

ANNUAL PROGRESS REPORT

SEATO Medic Study No. 101 Epidemiological Factors Related to
Formation of Urinary Tract Calculi

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

Task 01: Military Medical Research Program
S.E. Asia

Subtask 01: Military Medical Research Program
SEASIA (Thailand)

Reporting Installation: US Army-SEATO Medical Research Laboratory
APO 146, San Francisco, California

 Division of Medical Research Laboratories

 Department of Virology (Special Project)

Period Covered by Report: 1 April 1963 to 31 March 1964

Principal Investigator: Major Scott B. Halstead, MC

Associate Investigator: Dr. Aree Valyasevi

Reports Control Symbol: MEDDH-288

Security Classification: UNCLASSIFIED

ABSTRACT

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The objective of this study is to determine epidemiological factors related to formation of urinary tract calculi. Bladder stone is an acute and chronic disease occurring among the rural inhabitants of North and North-east Thailand. In a survey conducted in 1963 in Ubol Province no inhabited area was found to be free of bladder stones; however, prevalence in urban areas was very low. Disease prevalence did not vary significantly with ethnic group, heredity or economic status. Symptoms begin most frequently during the hot, dry weather before and after the rainy season. Burning or painful urination, the passing of urinary sand or obstruction of urinary flow may be the only symptoms of the disease; and 8 persons have these lesser symptoms to every 1 person hospitalized. Spontaneous stone passing is three times as frequent as symptoms requiring operation. Stone passing and obstruction of GU tract occur primarily in males but the lesser symptoms

occur nearly as frequently in females as males. The disease is most prevalent in children under the age of 5, however, stone formation occurs at a significant rate throughout life. Stones recur in 8% of cases or 7 times as frequently as the original attack rate. Finally, persons who share the same food and household environment with positive cases are twice as likely to develop a stone as the average.

BODY OF REPORT

SEATO Medical Study No. 101

Epidemiological Factors Related to Formation of Urinary Tract Calculi

Project No. 3A 025601 A 811

Military Medical Research Program
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Task 01:

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Military Medical Research Program
SEASIA (Thailand)

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Objective: The objective of this study is to determine epidemiological factors related to formation of urinary tract calculi particularly bladder stone.

Description: Bladder stone is the most common surgical problem in North and Northeast Thailand. The condition is considered by most authorities to be a nutritional disorder. In January, 1963 selected rural and urban areas of Ubon Province were surveyed for prevalence of bladder stone. Sample populations of 44 villages and 3 towns were selected randomly from village rosters. Interviewees were asked whether they or any member of their family remembered history of: (1) stone operation (2) passing a stone per urethra (3) episode of sandy or cloudy urination (4) episode of dysuria

(5) episode of painful urination (6) hematuria. The first 2 occurrences are classified as positive episodes (of bladder stone disease) and the latter 4 episodes are classified as presumptive episodes.

Progress: Altogether, families representing 20,806 persons were interviewed. Of these, 15,154 lived in 44 villages and 5,654 persons lived in 3 towns with populations of 5,000 or greater. As seen in Table 57, of the persons interviewed 253, or 1.2% had either passed a stone or had an operation and 540 or 2.6% had had presumptive symptoms. For each person hospitalized there were 3 sufferers who passed calculi spontaneously without medical attention and 8 persons with presumptive symptoms.

Geographical Distribution

No area surveyed was free of stone disease. Stones were 4 times as prevalent among some persons who lived near the Maekong as in persons who were remote from large bodies of water. In general, however, stone prevalence assumed a somewhat random distribution within each area studied. Several adjacent villages were found to have high and low stone prevalence even though they shared water and sources of food.

Rural and Urban Prevalence

The prevalence of positive and presumptive symptoms of bladder stone among residents of towns was uniformly low compared with residents of surrounding villages. Only 0.25% of inhabitants of the town of Ubol had positive evidence of stones while stones occurred at rates which were average (1-2%) for the Province as a whole in each of surrounding suburban villages.

Season of Occurrence of Stone Episodes

Positive and presumptive episodes of bladder stone disease showed a bimodal seasonal variation. The highest incidence of stone passing and presumptive symptoms occurred before and after the rainy season in March and November.

Age of Onset

Bladder stone is a disease of all ages of life, with a marked tendency to involve the very young. The modal age of presumptive symptoms is 2 years while the modal age of stone passing and operations is 3. Operations are performed rarely after childhood (confirmed by hospital statistics) but presumptive symptoms and stone passing episodes starting in the 3rd decade occur at a steady rate through life (about one half the rate observed in 3 year old).

Sex

Symptoms of bladder stone disease occur more frequently in males than females. Males accounted for 208 positive histories and females for 45 (4.6:1, M:F). Sex ratio for presumptive symptoms was 2:1 males to females while the ratio in hospitalized patients (Ubol Hospital 1958-1962) was 9:1 males to females.

Ethnic Group

Bladder stone prevalence did not vary significantly with any of the major ethnic groups living in Ubol. Each of the ethnic groups sampled with large enough numbers had approximately the same incidence of stones as did the Lao-Thai people living in the same area (Table 58).

Duration and Recurrence of Bladder Stone Disease

Spontaneous passage of stone or acute urinary retention occurred abruptly without prodromal symptoms in over one-half of the positive group. The rest had fairly continuous presumptive symptoms which preceded operation or stone passing by an average of over 2 years. In contrast to bladder stone operations stone passing recurred relatively frequently. Twenty-one of 253 persons or 8% passed stones on two or more occasions. As is shown in Table 59, the average interval between these positive episodes was 9 years and 5 months with intervals as long as 35 years being recorded. Of 68 persons with stone operation, 2 had operative recurrence. The intervals between first and second operations were 6 and 51 months, respectively.

