

## STUDY REPORTS

1. Title: Occurrence of crystalluria upon DL-methionine and orthophosphate supplementation (Bangkok Infants)

Principal Investigators: Sakorn Dhanamitta, M.D.  
Aree Valyasevi, M.D.  
Robert Van Reen, Ph.D.

Assistant Investigators: Sirinadh Pengruangrojanachai, B.Sc. (Med. Tech)  
Prapaisri Phuwastien, B.Sc. (Med. Tech)

### OBJECTIVE

To study the effect of DL-methionine and orthophosphate supplementation on the occurrence of crystalluria in Bangkok infants and compare with results reported previously in Ubol village infants (stone area).

### DESCRIPTION

Twenty-two male infants ranging in age from 6 to 24 months who live in the Rajavithi Children Home and Pak-Kred Preventorium in Bangkok were included in this study. Their routine feeding was cow's milk formula and ordinary rice. There were no histories of bladder stone disease.

300 mg of DL-methionine in 1 ml of 80% Sucrose syrup were administered orally to the infants once daily for 6 days following a 3 day control period. The orthophosphate was given in the form of buffer solution of neutral pH containing 2.32 g  $\text{Na}_2\text{HPO}_4$  and 0.36 g  $\text{KH}_2\text{PO}_4$  in 6.6 ml solution ( $\sim$  P 600 mg) per day for 5 days following the methionine supplementation.

Twenty-four hour urine samples were collected on the last day of control period and immediately after giving the 6th dose of methionine by utilizing pediatric urine collecting bags. Aliquots of the 24 hr urine samples were analyzed for the urinary excretion of various constituents (see next report).

Freshly voided early morning urine samples were collected daily and examined qualitatively for pH, protein, and sugar by COMBISTIX paper strip. Microscopic examinations were performed on centrifuged specimens within two to three hours after collection.

### PROGRESS

The age, weight and height of each subject, sequences of the supplementation and locations are shown in Table 1. No changes in the amounts of foods consumed were observed during the orthophosphate supplementation. A number of subjects developed mild diarrhea during the course of study (Control period B<sub>1</sub> B<sub>2</sub> B<sub>4</sub> B<sub>5</sub> B<sub>6</sub>), (Methionine period B<sub>1</sub> B<sub>2</sub> B<sub>3</sub> B<sub>4</sub> B<sub>5</sub> B<sub>6</sub> B<sub>10</sub> B<sub>11</sub> B<sub>13</sub> B<sub>14</sub>), and most of the subjects had loose stools, during the orthophosphate administration. The Average pH of the 3 periods were 5.31, 5.19 and 5.29 respectively.

Table 2. shows the occurrence of oxalate and uric acid crystalluria following the supplementation of methionine and orthophosphate in Bangkok infants compare with Ubol village infants (data from the previous reports).

Bangkok infants were found to have a less occurrence of oxalate crystalluria (9.1, 9.1%) in comparison with those in Ubol village infants (26.9, 28.6%) during placebo and methionine supplementations. However it was found that oral orthophosphate supplementation could not eliminate the oxalate crystalluria in Bangkok Infants as it did in Ubol village infants. On the other hand Bangkok infants demonstrated a more frequent occurrence of uric acid crystalluria when compared with those of Ubol village infants but

demonstrated a reduction in the occurrence of this crystal when orthophosphate was supplemented the same as Ubol village infants did. It was further observed that Bangkok infants demonstrated more calcium phosphate crystalluria after methionine supplementation and increasing further during orthophosphate supplementation. These findings were not found in Ubol village infants.

It would be interesting to study further the finding that oral orthophosphate supplementation can eliminate the oxalate crystalluria in Ubol village infants and Chiangmai villages infants (Hyper-endemic area) but not in Bangkok infants (Hypo-endemic area of Bladder stone disease). Since the pH of the urine in Ubol and Chiangmai infants were increased during orthophosphate supplementation but in Bangkok infants it was not changed, the kidney function of these two groups of infants should be studied.

