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Serum Phosphatase, Calcium and Phosphorus Values in Infancy.*

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Investigators who have been studying diagnostic procedures and standards for judging the healing or development of early rickets in infants have commented on the difficulty of making accurate judgments when these must be based upon the physical findings, roentgenological examinations, the serum calcium and serum phosphorus determinations. We have previously cited[1] our belief that, through the determination of the serum phosphatase, we have a more accurate means of recognizing the early development of the disease. In this we simply agree with other investigators[2, 3] and offer additional supporting evidence. However, with our interest in this abnormal state in the infant, we were struck by the lack of any considerable data defining the *normal* serum phosphatase for the infant in the first year of life. The data of Jeans and Stearns[4] show that the plasma phosphatase, which is low at birth, rises abruptly to a maximum during the first month, maintains this peak only a short time, and then falls rather rapidly during the second or third month, gradually declining through the remainder of the year, although the phosphatase level remains higher than that found in older age groups.

Our data, based on 630 observations made upon infants during the first year of life, do not entirely coincide with those of Jeans and Stearns but we feel that they represent a good sampling of population of this age for this section of the country. Part of the patients, differentiated as "Harper Babies", upon whom 390 observations were made, were born at Harper Hospital and were followed in our outpatient clinic. They received adequate amounts of milk, vitamin D

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1 Barnes, D. J., and Carpenter, M. D., *J. Pediatrics*, 1937, **10**, 596.

2 Bodansky, A., and Jaffe, H. L., *Arch. Int. Med.*, 1934, **54**, 88; *Am. J. Dis. Child.*, 1934, **48**, 1268.

3 Morris, N., Stevenson, M. M., Peden, O. D., and Small, J., *Arch. Dis. Childhood*, 1937, **12**, 45.

4 Stearns, G., and Warweg, E., *J. Biol. Chem.*, 1933, **102**, 749.

as cod liver oil, and accessory foods as their ages warranted. Where there was any evidence of developing anemia, iron was added to the dietary. Any infants who showed signs or symptoms of rickets, either physical or as judged roentgenologically, were dropped from the group. The average serum phosphatase from these patients did not show the peak rise during the first month noted by Jeans and Stearns.

A second group of patients, known as "Welfare Babies", on which 240 of the observations were made, were selected from those sent to our clinic from Child Welfare stations because they were thought to be rachitic and in need of treatment. From the large number sent, those were selected who were roentgenologically negative and

TABLE I.