Family Prevalence

Bladder stone symptoms occurred more frequently among household relatives than among other relatives of persons with the disease. In Table 60 it is seen that the secondary prevalence rate for bladder stone among the household relatives of positive cases was twice as high as the over-all prevalence rate. However, secondary episodes among near relatives living in other household occurred only at the frequency of primary occurrences.

Economic Status

The prevalence of positive or presumptive symptoms of stones was not found to vary significantly with family or village economic status (see Table 61).

Summary and Conclusions: Bladder stone is an acute and chronic disease occurring among the rural inhabitants of North and Northeast Thailand. In a survey conducted in 1963 in Ubol Province no inhabited area was found to be free of bladder stones; however, prevalence in urban areas was very low. Disease prevalence did not vary significantly with ethnic group, heredity or economic status. Symptoms begin most frequently during the hot, dry weather before and after the rainy season. Burning or painful urination, the passing of urinary sand or obstruction of urinary flow may be the only symptoms of the disease; and 8 persons have these lesser symptoms to every 1 person hospitalized. Spontaneous stone passing is three times as frequent as symptoms requiring operation. Stone passing and obstruction of the GU tract occur primarily in males but the lesser symptoms occur nearly as frequently as the original attack rate. Finally, persons who share the same food and household environment with positive cases are twice as likely to develop a stone as the average.

Table 57. Prevalence of positive episodes and presumptive symptoms in sample. Ubol, January 1963.

Total Interviewed		20,806
Total positive cases		253
Passed stone only	185	
Stone passed and operation	41	
Operation only	27	
Two operations	2	
Total presumptive cases		540

Table 58. Prevalence of positive bladder stone episodes in several ethnic groups. Ubol, 1963.

Ethnic group	Number sampled	Positive episodes	Attack rate per 1000	Attack rate per 1000 Lao-Thai in same area
Chinese	595	2	3.4	4.9
Vietnamese	447	1	2.2	3.8
Cambodian	949	5	5.3	7.0

125

Table 59. Duration and recurrence of bladder stone disease, Ubol, 1963.

	Number Cases	Average duration or interval	Extremes
Abrupt onset of positive symptoms	136	--	--
Presumptive symptoms precede positive	114	2.3 years	2 wks.- 36 yrs
Stone passing recurrence	21	9.4 years	5 mos.- 34 yrs

Table 60. Familial prevalence of bladder stone, Ubol, 1963.

	Total study	Near relatives of primary cases	
		Same household	Different household
No. at risk	20,806	1,348	3,105
Positive occurrence	253	31	43
Prevalence	1.2% (primary attack rate)	2.3% (secondary attack rate)	1.4% (secondary attack rate)

Table 61. Bladder stone prevalence and economic status of lifelong village residents, Ubol, 1963.

	Economic Rating by Village Headman					
	Poor	%	Average	%	Good	%
All families	930	38.9	1,328	56.5	135	5.6
Positive episodes	78	37.9	111	53.9	17	8.2
Presumptive symptoms	168	34.5	299	61.4	20	4.1

Publication: Halstead, S.B. and Valyasevi, A.
Epidemiology of Bladder Stone in Ubol Province
J. Med. Assoc. Thailand
47: 1-12, 1964.

ANNUAL PROGRESS REPORT

SEATO Medic Study No. 102 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
S.E. Asia

Subtask 01: Military Medical Research Program
SEASIA (Thailand)

Reporting Installation: US Army-SEATO Medical Research Laboratory
APO 146, San Francisco, California
Division of Medical Research Laboratories
Department of Virology (Special Project)

Period Covered by Report: 1 April 1963 to 31 March 1964

Principal Investigator: Dr. Aree Valyasevi

Associate Investigator: Major Scott B. Halstead, MC

Reports Control Symbol: MEDDH-288

Security Classification: UNCLASSIFIED

ABSTRACT

SEATO Medic Study No. 102 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
 S.E. Asia

Subtask 01: Military Medical Research Program
 SEASIA (Thailand)

Reporting Installation: US Army-SEATO Medical Research Laboratory
 APO 146, San Francisco, California

 Division of Medical Research Laboratories

 Department of Virology (Special Project)

Period Covered by Report: 1 April 1963 to 31 March 1964

Principal Investigator: Dr. Aree Valyasevi

Associate Investigator: Major Scott B. Halstead, MC

Reports Control Symbol: MEDDH-288

Security Classification: UNCLASSIFIED

The objective of this study is to elucidate the pathogenesis of vesical calculi. 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 even when corrected for volume in the samples from Nong Kohn than from the city. However, the lower volume of urinary excretion in the children under 5 years old is probably partly responsible for the higher urinary calcium concentration. Urinary crystals, mainly oxalate, were found more frequently in urine specimens from the village

than from the city. It seems probable that a stage of dehydration during the hot, dry season leads to lower urinary output with high urinary calcium, oxalate and uric acid may play a factor in the stone formation. Determinations of creatinine and uric acid in 24-hour samples are in progress. Further studies comparing the capacity of urine obtained from village and city to dissolve oxalate and studies of oxalate and uric acid metabolism will be done in the future.

BODY OF REPORT

SEATO Medic Study No. 102	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 S.E. Asia
Subtask 01:	Military Medical Research Program SEASIA (Thailand)
Reporting Installation:	US Army-SEATO Medical Research Laboratory APO 146, San Francisco, California Division of Medical Research Laboratories Department of Virology (Special Project)
Period Covered by Report:	1 April 1963 to 31 March 1964
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Reports Control Symbol:	MEDDH-288
Security Classification:	UNCLASSIFIED

Objectives: To study seasonal variation in the amount and type of foodstuff and urine findings in residents of hyper- and hypoendemic areas for bladder stone with a view to elucidating the pathogenesis of vesical calculi.