Table 1  
Description of Subjects, Location, Age, Weight,  
Height and Types of the Supplementation  
Bangkok, Thailand

| Location                | Subject | Ages<br>Months | Weight<br>Kg. | Height<br>Cm. | Supplementation              |
|-------------------------|---------|----------------|---------------|---------------|------------------------------|
| Rajavithi Children home | B1      | 11             | 7.25          | 72.5          | Control—Methionine—Phosphate |
|                         | B2      | 10             | 6.7           | 67.5          | "                            |
|                         | B3      | 9              | 7.0           | 65.0          | "                            |
|                         | B4      | 8              | 6.2           | 62.5          | "                            |
|                         | B5      | 14             | 8.0           | 72.5          | "                            |
|                         | B6      | 24             | 6.5           | 72.5          | "                            |
| Pak Kred Preventorium   | B8      | 14             | 7.3           | 65.0          | "                            |
|                         | B9      | 9              | 9.0           | 65.0          | "                            |
|                         | B10     | 9              | 7.8           | 63.8          | "                            |
|                         | B11     | 7              | 6.65          | 60.63         | "                            |
|                         | B12     | 10             | 6.14          | 65.0          | "                            |
|                         | B13     | 8              | 5.84          | 59.38         | "                            |
|                         | B14     | 11             | 7.88          | 67.5          | "                            |
|                         | B15     | 8              | 2.51          | 65.0          | "                            |
|                         | B16     | 10             | 10.0          | 78.75         | "                            |
|                         | B17     | 21             | 9.0           | 76.25         | "                            |
|                         | B18     | 22             | 11.0          | 78.75         | "                            |
|                         | B19     | 18             | 9.5           | 76.25         | "                            |
|                         | B20     | 16             | 8.0           | 43.75         | "                            |
|                         | B21     | 6              | 7.0           | 66.25         | "                            |
|                         | B22     | 23             | 10.0          | 79.38         | "                            |
|                         | B23     | 21             | 10.0          | 80.0          | "                            |

Table 2

Occurrence of crystalluria following supplementation with methionine and orthophosphate in Bangkok infants as compared with Ubol village infants

| Supplement and Type of Crystalluria | No. of Infants | Crystalluria       |                     |                        | No. of infants with crystalluria |
|-------------------------------------|----------------|--------------------|---------------------|------------------------|----------------------------------|
|                                     |                | No. of Occurrences | No. of Examinations | Percent of Occurrences |                                  |
| <b>Bangkok</b>                      |                |                    |                     |                        |                                  |
| <u>Placebo</u>                      |                |                    |                     |                        |                                  |
| Oxalate                             | 22             | 4                  | 44                  | 9.1                    | 3                                |
| Uric Acid                           | 22             | 19                 | 44                  | 43.2                   | 10                               |
| <u>Methionine</u>                   |                |                    |                     |                        |                                  |
| Oxalate                             | 22             | 8                  | 88                  | 9.1                    | 5                                |
| Uric Acid                           | 22             | 45                 | 88                  | 51.1                   | 19                               |
| <u>Orthophosphate</u>               |                |                    |                     |                        |                                  |
| Oxalate                             | 22             | 16                 | 110                 | 14.5                   | 8                                |
| Uric Acid                           | 22             | 37                 | 110                 | 33.6                   | 17                               |
| <b>Ubol villages</b>                |                |                    |                     |                        |                                  |
| <u>Placebo</u>                      |                |                    |                     |                        |                                  |
| Oxalate                             | 17             | 25                 | 93                  | 26.9                   | 17                               |
| Uric Acid                           | 15             | 22                 | 83                  | 26.5                   | 15                               |
| <u>Methionine</u>                   |                |                    |                     |                        |                                  |
| Oxalate                             | 14             | 20                 | 70                  | 28.6                   | 10                               |
| Uric Acid                           | 16             | 18                 | 80                  | 22.5                   | 11                               |
| <u>Orthophosphate</u>               |                |                    |                     |                        |                                  |
| Oxalate                             | 17             | 0                  | 83                  | 0.0                    | 0                                |
| Uric Acid                           | 15             | 6                  | 73                  | 8.2                    | 3                                |