

BODY OF REPORT

SEATO CRC Study No. 8 Urologic and Nutritional Studies of Calculous Disease of the Bladder *

Project No. 3A 025601 A 811 Military Medical Research Program
S. E. Asia

Task 01: Military Medical Research Program
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Subtask 01: Military Medical Research Program
SEASIA (Thailand)

Reporting Installation: US Army-SEATO Medical Research Laboratory
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 Division of Clinical Research

 Department of Clinical Studies

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Objectives:

1. To study seasonal variation in the amount and type of foodstuffs consumed by inhabitants of hyper- and hypo-endemic areas for bladder stone.
2. To study seasonal variation in urinary findings of freshly voided morning specimens and urinary metabolites in 24-hour specimens in inhabitants of hyper- and hypo-endemic areas for bladder stone.

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Description: Previous epidemiological studies have established that prevalence of bladder stone varies markedly between the city of Ubol and Nong Kohn village (only 15 kilometers apart). Highest incidence of stone passing and presumptive symptoms occur during the hot, dry weather in February, March and April and after the cessation of the rainy season in November. Bladder stone is most prevalent in children under the age of 5 years. Infants under 1 year old also suffer from this disease.

Sixteen families with a history of either positive or presumptive episodes of bladder stone disease in Nong Kohn village were subjected to dietary survey for 3 days each during April (hot and dry), August (rainy) and November (cool and dry) of 1963. Another 17 families randomly selected from Ubol city were also studied in the same fashion. A nurse investigator, well-trained in dietary survey technique, was assigned to each house. She weighed and recorded all food prepared for the family and all left over food or food not consumed by the family. During each family dietary survey, the nurse investigator also inquired about infant-feeding practice, foods (tree leaves, plants, vegetables, insects, etc.) consumed in different seasons and foods which are best taken or not allowed during menstruation, pregnancy and lactation.

Previous urologic studies have demonstrated that the volume of 24-hour urine excretion in subjects living in Nong Kohn village (endemic for bladder stone) was about half that of subjects living in Ubol city during the hot, dry weather (April 1963). The same group of villagers excreted about half as much during the hot, dry weather as compared to the rainy (August 1963) and cool, dry seasons (November 1963). Urinary calcium concentration was higher in the freshly voided morning urine samples from Nong Kohn than from the city. Urinary crystals, mainly oxalate, were found more frequently in urine specimens from the village than from the city.

Seventy three urine samples from Ubol city and 134 samples from Nong Kohn village obtained from children between the age of 2 to 10 years were studied for creatinine, calcium, phosphorus, uric acid, oxalate and magnesium. These 24-hour urine specimens were collected on 4 different occasions as follows: April (hot and dry), August (raining), November (cool and dry) of 1963 and May (hot and some rains) of 1964. Collection was made from the same household member in each season. A nurse stayed with each family for a period of not less than 16 hours daily and supervised the collection. Since there is no latrine in the house, individuals had to go outside for voiding or used the supplied container. Collection was made under toluene and the amount was measured. After the 24-hour samples were thoroughly mixed, a portion was put in a small glass container and kept in a freezer. Uric acid, inorganic phosphate, creatinine and calcium were determined by automated technics. (1). Oxalate determination was done by the method described by Archer et. al. (2).

(1) Technicon Autanalyzer, Chauncey, N.Y., U.S.A.

(2) Archer, H.E. et. al.: Studies on the Urinary Excretion of Oxalate by Normal Subjects. Clin. Sci. 16: 405, 1957.

Table I

NUTRIENT INTAKE PER CAPITA PER DAY CALCULATED FROM FOOD INTAKE *
UBOL CITY AND NONG KOHN VILLAGE, 1963

Season	Village	Calories intake	Protein (GM)			Ca mg	Fe mg	Vit A I.U.	Vit B ₁ mg	Vit B ₂ mg	Niacin mg	Vit C mg
			A	V	Total							
H	N.K.	1904	15.5	28.0	43.5	531	8.4	861	0.69	0.33	13.2	29.5
R	N.K.	1912	14.1	36.5	50.6	385	7.9	1,133	0.84	0.36	14.6	23.6
C	N.K.	1996	15.6	25.2	40.8	352	6.8	724	0.72	0.34	14.0	21.4
H	U.C.	1888	21.1	32.0	53.1	285	10.4	2,528	0.81	0.47	15.8	35.0
R	U.C.	1900	24.7	31.1	55.8	261	10.3	1,810	0.83	0.44	16.5	46.4
C	U.C.	1775	25.7	29.7	55.4	332	10.1	1,720	0.72	0.42	15.4	43.3