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.

Sixteen families each in Nong Kohn and Ubol were subjected to dietary survey for 3 days each during April (hot and dry), August (rainy) and November (cool and dry) of 1963. In addition to nutritional study, 24-hour urine specimens have been collected from each study household member and freshly voided morning specimens obtained from a larger group. A nurse investigator stayed with each family for a period of not less than 16 hours daily and closely supervised the collection. Since there is no latrine in the house, individuals have to go outside for voiding or use the supplied container. Each household member has been restudied 3 times.

Complete urinalysis, included determination of pH, protein, sugar, calcium and specific gravity. A microscopic examination was performed within 2 hours after the collection. Twenty-four hour samples were thoroughly mixed, measured for amount, specific gravity, calcium, protein, creatinine and uric acid.

Progress: The number of casual urinary samples and age distribution of the subjects studied in 1963 are shown in Table 62. Age of these subjects varies from 1 month to 90 years old.

The number of 24-hour urine samples collected are shown in Table 63. Children up to the age of 19 in Nong Kohn village excreted about half the volume of children in the city of Ubol during the hot, dry season in April, 1963. As controls five medical students who were working in the project at that period of time excreted almost the same amount as adults living both in the village and the city. At any sample period, the amount of urine excretion in village children was always lower in the 2 to 4 year age group than city children, however, other than in April, there was no significant difference between other age groups. Volume of urine excreted by villagers in Nong Kohn was about half as much in April as in August and November. However, the subjects living in the city excreted almost the same amount during these three studied periods.

Calcium concentration in the urine: Sulkowitch test showed higher concentration of urinary calcium in persons of less than 20 years of age living in the village than in the city. This finding is demonstrated in both freshly voided morning specimens and 24-hour samples (see Figures I, II and IV). Higher concentrations of urinary calcium are found more frequently in village children of less than 5 years of age than in older individuals. These findings were confirmed in 24-hour samples (see Figures III and V). The lower volume of urinary excretion in 0-4 year old village children is probably partly responsible for this higher urinary calcium concentration (Table 63). However, there is no significant difference in the volume of urine excretion in other age groups; yet calcium excretion appears to differ.

Urinary Crystals

Microscopic examination of freshly voided morning specimens revealed more crystals found in village than in city subjects as shown in Figure VI & VIII. About 70 to 80 percents of the crystals were oxalate; uric acid comprised the bulk of the remainder. Phosphate and sulfate crystals were only occasionally found.

Urinary Leucocytes and Erythrocytes

Microscopic examination showed no difference in the numbers of leucocytes and erythrocytes found in the centrifuged urinary specimens from the subjects living in Nong Kohn and Ubol city.

Urinary pH

There was no difference in pH between the specimens from Nong Kohn and Ubol city. About 70 percent of the children under 2 years old gave acid reaction to the pH paper; this increased to 90 percent in the older age groups.

Urinary Protein Concentration

The protein concentration tested was the same in the specimens from Nong Kohn and Ubol city. Less than 10 percent in both samples contained 30 mg of protein or more per litre of urine.

Summary and Conclusions: 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 even when corrected for volume in the samples from Nong Kohn than from the city. However, the lower volume of urinary excretion in the children under 5 years old is probably partly responsible for the higher urinary calcium concentration. Urinary crystals, mainly oxalate, were found more frequently in urine specimens from the village than from the city. It seems probable that a stage of dehydration during the hot, dry season leads to lower urinary output with high urinary calcium, oxalate and uric acid may play a factor in the stone formation. Determinations of creatinine and uric acid in 24-hour samples are in progress. Further studies comparing the capacity of urine obtained from village and city to dissolve oxalate and studies of oxalate and uric acid metabolism will be done in the future.

Table 62. Number of "Casual Urinary Samples" studied in three different seasons, Ubol City and Nong Kohn Village, 1963.

Age (yrs.)	City			Nong Kohn		
	April	August	November	April	August	November
Under 1	25	22	25	19	33	15
1 to under 2	15	27	26	8	16	17
2 to 4	38	46	71	44	63	63
5 to 9	65	56	66	67	67	77
10 to 19	63	75	90	72	70	74
20 to 39	63	58	64	66	59	70
40 to 60	38	43	40	48	54	56
over 60	24	28	39	10	21	26
Total	308	355	421	321	383	398

Table 63. Average 24 hour urine volume collected in different seasons, Ubol City and Nong Kohn Village, 1963.

Age (yrs.)	City			Nong Kohn		
	April	August	November	April	August	November
2 to 4	1,140(1)	530(3)	680(4)	176(8)	384(8)	390(11)
5 to 9	655(13)	507(15)	612(18)	310(22)	530(22)	574(21)
10 to 14	811(16)	855(17)	938(21)	484(13)	947(15)	712(14)
15 to 19	834(11)	695(17)	924(23)	484(11)	1,222(15)	1,183(10)
20 and over	723(42)	1,060(55)	1,008(55)	661(39)	1,063(38)	1,056(43)
Med Student	--	--	--	676(5)	--	--

The number in bracket indicates number of subjects studied.

