RESULTS FOLLOWING THE ADMINISTRATION OF
ALKALI PHOSPHATES TO SPASMOPHILIC,
RACHITIC AND NORMAL
INFANTS *

JOSEPH K. CALVIN, S.B., M.D.
AND
MAXWELL P. BOROVSKY, S.B., M.D.
CHICAGO

Considerable research has been conducted recently, investigating the influence of the alkali phosphates, especially sodium and potassium diortho-phosphates, on normal and spasmophilic infants. Binger ¹ produced tetany by the intravenous injection of ortho-phosphates. Howland and Marriott ² found that when the inorganic phosphorus of the serum was high in severe nephritis that the calcium of the serum was greatly diminished. They considered the question, therefore, whether there was a sufficient accumulation of inorganic phosphates in the serum in tetany to account for the reduction of the calcium. Their determinations in cases of active tetany showed a low calcium content in the blood serum but no significant increase in phosphorus. Kramer, Tisdall and Howland ^{2a} have very recently confirmed this work and state that an increase in the inorganic phosphorus of the serum does not seem to be responsible for infantile tetany, although in cases of rickets complicated by tetany there is a relatively high phosphate content (as compared with uncomplicated rickets), the significance of which is not as yet clear. Jones and Nye ³ and Howland and Kramer ⁴ have very recently found in normal infants that the concentration of calcium is from 9 to 11 mg. and inorganic phosphorus about 5 mg. per hundred c.c. of serum.

Jeppson and Klercker ⁵ found that by the feeding of 0.20 gm. of phosphorus pentoxid per kilogram body weight to normal infants and 0.10 to latent spasmophilic infants, symptoms similar to those of active

* Received for publication Oct. 24, 1921.

* From the Department of Pediatrics, University of Illinois and the Children's Department, Cook County Hospital.

1. Binger: J. Pharmacol. & Exper. Therap. **10**:105, 1917.

2. Howland, J., and Marriott, W. McK.: Quart. J. M. **11**:289, 1917.

2^a. Kramer, B.; Tisdall, F., and Howland, J.: Am. J. Dis. Child. **22**:431 (Nov.) 1921.

3. Jones, M., and Nye, L.: J. Biol. Chem. **47**:321, 1921.

4. Howland, J., and Kramer, B.: Am. J. Dis. Child. **22**:105 (Aug.) 1921.

5. Jeppson and Klercker: Ztschr. f. Kinderh. **28**:71, 1921.

spasmophilia were produced.⁶ These results were often evident in a few hours when the potassium salts were employed while larger quantities of sodium salts were needed. Often it required two or three days to produce symptoms with the latter. They conclude that especially during the first and second years, with the exception of the first few months of life, that an excess of alkali phosphates is received by most of the spasmophilic children. An 8 months old infant, weighing 8 kg., receiving 1 liter of cow's milk daily, will get from 0.25 to 0.3 gm. phosphorus pentoxid per kilogram. A large percentage of this will be in the form of alkali phosphates. These authors found that whey produced less irritation in latent spasmophilics when the phosphates had been precipitated and removed.

Howland and Kramer⁴ in a series of experiments found that the inorganic phosphorus of the serum is regularly reduced in active rickets, (except when complicated by tetany) sometimes to an extreme degree, and that by administering cod liver oil, the phosphorus content of the serum gradually rises to a normal figure and often somewhat above this. Sherman and Pappenheimer⁷ have reached the conclusion that lesions resembling rickets uniformly appeared in the absence, and were uniformly prevented by the presence of, sufficient phosphates in the diet. Similarly, Park⁸ and co-workers believe that the phosphate ion in the diet may be a determining factor for or against rickets. They found that if the phosphate content of the diet is sufficiently high, rickets-like changes in the skeleton do not occur in rats.

It is a well established fact that rickets and spasmophilia are very closely associated clinically. Very few cases of spasmophilia are observed which do not show evidences of rickets. In fact, Kassowitz and others have referred to spasmophilia as the nervous manifestation of rickets. According to our present knowledge it appears confusing to accept Jeppson and Klercker's view that an increased intake of phosphates alone is responsible for the precipitation of infantile tetany while a diminished phosphorus intake and content of the blood is a dominant factor in the development of rickets. The administration of cod liver oil and phosphorus prevents, arrests or cures both rickets and spasmophilia and yet increases the phosphorus content of the blood.