* Interdepartmental Committee on Nutrition for National Defense: The Kingdom of Thailand Nutrition Survey, Oct. - Dec. 1960. Washington, D.C. (1962)

Food Composition tables by the Nutrition Division, Ministry of Health, Thailand

** H - Hot and dry
R - Rainy
C - Cool and dry'

*** N.K. - Nong Kohn
U.C. - Ubol City

Progress: The average daily intake for each food item within a village was determined by tabulating the foods consumed by each family, obtaining the total amount of each food item consumed, and dividing by the number of person days. The nutrient intake was calculated using standard tables of food composition from the average daily food intake for each village. Technique used here is the same as the ICNND survey in 1960 (3).

Nutrient intake per capita per day is shown in Table I. City inhabitants consume more protein (mainly animal protein), vitamin A, B₁, B₂, niacin, C and iron than villagers. However, calcium intake among villagers is significantly higher than city people, especially in hot, dry season in which small animals including insects and reptiles are frequently eaten among school-age children and adults. Vitamin A intake among villagers is about half that of city inhabitants. The over-all dietary intake in rainy season is better than dry season (see Figures 1-6).

The same kinds of tree leaves, plants and vegetables are available for consumption both in Nong Kohn and Ubol city. There are also no differences in dietary habits during pregnancy and lactation in the two areas. Source of drinking and cooking water is from local wells both in the village and city.

(3) Interdepartmental Committee on Nutrition for National Defense: The Kingdom of Thailand. Nutrition Survey, Oct - Dec 1960. Washington, D.C. (1962).

Table II
 INFANT FEEDING PRACTICES IN 90 FAMILIES
 NONG KOHN VILLAGE, 1964

Feedings	AGE						No		Total	
	1 wk	2-4 wk	2-3 mo	4-5 mo	6-11 mo	1 yr	2 yr	2 yr Inf.		
Beginning of glutinous rice	51	25	4	1	3	0	0	0	6	90
Beginning of ordinary rice	0	0	0	0	0	0	0	0	0	90
Beginning of fermented fish (raw)	0	0	0	0	0	8	10	28	44	90
Beginning of fermented fish (cooked)	0	0	0	0	4	35	25	20	6	90
Beginning of vegetables	0	0	0	0	0	7	19	64	0	90
Beginning of meat	0	0	0	0	1	17	30	42	0	90
Beginning of spicy food	0	0	0	0	0	4	13	71	2	90
Beginning of adult food	0	0	0	0	0	0	3	82	5	90

Ninety households, randomly selected from 3 villages close to Nong Kohn, were questioned for infant-feeding practices. In addition, 114 households from Ubol city were also studied. Data including types of milk feedings, age at starting solid foods (rice, vegetables, meat and fish) and age at weaning are shown in Tables II and III. There are striking differences in the infant-feeding practices, mainly in introduction of solid food, between Nong Kohn and city inhabitants. Fifty-seven per cent of village infants have glutinous rice (baked and chewed) supplementation in the first week of life. On the contrary, only 2 per cent of city infants are started at this age.

The number of urine samples, age and sex distribution of the subjects and time of collection are shown in Table IV.

Urinary calcium excretion as expressed in mg. per cent or per gm. creatinine in age groups, 2 to 6 and 7 to 10 years, of children from Nong Kohn is significantly higher than from Ubol city throughout the year. The excretion in the hot, dry season is significantly higher than in the rainy and cool seasons. There is no significant difference in urinary calcium excretion during the three seasons in children from Ubol city (see Graph 1).