FIGURE I

URINARY CALCIUM (SULKOWITZ'S TEST) IN FRESHLY VOIDED MORNING SPECIMENS,
UBOL AND NONG KOHN, APRIL 1963

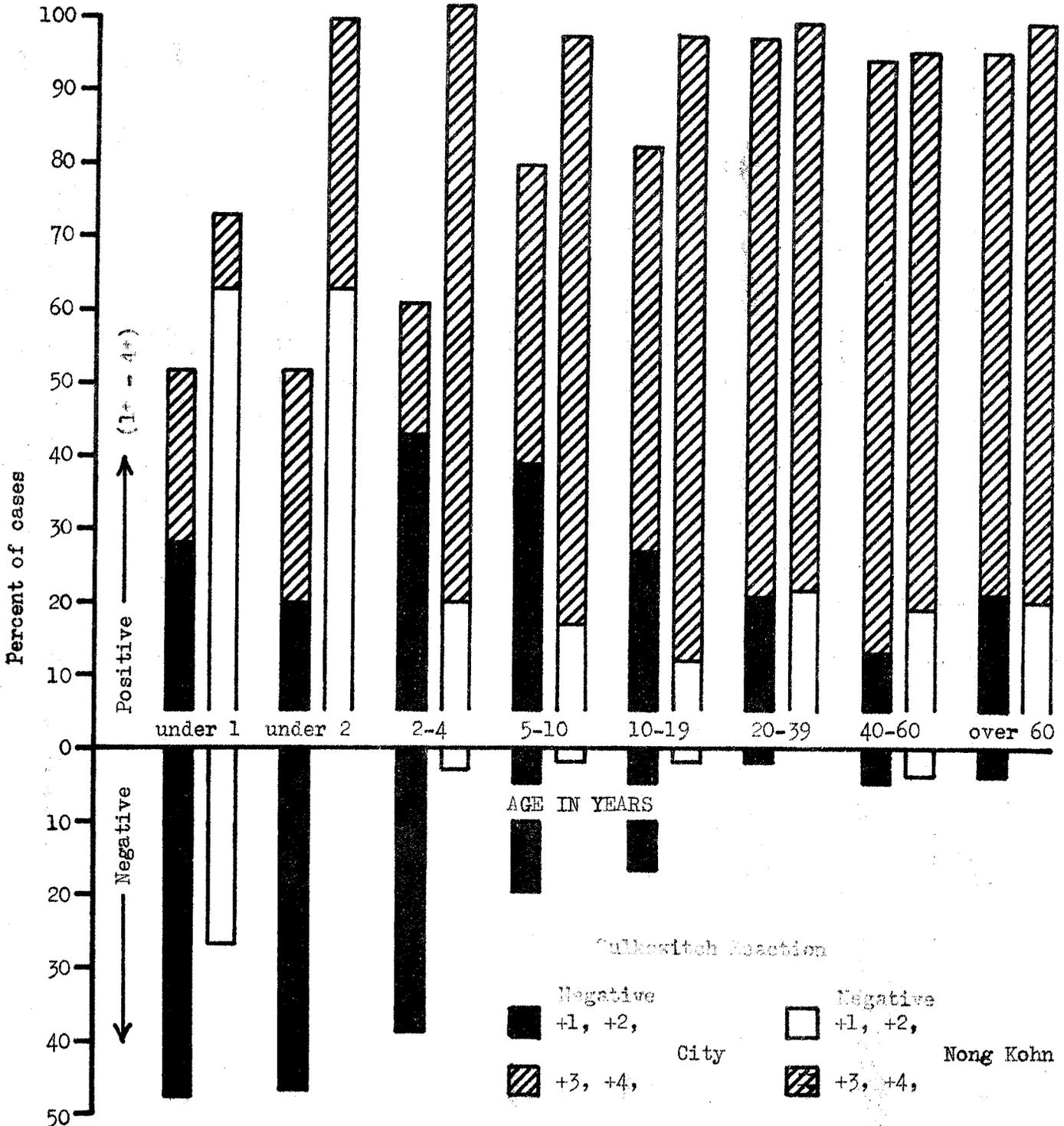


FIGURE II

