

REPORT NUMBER 601

THE EFFECTS OF ORAL ADMINISTRATION OF MAGNESIUM OXIDE
ON RENAL CALCIUM EXCRETION IN CREW MEMBERS
DURING A SUBMARINE PATROL

by

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Bureau of Medicine and Surgery, Navy Department
Research Work Unit MF099.01.01.04

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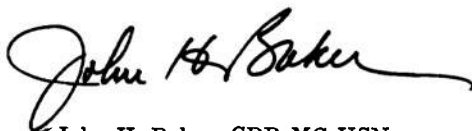
LCDR Clayton T. Drake, MC, USN

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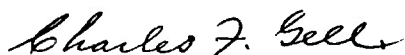
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SUMMARY PAGE

THE PROBLEM

To study the urinary mineral excretions of submarine personnel involved in prolonged submergence, and specifically, to determine the effects of oral administration of magnesium oxide on the excretion of urinary calcium and phosphorus. A group of forty submariners were chosen at random from among the crew of a Polaris submarine to participate in this study.

FINDINGS

Total urinary calcium excretion in the control group fell from a mean of 178 mg in pre-patrol tests to 135 mg post-patrol, while the group ingesting magnesium oxide exhibited a sample mean of 162 mg in the post-patrol tests. These figures show a significantly different mean value ($p=0.05$).

APPLICATION

The results of this study are of interest to all Naval medical officers, and particularly those charged with the maintenance of the health of submarine personnel making prolonged patrols. It could lead to the use of magnesium to control the formation of urinary calculi.

ADMINISTRATIVE INFORMATION

The study reported herein was conducted as partial fulfillment of the requirements for qualification as a Submarine Medical Officer. The author's thesis was chosen by the Qualification Committee for revision and publication as a Submarine Medical Research Laboratory report. It was approved for publication on 28 October 1969 and designated as Report No. 601.

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ABSTRACT

Twenty-four urine specimens were collected from randomly selected members of the crew of the U.S. Navy Submarine NATHAN HALE, SSBN-623, while at sea on a routine patrol mission. Specimens were collected three days after submergence, and again a few days before return to port. Twenty-one men received daily dosages of 310 mg of magnesium oxide orally, while nineteen served as controls. Urine specimens were examined microscopically, then measured for calcium, phosphorus, and routine factors.

No urine specimen examined was found to contain bacteria or white blood cells, nor was there any alteration in the routine chemistries.

Total urinary calcium excretion in the control group fell from a mean of 178 mg pre-patrol to 135 mg post-patrol, while the group ingesting magnesium oxide exhibited a sample mean of 162 mg calcium post-patrol, which is a significantly different mean value ($p=0.05$). Phosphorus excretion was not significantly variant.

These data indicate that magnesium oxide does have an ionic effect on urinary chemical excretion and may explain the so-called "protective mechanism."

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THE EFFECTS OF ORAL ADMINISTRATION OF MAGNESIUM OXIDE ON RENAL CALCIUM EXCRETION IN CREW MEMBERS DURING A SUBMARINE PATROL

INTRODUCTION

The magnesium ion has long been suspected (1-5) of exerting a protective effect on calcium urolithiasis. An interrelationship between the two has not been clearly elucidated, but it is postulated that the protective mechanism has to do with a decrease in urinary calcium excretion (4). However, there is no clear-cut data to indicate that a high urinary calcium, per se, increases the risk of renal stone formation (6-9).

The controlled environmental conditions encountered aboard one of the Polaris submarines where subjects live in the same atmosphere, eat identical food, and, generally, have similar schedules of work and sleep, afforded an excellent opportunity to study the urinary excretion of calcium.

The submarine patrol by necessity causes many changes in daily lives: no sunlight, an almost completely sedentary existence, exposure to an atmosphere with an increased carbon dioxide content, and probable decreased water intake. These alterations might predispose the crew to a higher incidence of urinary tract stone formation.