Urinary phosphorus excretion: The data concerning the excretion of phosphate in children from Nong Kohn and Ubol city is shown in Graph II. There is no significant difference in the phosphate excretion between the samples from Nong Kohn and Ubol city. However, the phosphorus excretion in samples from Nong

Table III

INFANT FEEDING PRACTICES IN 114 FAMILIES
UBOL CITY, 1964

Feedings	AGE					1 yr	2 yr	2 yr	No info.	Not take	Total
	1 wk	2-4 wk	2-3 mo	4-5 mo	6-11 mo						
Wean from breast feeding	0	0	2	5	3	27	42	14	9		102
Wean from bottle feeding	0	0	0	0	0	2	1	6	3	104	114
Beginning of glutinous rice	1	5	9	0	2	1	0	0	0	96	114
Beginning of ordinary rice	2	1	42	8	35	5	2	0	1	18	114
Beginning of (raw fermented fish	0	0	0	0	5	8	15	50	20	16	114
Beginning of (cooked) fermented fish	0	0	0	0	3	11	13	47	24	16	114
Beginning of vegetables	0	0	1	0	15	24	41	23	8	3	114
Beginning of meat	0	0	1	0	15	24	35	30	8	1	114
Beginning of spicy food	0	0	0	0	0	2	22	85	4	1	114
Beginning of adult food	0	0	0	0	0	3	28	46	37	0	114

Table IV

NUMBER OF SUBJECTS, AGE AND SEX DISTRIBUTION AND MONTH OF COLLECTION

Description	Nong Kohn	Ubol City
Number of families	17	16
Total Subjects	48	44
Ages: 2-6 years	29	19
7-10 years	19	25
Sex: Male	22	19
Female	26	25
Total Samples	134	73
Period I April 1963	24	13
Period II Aug - Sept 1963	34	20
Period III November 1963	35	16
Period IV May 1964	41	24

Kohn is lowest in May 1964, at which time the urinary calcium excretion is the highest.

Urinary creatinine excretion (Graph III): The data demonstrate that the highest creatinine concentration is in the sample from Nong Kohn collected during the hot dry season (April 1963).

Urinary uric acid and oxalate excretion: The data are shown in Graph IV and V. There are no significant differences between the samples from Nong Kohn and Ubol city. No seasonal variations are observed both in samples from Nong Kohn and Ubol city.

Urine samples were sent to Dr. Saubertich at the Fitzsimmon General Hospital for magnesium determination.

Summary and Conclusions: Dietary surveys and urinary studies were carried out in Nong Kohn village (hyper-endemic area for stone) and Ubol city (hypo-endemic for stone) with the objective to determine the differences in which may lead to an explanation for a high prevalence in villages and low in city.

Early feeding of glutinous rice to less than 1 week old babies is frequently practiced in Nong Kohn village, whereas it is rarely practiced in Ubol city. City infants are usually supplemented with ordinary rice at the age of 3 to 6 months. The amount of rice, given to the newborn baby in the village, is enough to cut down the number of milk feedings. This will allow the mothers to have more time available for doing housework or field-work.

Urinary calcium excretion is higher in the samples from Nong Kohn than from Ubol city during three seasons of 1963. Urinary calcium concentration is about double in the hot, dry season as compared to the rainy and cool seasons. High calcium intake is partly responsible for this. High excretion of urinary calcium was demonstrated in experimental rats with urolithiasis. (4,5,6). These rats were fed a diet containing low casein (15% by weight). Calculi are prevented by increasing the protein level to 30% with either casein or soybean protein although gelatin is ineffective. Supplementation of methionine and/or lysine monohydrochloride can also reduce or prevent stone formation in these rats. (7) The excretion of calcium was inversely related to the casein level of the diet. The greatest excretion was observed in rats fed the low casein diet and the least excretion of calcium in rats receiving the high casein diet.

Our findings are consistent with the studies in rats where the protein-mineral ratio of the diet is important. It is further supported by infant-feeding study. Early rice supplementation in newborn babies among the villagers would reduce the protein intake at the age at which maximum protein intake is required. The study of urinary lysine and methionine excretion is in progress.

The possible role of vitamin A deficiency in the pathogenesis of vesical calculi cannot be ruled out. However, in the south where the vitamin A intake is low

and signs of vitamin A deficiency are found more commonly than in the other parts, bladder stones are rarely found.

From our study, it appears unlikely that unusual tree leaves, plants or vegetables consumed by villagers are a possible factor in stone formation.