URINARY CALCIUM (SULKOWITZ'S TEST) IN FRESHLY VOIDED MORNING SPECIMENS,
UBOL AND NONG KOHN, AUGUST 1963

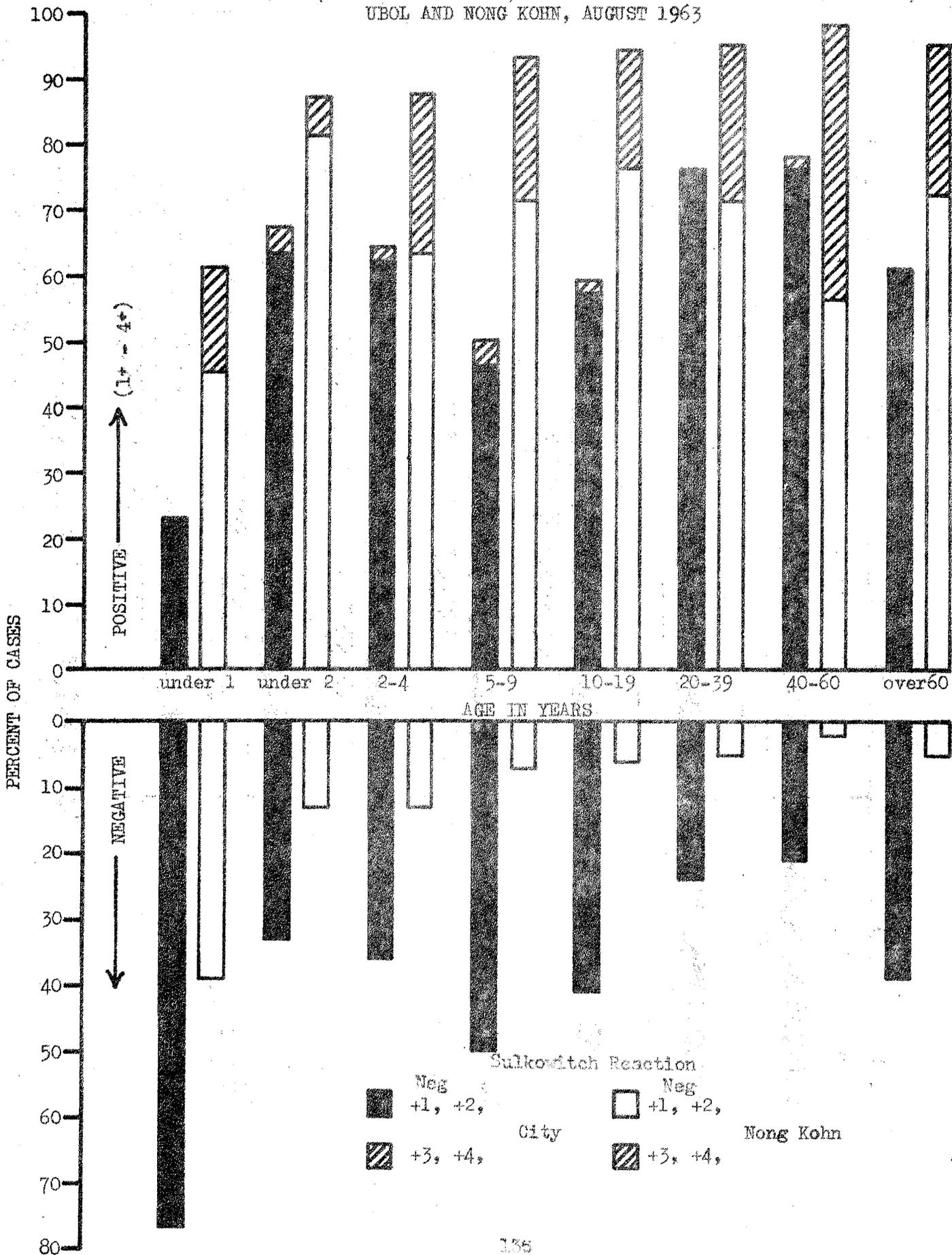
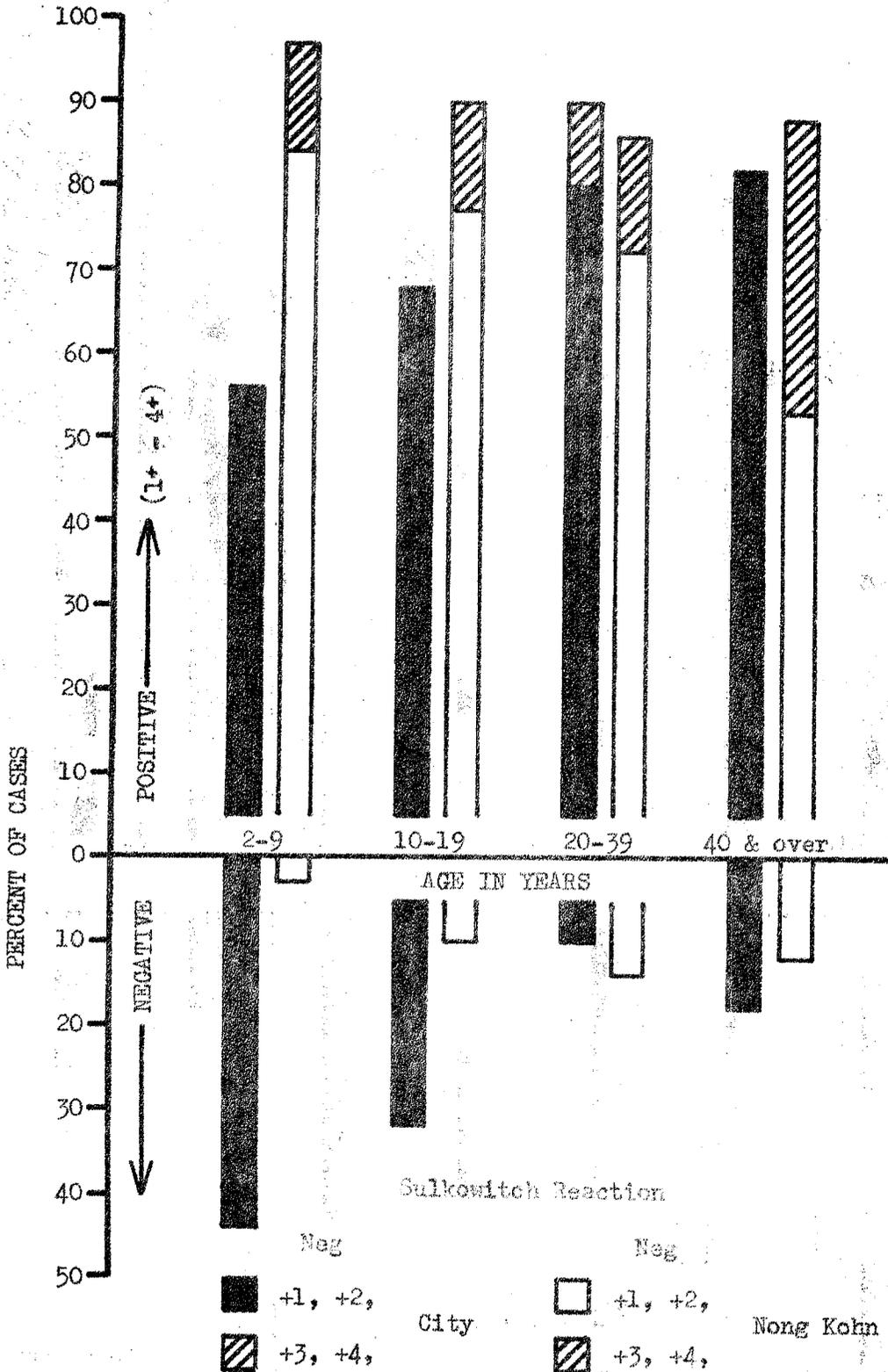