Because of these apparent discrepancies we made a number of observations on infants who were receiving various amounts of the

6. 0.20 gm. of phosphorus pentoxid (P_2O_5) represents in alkali diorthophosphates 0.27 gm. of potassium oxid (K_2O) and 0.18 gm. sodium oxid (Na_2O) or 0.49 gm. of potassium phosphate (K_2HPO_4) and 0.39 gm. of sodium phosphate (Na_2HPO_4).

7. Sherman, H. C., and Pappenheimer, A. M.: *Proc. Soc. Exper. Biol. & Med.* **18**:193, 1921.

8. Shipley, P. G.; Park, E. A.; McCollum, E. V.; Simmonds, N.: *Johns Hopkins Hosp. Bull.* **32**:160, 1921.

diortho-phosphates of sodium and potassium. A brief summary of the history and observations on these cases follows:

REPORT OF CASES

CASE 1.—G. D., aged 15 months, colored, weight 14 pounds, was admitted April 3, 1921, with evidence of an early bronchopneumonia and signs of active tetany, consisting of marked laryngospasm, Chvostek, Trousseau and an electrical reaction of 3.5 ma. with the C.O.C. There were signs of marked rickets. Calcium bromid, 5 grains, three times daily and cod liver oil with phosphorus, one dram three times daily were administered. Twelve days of this treatment brought the C.O.C. to 12 ma. April 15, and there were no signs of active tetany. Temperature was normal. Cod liver oil and calcium bromid were stopped and sodium chlorid, 15 grains, and potassium citrate, 10 grains, were given every morning. Six days later, April 21, the C.O.C. was 2.5 ma.; there was a definite Chvostek, a moderate Trousseau but no spontaneous carpopedal spasm. The sodium and potassium salts were then stopped and calcium lactate, 3 grains twice daily, cod liver oil with phosphorus, one dram three times daily and orange juice one ounce twice daily were begun. Six days later the C.O.C. was 15 + ma. No carpopedal spasm was present and there was merely a suggestion of a Chvostek.

May 27, 1921, the cod liver oil and phosphorus, calcium lactate and orange juice were discontinued and sodium diortho-phosphate, 17 grains, was given three times daily (a dosage amounting to 0.53 gm. per kg. in twenty-four hours) and continued until June 10. There were no signs of spasmophilia and the C.O.C. was 15 + ma. June 1, 1921, five days after beginning the administration of the phosphate, there were no signs of spasmophilia. June 8, 1921, there was no evidence of tetany, no diarrhea; cheerful, appetite and sleep normal. June 10, 1921 the phosphate was changed to the potassium salt and 0.53 gm. per kg. in twenty-four hours were given until June 14. There was no evidence of spasmophilia, the C.O.C. was 15 + ma. and the C.C.C. 8 ma. There was a moderate diarrhea. On June 11, 1921 the child was very irritable and restless. There were no clinical manifestations of tetany. The C.O.C. was 10 ma., the C.C.C. 3 ma. The diarrhea had subsided. June 13, the child was still irritable. The irritability for the past few days was discovered to have been due to cellulitis about the neck. June 14, 1921, the potassium diortho-phosphate was stopped and the cellulitis was treated. There was no evidence of spasmophilia and the C.O.C. was 15 ma. June 15, 18 and 20 there were no clinical manifestations of tetany and the electrical reactions were normal. June 20 the temperature was again normal and the infection practically cleared up.

This case shows that in spite of the presence of an acute infection, along with the administration of massive doses of phosphates, tetany was not induced. The moderate diarrhea probably due to the sodium salt was not aggravated by changing to the potassium salt.

CASE 2.—E. M., aged 3 years, colored, weight 17 pounds, was admitted May 23, 1921, suffering from pertussis, very marked rickets and active tetany, consisting of marked laryngospasm, Chvostek, Trousseau and C.O.C. of 4.5 ma., with generalized convulsions. She was placed on calcium lactate 5 grains three times daily; cod liver oil, 1 dram, and orange juice $\frac{1}{2}$ ounce, three times daily, in addition to antispasmodics and pertussis vaccine. June 2, there were still present signs of tetany, the C.O.C. was 4.5 ma. but the paroxysms of coughing were less frequent. June 10, the Chvostek sign was only suggestive; no Trousseau; C.O.C. 8 ma.; pertussis much less severe. June 14, no clinical evidence of spasmophilia and normal electrical reactions. June 19, developed measles but there were no signs of spasmophilia.

After complete recovery from the attack of measles July 15, 1921, the cod liver oil and calcium were stopped and potassium diortho-phosphate, 25 grains three times daily (0.62 gms. per kg. in twenty-four hours) was given for the following sixteen days. There were no signs of spasmophilia—the C.O.C. was 12 ma. and the C.C.C. 4 ma. July 18, no diarrhea or vomiting; cheerful; no signs of spasmophilia and electrical reactions normal. July 21, clinical record was the same, C.O.C. was 12 + ma. and C.C.C. 8 ma. The condition remained the same until the child was discharged July 31, 1921.