Table V

URINARY CALCIUM EXCRETION IN 24-HOURS SPECIMENS UBOL AND
NONG KOHN, 1963-1964

Seasons	Nong Kohn mg/gm Creatinine	Ubol City mg/gm Creatinine	Probability (P)
Hot, dry April, 1963	163.8 ± 21.8	77.2 ± 11.4	<0.01
Rainy August, 1963	105.5 ± 17.7	65.0 ± 12.1	<0.01
Cool, dry November, 1963	131.8 ± 10.8	70.0 ± 10.4	<0.01
Hot, dry May, 1964	285.8 ± 23.3	86.2 ± 10.9	<0.01

- (4) Van Reen, R. et. al. Urolithiasis in the Rat I. J. Nutr. 69: 392-396, 1956
 (5) Van Reen, R. et. al. Urolithiasis in the Rat II. J. Nutr. 69: 397-402, 1959
 (6) Van Reen, R. et. al. Urolithiasis in the Rat III. J. Nutr. 77: 137-141, 1962
 (7) Van Reen, R. et. al. Urolithiasis in the Rat IV. J. Nutr. 83: 358-364, 1964

Table VI

URINARY METABOLITES CONCENTRATION
IN 3 DIFFERENT SEASONS
NONG KOHN AND UBOL CITY, 1963

Urinary Metabolites mg%	Age	NONG KOHN			UBOL CITY				
		Apr 63	Aug 63	Nov 63	May 63	Apr 63	Aug 63	Nov 63	May 63
"Creatinine"									
2 - 6 years		67.0	36.8	35.3	47	32.8	39.3	34.5	50.8
7 - 10 years		76.9	50.4	60.6	56.3	40.5	42.4	47.2	88.7
"Uric Acid"									
2 - 6 years		69.5	48.9	41.1	23.0	43.8	70.5	75.3	27.8
7 - 10 years		96.2	56.8	73.2	26.2	43.5	55.1	66.8	38.5
"Calcium"									
2 - 6 years		9.9	4.9	4.96	12.02	2.5	1.95	3.35	3.4
7 - 10 years		8.4	4.5	7.7	13.57	2.1	3.2	2.85	6.87
"Phosphorus"									
2 - 6 years		35.1	18.8	20.1	18.06	15.0	24.4	29.5	37.3
7 - 10 years		36.8	25.1	38.2	21.05	20.2	22.7	31.4	36.3