Though it has been shown that respiration and acid-base balance are altered and that calcium mobilization does take place (10), no comprehensive data on calcium excretion after prolonged exposure to the submarine environment were available; therefore, this study was undertaken to determine whether significant increases in calcium and phosphorus excretion occurred and the "protective effect" of magnesium oxide in calcium oxalate stone formation.

PROCEDURE

For this study, forty healthy young men were followed for a period of approximately four months, in order to learn the effects of oral magnesium oxide on urinary calcium and phosphorus excretion. The project began with sixty volunteers, but those whose

medical history or physical examination indicated renal abnormality or infection, or who were suspected of having had a renal stone were excluded. The forty men included in the study were all members of the U.S. Navy, between the ages of 19 and 33. Blood plasma specimens were screened for calcium, phosphorus, and uric acid levels, all of which were within normal ranges.

For a portion of a routine Polaris submarine patrol, these forty volunteers were observed. Several days after submergence, 24-hour samples of urine were collected and measured, and routine microscopic examinations were performed. Ten ml aliquots of urine preserved in dilute hydrochloric acid were frozen to be analyzed upon return to a laboratory facility. A second 24-hour urinary specimen was collected shortly before surfacing at the end of patrol. It was treated in the same manner. During the intervening period, twenty-one men ingested 310 mg of magnesium oxide each day, while nineteen served as controls. These men were closely matched in age, race, body build, type of job, amount of exercise, type and amount of food consumed, water intake, and all environmental conditions. None of the men studied suffered any illnesses or abnormal stresses during the period of study. All were examined physically at the completion of the patrol and found to be in excellent physical condition.

RESULTS

Routine urinalysis indicated that both groups, after patrol, tended to have a more dilute urine. This finding is not explained simply, but change in the acid-base balance is not suspect, as the urinary pH remained approximately constant.

Microscopic analysis was carried out on the post-patrol urines only (see Figure 1). Of interest here is that no leucocytes or bacterial forms were noted in any urine specimen. The percentage of urines with amorphous forms, epithelial cells, and crystals,

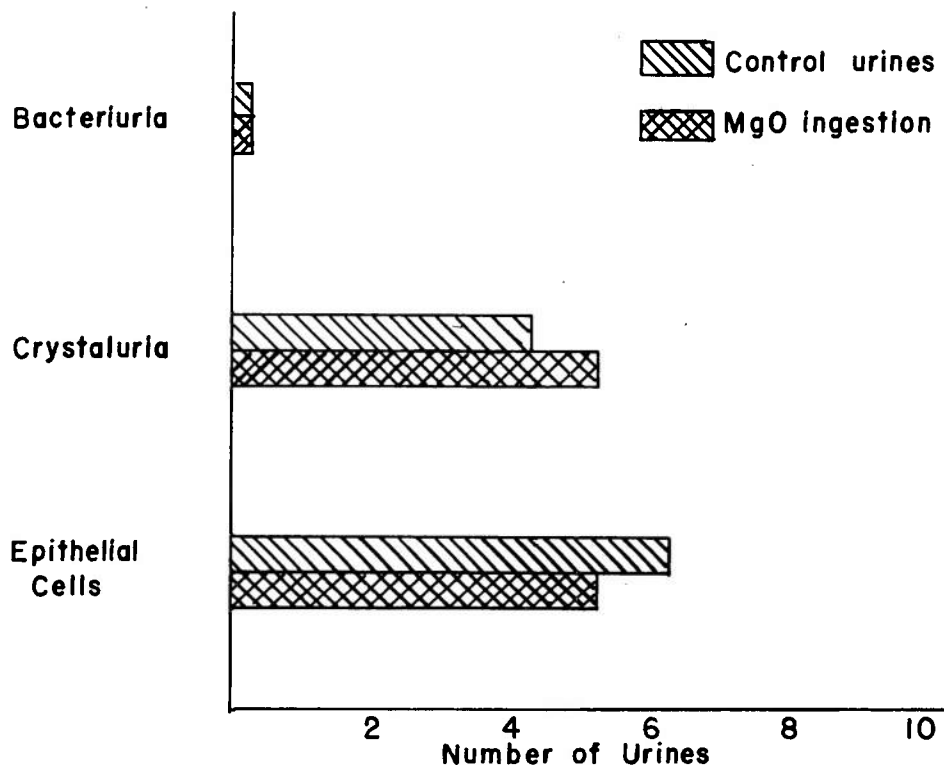


Figure 1.— Microscopic Analysis

does not differ from an average Stateside population in routine analysis. Each specimen was tested for glucose and protein, both pre- and post-patrol. Neither was detected at any time.