FIGURE III

URINARY CALCIUM (SULKOWITZ'S TEST) IN 24-HOUR SPECIMENS,
UBOL AND NONG KOHN, AUGUST 1963



NUMBER ABOVE COLUMN INDICATES NUMBERS OF SUBJECTS STUDIED

FIGURE IV

URINARY CALCIUM (SULKOWITZ'S TEST) IN FRESHLY VOIDED MORNING SPECIMENS,
UBOL AND NONG KOHN, NOVEMBER 1963

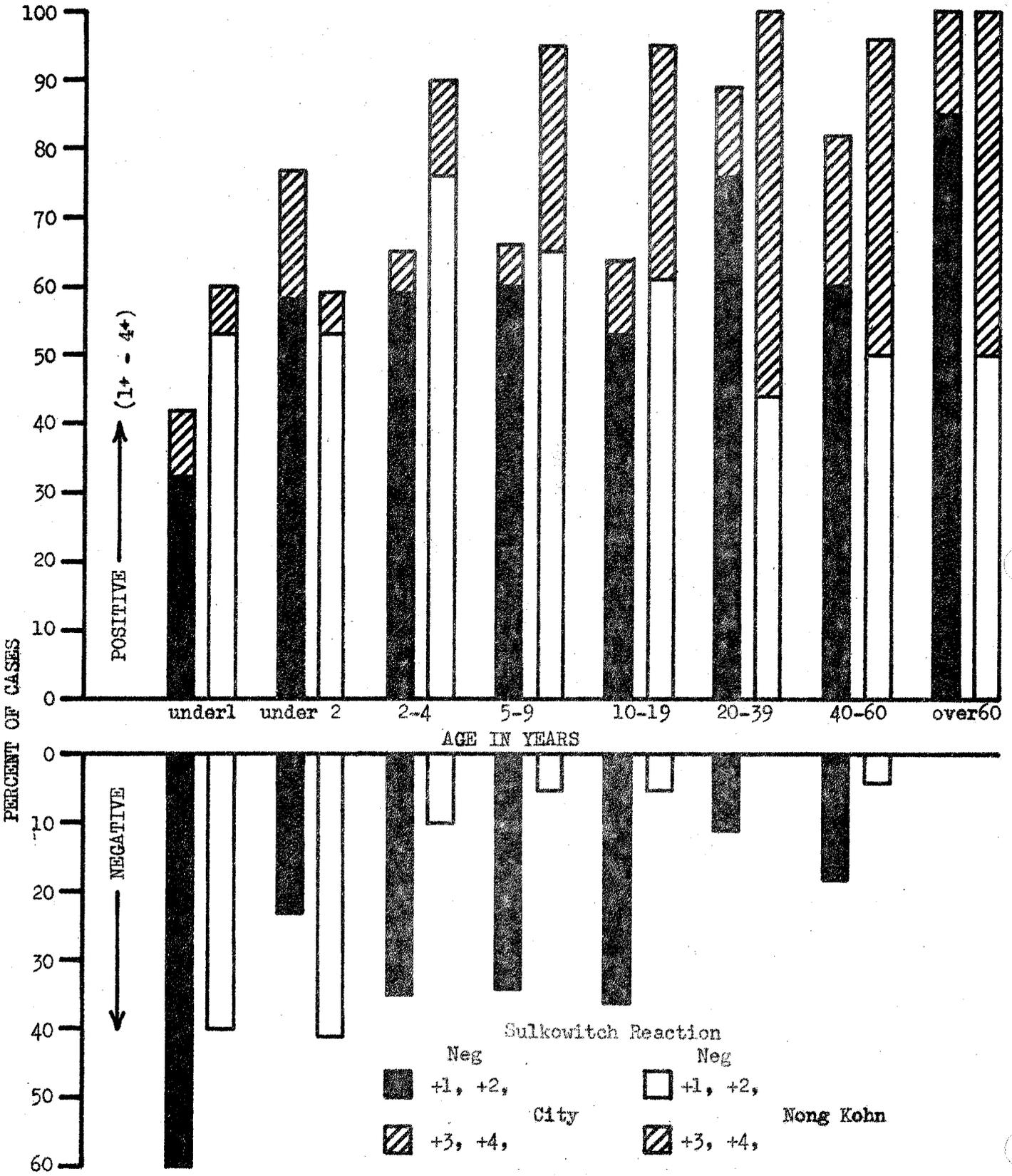
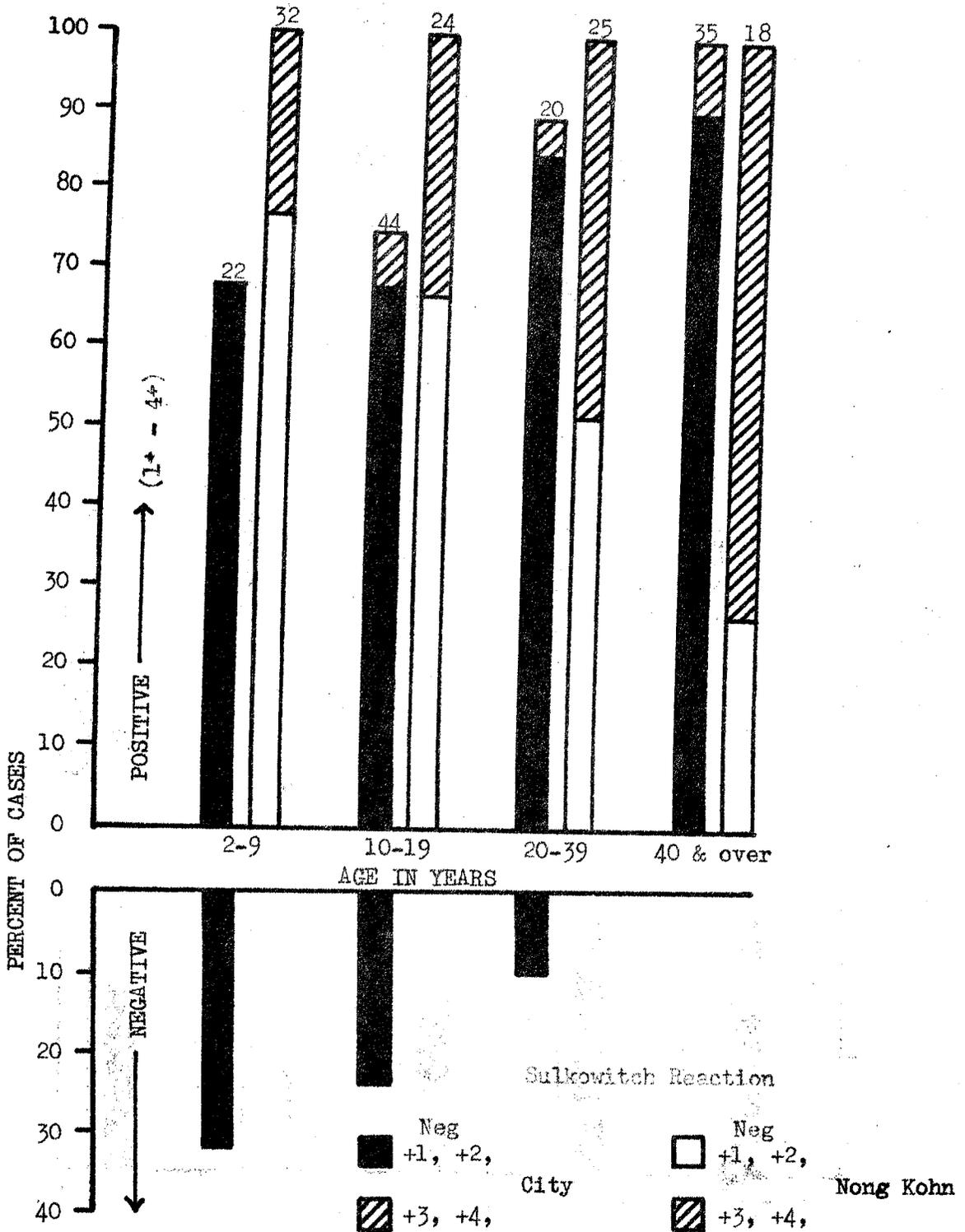