FIGURE I CALORIES INTAKE PER CAPITA PER DAY
SEASONAL VARIATIONS IN THE SAME HOUSEHOLD. UBOL, 1963

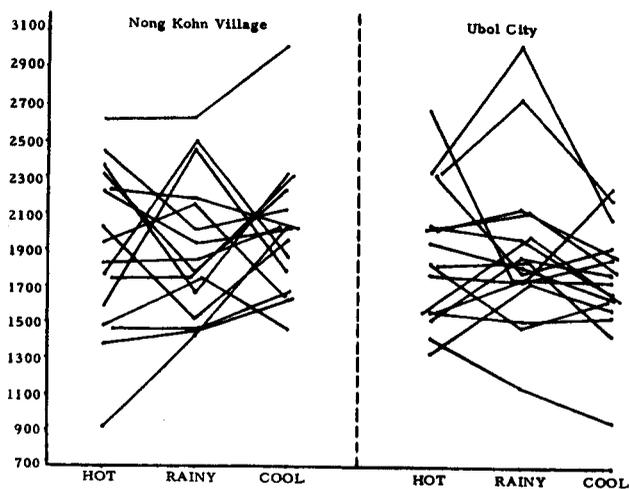


FIGURE II PROTEIN INTAKE (GM) PER CAPITA PER DAY
SEASONAL VARIATIONS IN THE SAME HOUSEHOLD. UBOL, 1963