Urinary volumes for the two groups were quite similar. The differences between pre- and post-patrol volumes were slight (Table I).

TABLE I.—Urinary Volume (24-hour samples) for MgO-Treated and Control Group

	Urinary Volume (cc)	
	Mean	Stan. Deviation
MgO-Treated Group (N — 21)		
Pre-Patrol	1300	509
Post-Patrol	1338	657
Control Group (N — 19)		
Pre-Patrol	1226	419
Post-Patrol	1218	547

Data on calcium and phosphorus excretion are summarized in Tables II and III, respectively. For the MgO-treated group there was

practically no difference in mean calcium excretion between the two sample periods, 168 mg pre-patrol compared with 167 mg post-patrol.

TABLE II.— Calcium Excretion (24-hour samples) for MgO-Treated and Control Group

	Calcium Excretion (mg)	
	Mean	Stan. Deviation
MgO-Treated Group (N—21)		
Pre-Patrol	169.1	49.3
Post-Patrol	166.6	89.2
Amount of change, pre- to post-Patrol	2.5	70.0*
Control Group (N—19)		
Pre-Patrol	187.2	83.5
Post-Patrol	135.5	69.6
Amount of change, Pre- to Post-Patrol	51.6	88.3*

* Interrelation between repeated measurements taken into account.

In contrast, the mean excretion of calcium by the control group dropped from 187 mg to 136 mg post-patrol, a decrease significant

at the ($p < .01$) level, by a t-test for repeated measurements. The difference between pre- and post-patrol change in calcium excretion by the two groups was significant at the ($p < .05$) level by a one-tailed t-test for repeated measurements ($t = 1.88$).

Both groups showed slight drops in phosphorus excretion from the pre- to post-patrol samples (Table III), the drop being slightly more for the control group. The changes, however, were not statistically significant, nor was there a significant difference in changes between the two groups.

TABLE III.—Phosphorous Excretion (24-hour samples) for MgO-Treated and Control Group

	Phosphorous Excretion (mg)	
	Mean	Stan. Deviation
MgO-Treated Group (N—21)		
Pre-Patrol	1018.6	345.7
Post-Patrol	974.6	478.0
Pre- to Post-Patrol Change	44.0	546.1*
Control Group (N—19)		
Pre-Patrol	967.2	420.2
Post-Patrol	912.1	374.4
Pre- to Post-Patrol Change	55.1	531.3*

* Intercorrelations between repeated measurements taken into account.

DISCUSSION

In the United States the overall incidence of urologic stone is put at 0.7 percent, or 7 cases per 1,000 population per year (11). One would expect, therefore, several cases of renal stone to occur among submariners each year. Any method of decreasing this incidence should be thoroughly evaluated.

Oxalate stones account for over 90 percent of the urolithiasis encountered in North America (12). In contrast to uric acid and cystine stones, which are formed in urines with high concentrations of these components, the mechanism of formation of the oxalate stone is not yet known. Many authors (13-16) have compared the urinary output of calcium, phosphorus, and oxalic acid in patients with stones to that of normal

controls, finding no significant differences. However, other authors, noting the protective effects of magnesium, demonstrated that magnesium increases the solubility of calcium oxalate (17, 18). Takasaki and Shimano also measured urinary calcium, phosphorus, magnesium and oxalate. They concluded in an exhaustive study that the magnesium: oxalate ratio is the most important factor in oxalate stone formation. Any magnesium: oxalate ratio less than 2.0, or a magnesium: phosphorus ratio less than 0.1 (urinary oxalate and phosphorus were shown to be positively correlated) was said to be a "magnesium-oxalic acid unbalanced urine," in which stone formation would more likely take place (19).