FIGURE V

URINARY CALCIUM (SULKOWITZ'S TEST) IN 24-HOUR SPECIMENS,
UBOL AND NONG KOHN, NOVEMBER 1963



NUMBER ABOVE COLUMN INDICATES NUMBERS OF SUBJECTS STUDIED

FIGURE VI

URINARY CRYSTALS (MICROSCOPIC EXAMINATION) IN FRESHLY VOIDED MORNING SPECIMENS,
UBOL AND NONG KOHN, APRIL 1963

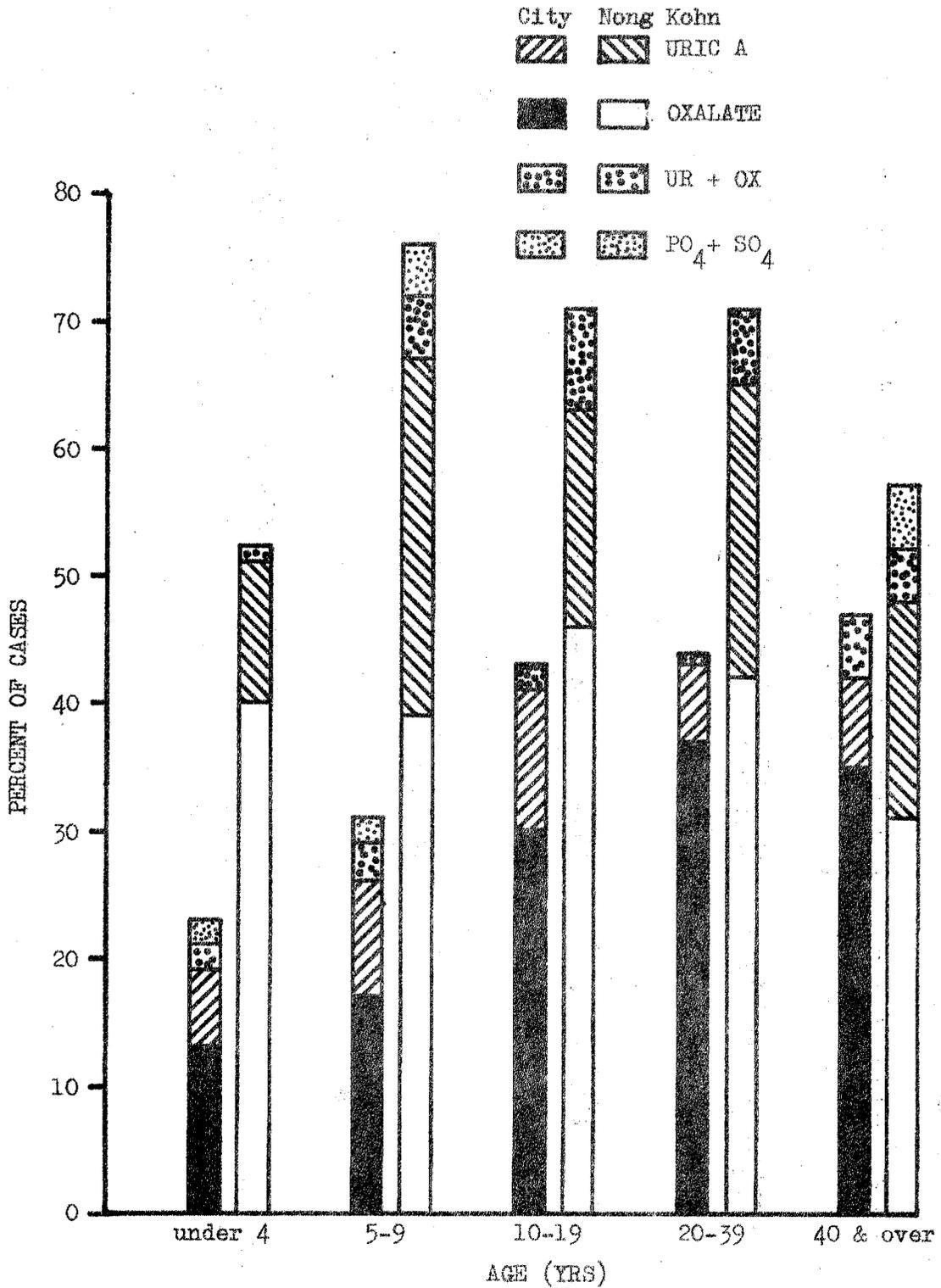