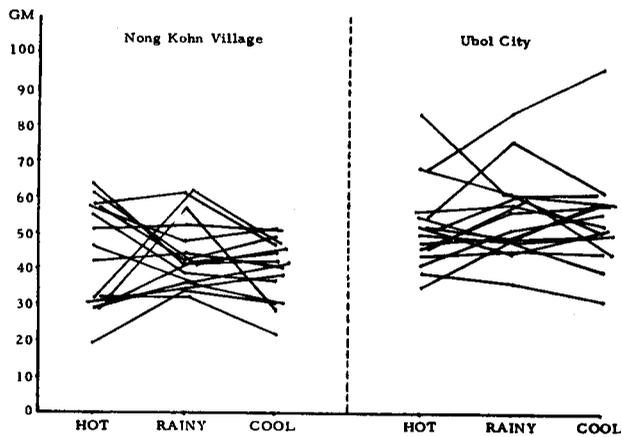
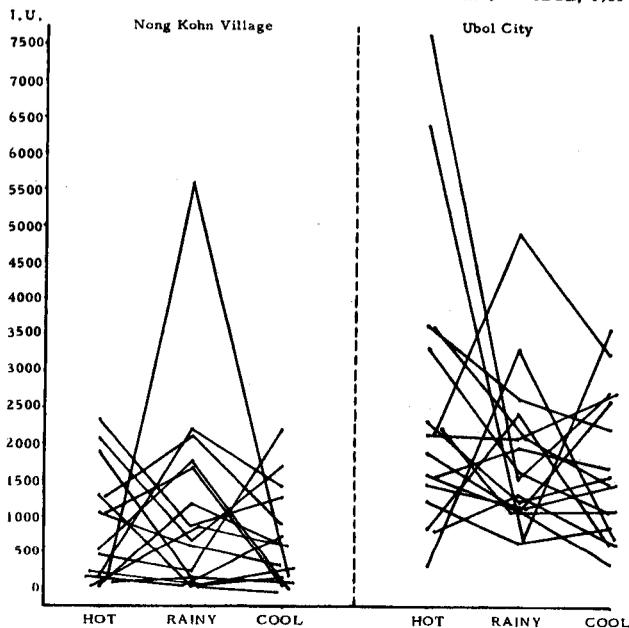
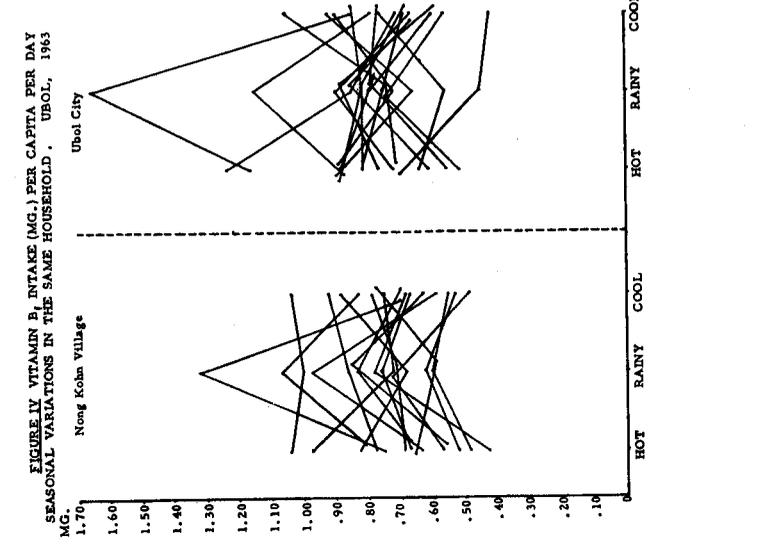
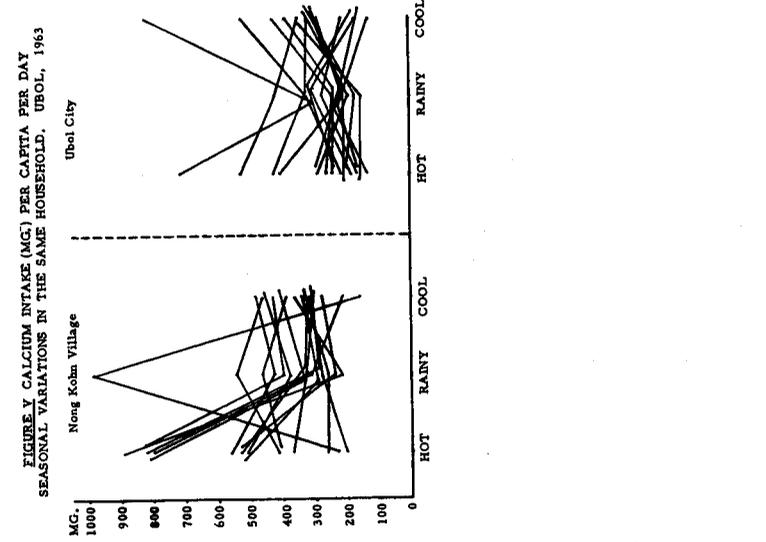
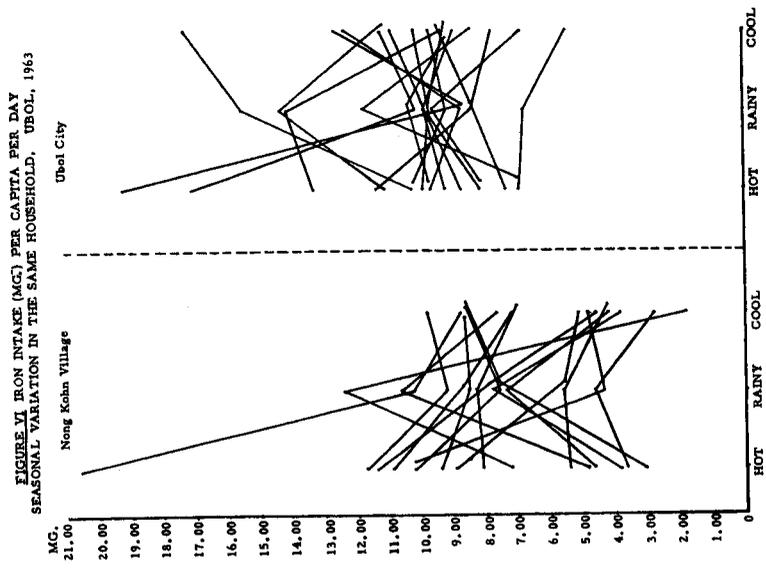