CASE 3.—M. M., twin of E. M., weight 18½ pounds, was admitted May 23, 1921, with the same condition as that of her sister. The findings were the same, except for the electrical reaction, which was C.O.C. 4 ma. The same treatment was instituted. June 2, the C.O.C. was 5 ma.; the Chvostek sign still present; paroxysms of coughing less frequent. June 7, practically the same. June 10, only a suggestion of a Chvostek; no other signs of tetany; C.O.C. 15 ma., C.C.C. 3 ma. June 19, the child developed measles, and there were no clinical signs of tetany.

After complete recovery from the attack of measles, the cod liver oil and calcium were stopped and potassium phosphate, 25 grains, three times daily (0.600 gm. per kg. in twenty-four hours) was begun July 5, and continued for six days. There were no signs of spasmophilia; the C.O.C. was 15 + ma., the C.C.C. was 5 ma. July 7, no vomiting or diarrhea, no signs of tetany; July 8, moderate diarrhea; no vomiting; no signs of tetany; the C.O.C. was 15 ma. and the C.C.C. 7 ma. July 10, discharged.

CASE 4.—F. D., 18 months of age, colored, weight 13 pounds, was admitted May 18, 1921, with malnutrition, marked rickets and no clinical manifestations of spasmophilia. May 23, sodium phosphate, 17 grains, three times daily (0.57 gm. per kg. per twenty-four hours) was given for seventeen days. June 1, there were no signs of tetany, the C.O.C. was 15 ma. June 5, the patient ate and slept well, no diarrhea and no clinical signs of tetany. June 8, the C.O.C. was 6 ma. but still there was no clinical evidence of tetany. June 9, the phosphate was changed to the potassium salt which was given in same dosage for the next eleven days. June 10, moderate diarrhea, no signs of spasmophilia. June 11, the C.O.C. was 5 ma.—no other definite signs of tetany. June 18 and June 20, electrical reaction C.O.C. 12 + ma. and no signs of tetany. Discharged.

CASE 5.—J. F., age 1 year, white, weight 16 pounds, was admitted April 29, 1921, with furunculosis, no signs of spasmophilia and only moderate rickets. The furunculosis cleared up, and May 23, sodium phosphate, 19 grains, three times daily (0.52 gm. per kg.) was given for eleven days. The C.O.C. was 15 ma. June 1, still no evidence of spasmophilia, the C.O.C. was 12 ma. June 7, developed an acute encephalitis; no evidence of tetany. Died of acute infection one week later.

CASE 6.—J. L., aged 8 months, white, weight 12 pounds, was admitted June 6, 1921, with malnutrition and no evidence of rickets. June 10, sodium phosphate, 17 grains, three times daily, was given (0.62 gm. per kg. per twenty-four hours). The C.O.C. was 15 ma.; the C.C.C. was 3.5 ma. After being on this preparation for about four days the electrical reaction was unchanged and there were no clinical manifestations of spasmophilia.

CONCLUSIONS

1. The administration of from 0.55 to 0.60 gm. of potassium diorthophosphate (K_2HPO_4) or sodium diorthophosphate (Na_2HPO_4) per kilo body weight per twenty-four hours to the infants neither activated latent spasmophilia nor produced symptoms resembling

spasmophilia. In one case of rickets the electrical excitability approached the spasmophilic reaction for about thirty-six hours although no other manifestations of tetany were present notwithstanding the fact that the potassium phosphate was continued.

2. Several of the cases selected were at the most susceptible age for spasmophilia to develop.

3. Several of the infants showed marked evidences of rickets, supposedly making them more prone to develop spasmophilia.

4. Even the superimposing of acute intercurrent infections in a number of cases, plus the administration of the phosphates did not precipitate spasmophilic manifestations.

5. Three of the patients had just recovered from active spasmophilia and yet it could not be reprecipitated by administering the phosphates.

6. These patients had recovered from the active spasmophilia rapidly on receiving phosphorized cod liver oil, which is known to increase the phosphorus content of the blood.

7. It is evident, therefore, that the most susceptible cases which could be selected did not develop spasmophilia when placed on large doses of diorthophosphates and so we are unable to confirm the results of Jeppson and Klercker.

We wish to express our sincere thanks to Dr. Julius H. Hess for suggesting this research, for his kindly interest and the opportunity of reporting cases from his ward.