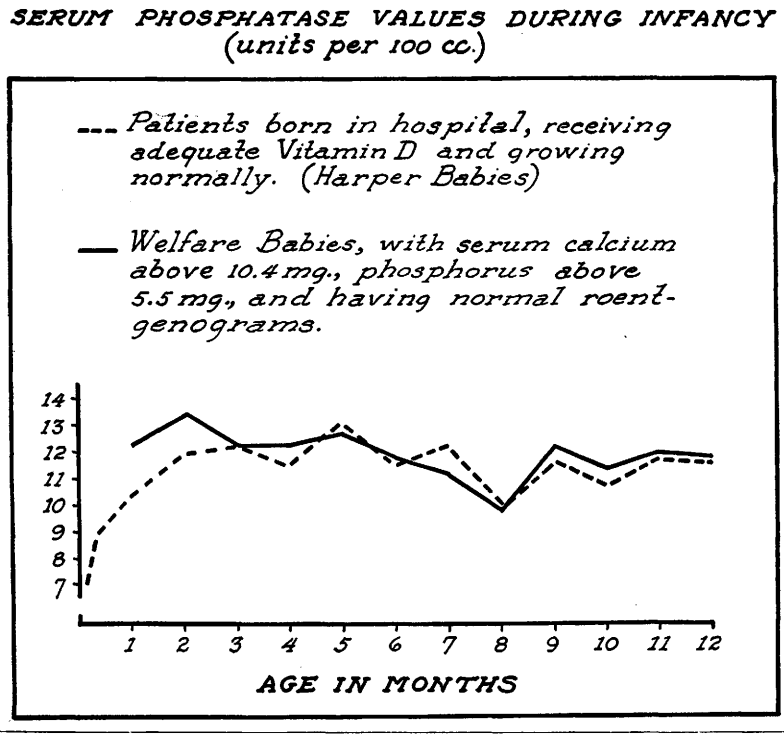
Age groups	"Harper babies" No. cases	Mean, mg per 100 cc serum	Standard deviation, mg	"Welfare babies"* No. cases	Mean, mg per 100 cc serum	Standard deviation, mg
(a) Statistical evaluation of calcium data.						
0 - 3 days	20	11.3	.83	—	—	—
3 -15 "	17	10.8	1.09	—	—	—
½- 1½ mo	31	12.1	.70	8	11.9	.80
1½- 2½ "	28	11.6	.71	30	11.9	.67
2½- 3½ "	28	11.9	.62	27	11.9	.69
3½- 4½ "	33	12.1	1.09	23	12.1	.92
4½- 5½ "	34	11.8	.66	23	12.1	.77
5½- 6½ "	27	11.9	.63	21	12.0	.63
6½- 7½ "	26	11.8	.92	28	11.5	.74
7½- 8½ "	31	11.9	.79	21	11.9	.59
8½- 9½ "	25	11.9	.67	15	11.9	1.13
9½-10½ "	19	12.1	.64	18	12.0	.62
10½-11½ "	13	11.8	.58	12	12.1	.50
11½-12½ "	22	11.9	.65	10	12.3	.61
Total	354			236		
(b) Statistical evaluation of phosphorus data.						
0 - 3 days	45	6.4	.99	—	—	—
3 -15 "	23	6.8	.75	—	—	—
½- 1½ mo	33	6.4	.56	8	6.6	.58
1½- 2½ "	30	6.7	.78	30	6.3	.58
2½- 3½ "	28	6.5	.77	27	6.3	.52
3½- 4½ "	33	6.3	.93	23	6.1	.51
4½- 5½ "	34	6.3	.71	23	6.4	.51
5½- 6½ "	27	6.4	.61	22	6.2	.51
6½- 7½ "	26	6.2	.51	28	6.3	.42
7½- 8½ "	31	5.9	.62	21	6.1	.45
8½- 9½ "	26	5.9	.59	15	6.2	.49
9½-10½ "	19	6.1	.54	21	6.1	.43
10½-11½ "	13	5.9	.87	12	6.4	.54
11½-12½ "	22	5.8	.39	10	6.4	.59
Total	390			240		

*Patients had a serum calcium of at least 10.4 mg per 100 cc, and a serum phosphorus of 5.5 mg or higher.

who were found to have a serum calcium of at least 10.4 mg per 100 cc and a serum phosphorus of 5.5 mg or above, values which are considered well above the minimal normal levels. From this group, consisting of colored and white babies, we obviously could not get data at birth and relatively few were seen during the first month. Some of them had had vitamin D, generally in small amounts.

The serum calcium, phosphorus and phosphatase were determined on blood drawn from the femoral vein. Clark and Collip's modification of the Kramer, Tisdall method[5] was used for calcium determinations, and Bodansky's method[6] for phosphorus and phosphatase determinations.

Table I shows that the calcium values from birth to 3 days for "Harper Babies" fell from an average of 11.3 mg per 100 cc serum to 10.8 mg during the second week, then rose to an average of 12.1 mg at the first month and were maintained rather consistently through the year. Phosphorus values averaged 6.4 mg per 100 cc serum for birth to 3 days of life and rose to an average maximum



[5] Clark, E. P., and Collip, J. B., *J. Biol. Chem.*, 1925, **63**, 461.

[6] Bodansky, A., *J. Biol. Chem.*, 1932, **99**, 197; *ibid.*, 1933, **101**, 93.

of 6.8 mg during the second week, receded slightly with the upswing of serum calcium at one month and then established a fairly constant though slightly falling value during the remainder of the year, to an average of 5.8 mg at 12 months. The "Welfare Babies" gave values which corresponded remarkably closely to those of the "Harper Babies."