FIGURE VII

URINARY CRYSTALS (MICROSCOPIC EXAMINATION) IN FRESHLY VOIDED MORNING SPECIMENS,
UBOL AND NONG KOHN, AUGUST 1963

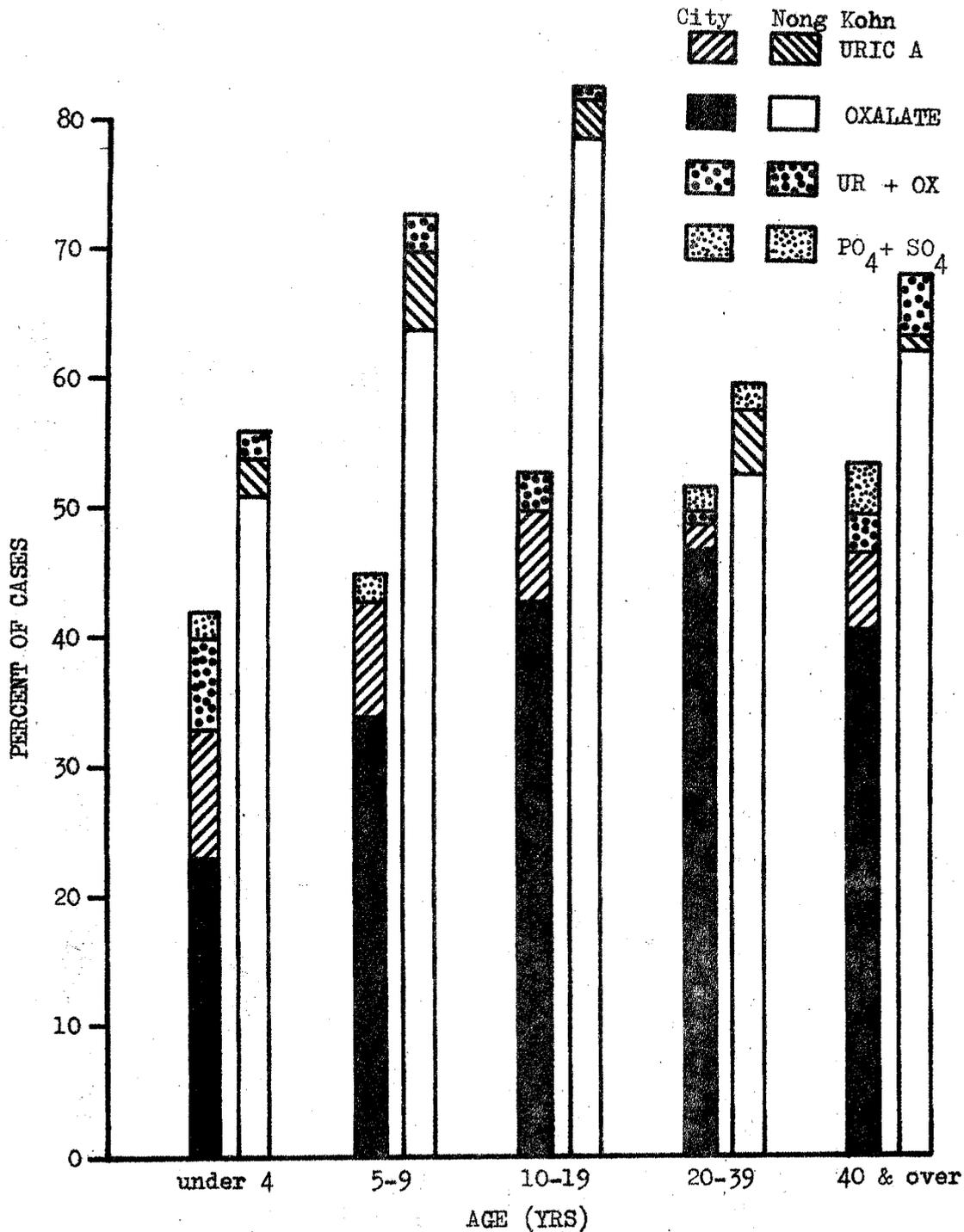


FIGURE VIII

URINARY CRYSTALS (MICROSCOPIC EXAMINATION) IN FRESHLY VOIDED MORNING SPECIMENS,
UBOL AND NONG KOHN, NOVEMBER 1963