The present study demonstrates that there is little change in urinary pH, sugar, protein, or sedimentation (Figures 1-4). Bacteriuria was not found in any urine tested. The volume of urine excreted by the submariners was found to average quite a bit less than the average normal adult excretion rate of 2-3 liters/24 hours. This finding reflects the stasis of the individual and the stability of his environmental conditions, and is a factor which could lead to a higher incidence of renal stone formation.

Of greater interest are the total calcium and phosphorus excretion rates. Significant differences (p is less than 0.05) are noted between the pre- and post-patrol values of calcium. Also, the administration of magnesium oxide significantly alters the observed excretion values of calcium. It is postulated that through this mechanism of chemical excretion rate alteration, magnesium oxide exerts its protective influence on stone formation. It is suggested that spacecraft, with a much more limited environment than submarines, might possibly utilize these data in the preservation of health and the utilization of manpower.

SUMMARY

After encountering two cases of renal urolithiasis while serving aboard the USS NATHAN HALE, SSBN-623 (G), the medical officer became interested in studying urinary mineral excretion in submarine personnel in-

volved in prolonged submergence. He realized that documented research in this area would be necessary to round out the existing body of knowledge of the effects of the submarine environment on submarine crews, and therefore planned and carried out the study reported herein.

In order to learn the effects of orally administered magnesium oxide on excretion of urinary calcium and phosphorus, a study was undertaken on a group of forty submariners while on a routine patrol. Approximately half of the group (21) received daily dosages of magnesium oxide, while the remainder of the group (19) served as controls.

This report reflects procedures and findings of that study. Significant alterations are reported, which, suggest that if further research confirms the author's hypothesis, and if the side effects of magnesium oxide are minimal, the drug may have some value on the medical supply table in the future for prevention of urinary stone.

CONCLUSIONS

In this study, exposure to the submarine environment causes no change in the results of the routine urinalysis. No Glaukosuria or proteinuria were noted, no pus cells or bacterial forms were found, and no unusual or large amounts of crystalline forms were noted.

In this study a decreased urinary calcium excretion was found in the control subjects. Magnesium oxide in this controlled pilot study led to an increased excretion of calcium in the urine. This finding does not agree with the "decreased urinary excretion" theory for the protective influence, but lends some support to the "magnesium-oxalate balance" theory.

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ADDENDUM

Since the time of the first draft of this paper, more studies have been published which pertain to oxalate renolithiasis. Resnick, et al., reports that an important factor in the stone formation is familial, through a polygenic mode of inheritance. In Volume 280 of *The New England Journal of Medicine*, Lemann, et al., discuss their study of urinary calcium excretion when a carbohydrate load is given. In a study structured much the same as that reported here, those with a family history of renal stone responded to oral sugar administration with a significantly higher calcium excretion.

These findings suggest that several factors influence the formation of renal oxalate stones, factors which, when discovered, can lead to better prophylaxis for our military forces.

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13. ABSTRACT

In order to learn the effects of orally administered magnesium oxide on the excretion of urinary calcium and phosphorus, a study was undertaken on a group of forty submariners while on a routine patrol. Half of the group received daily dosages of magnesium oxide, while the other half served as controls. Twenty-four-hour specimens were collected from these subjects three days after submergence, and again a few days before return to port.

Urine specimens were examined microscopically, then measured for calcium, phosphorous and routine factors. No specimen examined was found to contain bacteria, or white blood cells, nor was there any alteration in the routine chemistries.

Total urinary calcium excretion in the control group fell from a mean of 178 mg in pre-patrol tests to 135 mg post-patrol, while the group ingesting magnesium oxide exhibited a sample mean of 162 mg in the post-patrol tests. These figures show a significantly different mean value ($p = 0.05$) These results, if substantiated by further studies, would argue strongly for the prophylactic use of magnesium for protection against the formation of urinary calculi.

14.

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