The average serum phosphatase of the "Harper Babies", from birth to 3 days of age (Chart), has a value of 7.1 units per 100 cc. It shows no peak during the first month but rather a sharp rise to 11.9 units during the first 2 months, a very slow continuance of this rise through the fourth and fifth months to an average value of 13.0 units and then a gradual, slight decline through the rest of the year to a level of 11.5 units. There is a rather pronounced decline at the eighth month to a value of 9.9 units. The data, representing averages, together with standard deviations for the phosphatase values are shown in Table II.

It is noteworthy that the group labeled "Harper Babies" does not have the high average phosphatase levels at the first and second months reached by the "Welfare" patients. This probably is explained by the fact that the "Welfare Babies" were sent in as being possible cases of active rickets and their serum phosphatase values actually were elevated during the first and second months. In other words, some did have this deviation from the normal. It has been

TABLE II.
Statistical Evaluation of Phosphatase Data.

	"Harper babies"			"Welfare babies"*		
Age groups	No. cases	Mean, units per 100 cc serum	Standard deviation, units	No. cases	Mean, units per 100 cc serum	Standard deviation, units
0 - 3 days	45	7.1	2.66	—	—	—
3 -15 "	23	8.9	2.39	—	—	—
½- 1½ mo	33	10.4	3.05	8	12.3	3.84
1½- 2½ "	30	11.9	3.01	30	13.5	3.25
2½- 3½ "	28	12.1	2.52	27	12.3	2.87
3½- 4½ "	33	11.6	2.76	23	12.2	3.15
4½- 5½ "	34	13.0	2.92	23	12.8	2.81
5½- 6½ "	27	11.4	2.88	22	11.5	2.56
6½- 7½ "	26	12.3	2.44	28	11.1	2.51
7½- 8½ "	31	9.9	2.64	21	9.8	3.29
8½- 9½ "	26	11.6	2.58	15	12.2	3.18
9½-10½ "	19	10.8	3.11	21	11.0	3.58
10½-11½ "	13	11.8	2.56	12	12.0	3.84
11½-12½ "	22	11.5	2.87	10	11.7	3.21
Total	390			240		

*Patients had a serum calcium of at least 10.4 mg per 100 c, and a serum phosphorus of 5.5 mg or higher.

pointed out that this change in serum phosphatase is probably our earliest reliable sign of rachitic activity. Later on in the infant's life there was not the same relationship between slight physical signs and this evidence of activity. Beginning with the third month and continuing through the year, the phosphatase values for the "Welfare" group correspond fairly closely to those of the "Harper" group. We feel that the "Harper" group represents a sufficiently large, well controlled series so that we have not combined it with the "Welfare" group, rather showing each separately. As would be expected, our standard deviations are smaller in the "Harper" group than in the "Welfare" group.

The findings include both summer and winter values. Among the "Harper Babies," 170 cases tested between June 1 and November 1, constituting summer values, averaged 10.8 units for the year; while 220 cases observed from November 1 to June 1 in the winter grouping, averaged 11.0 units. During the first 6 months of life, the winter values of the "Harper Babies" averaged 1.3 units higher than the summer values, while from 6 months to one year of age, the summer values averaged 1.6 units greater than the winter values. There was not a sufficiently regular distribution of summer and winter cases in the "Welfare" group to warrant such comparisons.

These data represent, first, a series of serum phosphatase, calcium and phosphorus observations upon normal infants (Harper Babies) which should help to establish normal serum phosphatase values through the first year of life; second, a comparison with a group (Welfare Babies) which shows a slightly abnormal elevation of serum phosphatase at the first and second months but which, as judged by other serological and roentgenological standards, was normal. This supports the view that the serum phosphatase elevation is the earliest diagnostic sign of rickets, since this latter group was sent to us representing possible early cases of the disease. Furthermore, the "Welfare" group refutes, since it had such small amounts of vitamin D, the possible argument that the ingested vitamin D which was had in moderate amounts by the "Harper Babies" depressed the level of serum phosphatase below the physiological normal. In addition, further correlated data are presented concerning the serum calcium and phosphorus values during infancy.