FIGURE III VITAMIN A INTAKE (I.U.) PER CAPITA PER DAY
SEASONAL VARIATIONS IN THE SAME HOUSEHOLD. UBOL, 1963

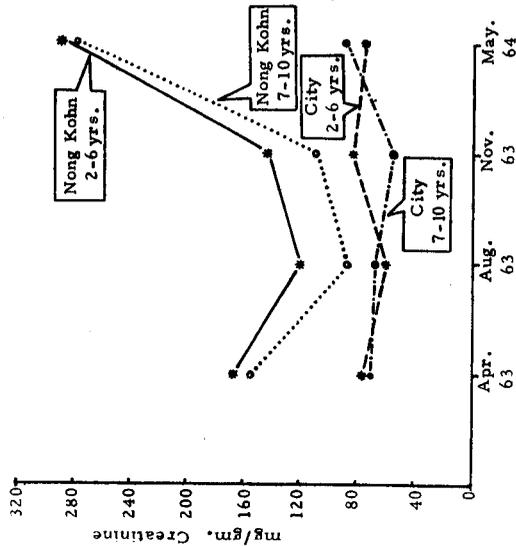




GRAPH I

URINARY CALCIUM IN 24 - HOUR SPECIMENS

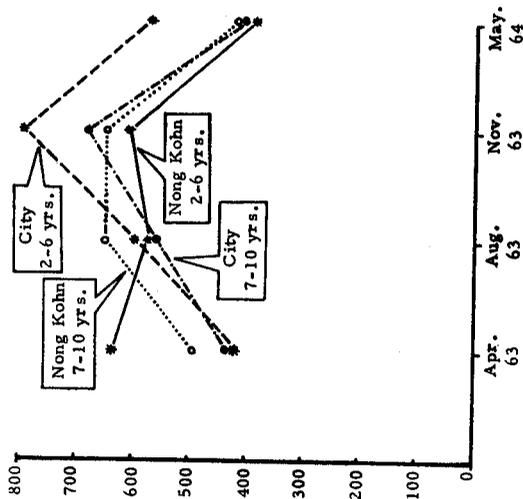
UBOL AND NONG KOHN, 1963 - 1964



GRAPH II

URINARY PHOSPHORUS IN 24 - HOUR SPECIMENS

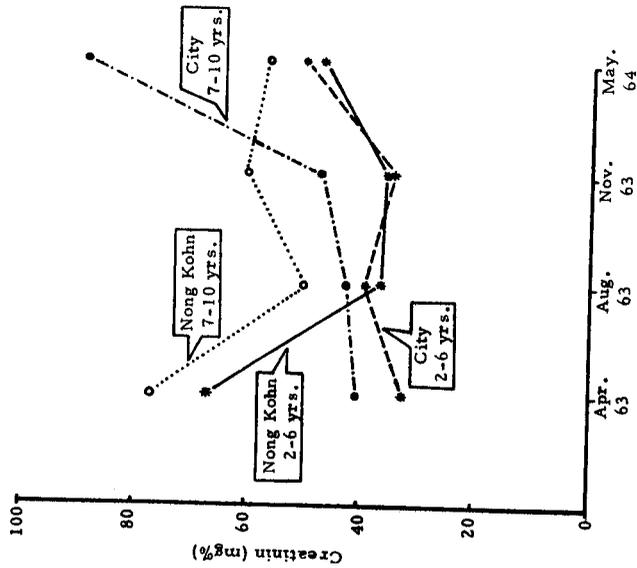
UBOL AND NONG KOHN, 1963 - 1964



GRAPH III

URINARY CREATININE IN 24 - HOUR SPECIMENS

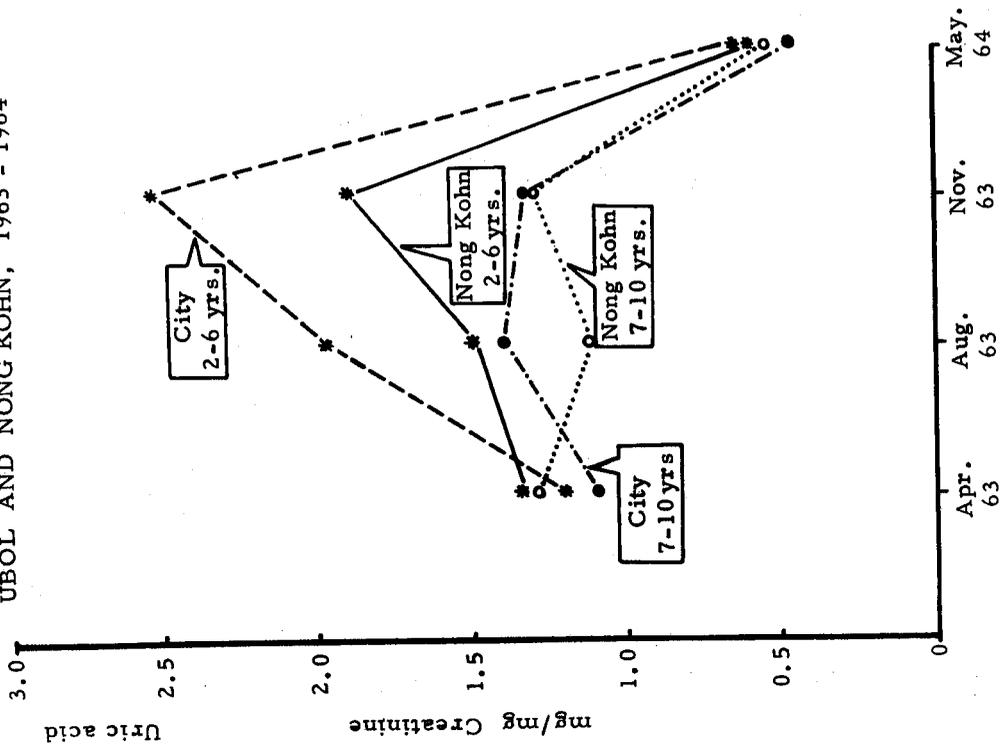
UBOL AND NONG KOHN, 1963 - 1964



GRAPH IV

URINARY URIC ACID IN 24 - HOUR SPECIMENS

UBOL AND NONG KOHN, 1963 - 1964



GRAPH V

URINARY OXALATE IN 24 - HOUR SPECIMENS

UBOL AND NONG KOHN, 1963 - 1964

