5.1	9.5
6.20	4.2	9.9	7.24	5.1	10.3
6.24	4.8	10.3	7.27	4.5	10.5
6.28	3.5	9.8	7.47	4.5	11.0
6.31	4.4	10.2	7.55	4.3	10.8
6.38	3.5	10.3	7.65	4.8	9.8
6.40	3.5	9.9	7.69	4.6	10.3
6.48	3.8	10.4			
6.50	3.3	10.0	7.16	4.6	9.9
6.51	4.4	10.6			
6.64	4.5	9.0			
6.70	4.9	10.4			
6.76	3.2	10.4			
7.20	4.2	9.2			
7.20	4.7	9.5			
7.33	3.7	9.2			
7.53	4.5	10.9			
7.63	3.6	10.1			
6.44	3.9	9.9			

The total nitrogen was determined by the micro-Kjeldahl method (7) and the determined nonprotein nitrogen subtracted to give the protein nitrogen, which was then multiplied by the factor 6.25 to obtain the total protein. The inorganic phosphorus was determined by the method of Benedict and Theis (8), and the calcium by the Clark-Collip (9) modification of the Kramer-Tisdall (10, 11) procedure.

The sera from the five series of women studied were grouped according to the protein content (Table I). Variations in calcium and phosphorus were then compared with the changes in protein concentration.

TABLE II
Summary

Blood serum determinations	Normal non-pregnant	Early pregnancy	Late pregnancy	Parturition	Post-partum 7-9 days
Number of observations	16	10	33	25	14
Protein (average per cent)	7.2	6.9	6.4	6.4	7.2
Phosphorus (mgm. per 100 cc.)	4.0	4.1	3.8	3.9	4.6
Calcium (mgm. per 100 cc.)	10.4	10.4	9.5	9.9	9.9

DISCUSSION

The correlation coefficients between serum protein and calcium and between serum calcium and phosphorus have been calculated from the experimental data in Table I, and are presented in Table III.

TABLE III
Correlation coefficients

	Protein : Calcium	Calcium : Phosphorus
Non-pregnant women.....	+ 0.65 \pm 0.098	+ 0.148 \pm 0.167
Early pregnancy.....	- 0.16 \pm 0.152	- 0.317 \pm 0.211
Late pregnancy.....	+ 0.355 \pm 0.102	+ 0.379 \pm 0.101
Parturient women.....	+ 0.082 \pm 0.134	+ 0.121 \pm 0.134
Puerperal women.....	+ 0.728 \pm 0.085	- 0.273 \pm 0.166

It is evident from Table III that there is a significant correlation between the protein and the calcium concentrations in the sera of non-pregnant and puerperal women only. In early pregnancy, the protein values tend to be somewhat diminished, while the serum calcium is unaffected, and the correlation completely disappears. (It is realized that the number of determinations in this group is too small to permit an accurate statistical survey.) In late pregnancy and during the post-partum period, all three constituents are reduced somewhat below the non-pregnant level, and again there is no mathematical correlation of significance.

Comparative study of the serum phosphorus and calcium values in the various groups fails to elicit any significant correlation.

A mathematical formula can be evolved expressing a relationship between any two blood constituents which normally exhibit comparatively narrow ranges. The proof of such a relationship, however, lies in the maintenance of a significant correlation between the two constituents under conditions allowing wide variation of either component. In normal non-pregnant women, the range of serum protein is slight, whereas in late pregnancy and during parturition the protein concentration tends to be lower and the range is considerably increased. The fact that in these latter groups there is no significant correlation between calcium and protein bears out the contention that the level of serum protein in these conditions is not the chief factor in determining the level of the serum calcium. The same reasoning can be applied to the relationship assumed to exist between serum calcium and inorganic phosphorus.

SUMMARY

1. Variations of serum calcium with changes of inorganic phosphorus at different protein concentrations were studied in non-pregnant women, in early pregnancy, in late pregnancy, during parturition, and after delivery.

2. The data indicate a significant correlation between the serum protein and the serum calcium in non-pregnant and puerperal women, which is completely lost in late pregnancy and parturition when the protein range is considerably widened.

3. No significant correlation between the serum calcium and the serum inorganic phosphorus was observed in any of the five groups studied.

ADDENDUM

Since the above was written, there has appeared a theoretical exposition by Greenwald (12), in which he derives a new equation for expressing the relationship between serum protein and serum calcium ($\text{Ca} = x + 0.875 \text{ protein}$). Considering only the groups of normal individuals cited by Greenwald, it is found that the protein is the more variable factor, and that the calculated value for x is dependent largely upon the levels of serum protein in the group studied.

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