BRIEF CLINICAL OBSERVATIONS

IS DIGITAL RECTAL EXAMINATION IN MEN A CAUSE OF TRANSIENT PROTEINURIA?

To the Editor:

Proteinuria is a relatively common laboratory abnormality (prevalence 0.4 to 1.9 percent) [1,2] that can be a transient and clinically unimportant finding or an indication of underlying disease. Among the causes of transient proteinuria are high fever, exposure to cold, strenuous exercise, emotional stress, and congestive heart failure [3,4].

Prostatic secretions have a high protein content (mean 4,000 mg/dl) [5], and digital rectal with prostate examination has been suggested as a possible cause of transient proteinuria. A prospective blind study was conducted in healthy young male medical students to determine if a standard digital rectal examination could be a cause of transient proteinuria.

The subjects were 101 healthy male freshman medical students at the Medical College of Georgia. No student had a prior history of proteinuria. As part of an introductory course in physical diagnosis, students are instructed in performing a digital rectal and prostate examination, and perform this examination on each other. We requested urine specimens from each student before and after the examination. Sterile specimen containers were numbered consecutively 1 to 250. Each subject was randomly given two containers, each labeled with a number, the student's name, and "before" or "after." After the specimens were collected in the labeled containers, the names and "before" or "after" designations were removed. In addition, nine urine specimens with negative to 4+ protein were randomly included as an internal control. Dipstick and Exton's reagent testing of the control specimens was performed by the clinic technician.

The subject and control blind specimens were tested for specific gravity and protein content both by dipstick and by Exton's reagent. The Exton's reagent was prepared by dissolving sulfosalicyclic acid 50 g and sodium sulfate 10 g in 800 ml water. Results of dipstick and Exton's reagent testing were recorded on a scale of negative to 4+ according to the manufacturer's directions. Trace and negative by the dipstick were considered "negative," and change to at least "plus one" by both dipstick and Exton's reagent was required to be considered a change from negative to positive.

Protein content of seven of the nine control specimens was accurately determined. The remaining two specimens were recorded as 2+, whereas the control reading was 3+. Both "before" and "after" urine specimens were obtained from 82 of the 101 eligible students. The remaining 19 students were unable to provide both specimens and were excluded from the study.

The specimens from 75 of the 82 students were negative both before and after the digital examination. Five specimens were negative before and positive after (range "1 plus" to "4 plus") the examination. One specimen was positive before and negative after and one positive both before and after. This change from negative to positive protein was not statistically significant ($p = 0.109$ using McNemar's test for significance of change [6]. Calculations of statistical power showed that this study had a 0.99 probability of detecting a true difference if one exists at the 0.05 level of significance. The mean specific gravity of these "before" specimens was 1.024 (range, 1.018 to 1.032), and of the "after" specimens, 1.027 (range, 1.021 to 1.032).

Idiopathic transient proteinuria is common in children and young adults and is not associated with subsequent development of renal disease [3]. Because the presence of proteinuria in young men may be a transient benign condition or may indicate underlying systemic disease, accurate testing of urinary protein, uncontaminated by other fluids, is important. In this study, although five urine specimens were negative before and positive after rectal examination, this change was not statistically significant. We conclude that rectal with prostate examination in healthy young men does not appear to be a clinically important cause of proteinuria.

RUTH-MARIE E. FINCHER, M.D.
TERRENCE T. KUSKE, M.D.
JOHN W. RICHARDS, Jr., M.D.
Medical College of Georgia
Augusta, Georgia 30912

1. von Bonsdorff M, Koskenvuo K, Salmi HA, Pasternak A: Prevalence and causes of proteinuria in 20-year-old Finnish men. Scand J Urol Nephrol 1981; 15: 285–290.
2. Wolman IJ: The incidence, causes and intermittancy of proteinuria in young men. Am J Med Sci 1945; 210: 86–100.
3. Abuelo JG: Proteinuria: diagnostic principles and procedures. Ann Intern Med 1983; 98: 186–191.
4. Castenfors J, Mossfeldt F, Piscator M: Effect of prolonged strenuous exercise on renal function and urinary protein excretion. Acta Physiol Scand 1967; 70: 194–206.
5. Walsh PC, Gittes RF, Perlmutter AD, Stamey TA: Campbell's urology, 5th ed. Philadelphia: WB Saunders, 1986; 255.
6. Siegel S: Nonparametric statistics for the behavioral sciences. New York: McGraw-Hill, 1956; 63–67.

Submitted December 8, 1986, and accepted in revised form January 14, 1988

SULFADIAZINE-INDUCED CRYSTALLURIA IN A PATIENT WITH THE ACQUIRED IMMUNODEFICIENCY SYNDROME: A REMINDER

To the Editor:

The treatment of choice for toxoplasmosis in patients with the acquired immunodeficiency syndrome (AIDS) is a combination of a sulfonamide and pyrimethamine [1]. We report herein a case of sulfadiazine-induced crystalluria and renal insufficiency in a patient with AIDS being treated for toxoplasmosis.

On August 3, 1987, a 45-year-old, 74-kg Hispanic man was admitted to the urology service with sudden onset of sharp right flank pain radiating to his right testicle, gross hematuria for two days, and an inability to void on the morning of admission. Past medical history was significant for AIDS and toxoplasmosis of the central nervous system. He was receiving sulfadiazine, 1.5 g (80 mg/kg) orally every six hours, and pyrimethamine, 25 mg orally every day, for six weeks prior to admission and had been compliant. He had not been advised to increase fluid intake despite the warm weather. Other medications included daily folinic acid 5 mg and clotrimazole 10 mg five times daily. Physical examination only revealed a moderately distended abdomen with involuntary guarding, decreased bowel sounds, and right lower quadrant and flank pain. Urinalysis showed cloudy urine with a pH of 6.0, three to five white blood cells per high-power field, gross hematuria, and many crystals identified under light microscopy by one of us (K.C.) and described as "shocks of wheat" (diagnostic of acetylsulfadiazine) by the Director of the Clinical Pathology Laboratory. Laboratory values included a serum creatinine of 3.9 mg/dl (baseline 1.2 mg/dl), and serum albumin of 4.2 mg/dl. An abdominal radiograph revealed multiple stones in the upper right ureter. Sulfadiazine was discontinued and fluid and oral sodium bicarbonate therapy started. On Day 3 of hospitalization, a ureteral stint was placed to relieve the obstruction. Acetylsulfadiazine crystals were again identified. Serum creatinine level returned to baseline on Day 6, and he was discharged receiving clindamycin and pyrimethamine after eight days of hospitalization.

Animal models and clinical reports have demonstrated that sulfonamides of low solubility such as sulfadiazine may form concretions in the urinary tract under appropriate conditions, such as dehydration [2]. Increasing fluid intake to 1 to 2 liters per day is recommended [3]. Because of this practice and the use of more soluble agents, sulfonamide-induced crystalluria is now uncommon. Sulfonamide-induced crystalluria has also been reported in two patients with hypoalbuminia [4]. Since many patients with AIDS are prone to hypoalbuminia [5], this may be an additional predisposing factor in this population. Physicians and pharmacists should continue to advise patients to increase their fluid intake when taking sulfonamides.

JAN SAHAI, Pharm.D.
TRACY HEIMBERGER, M.D.
KENNETH COLLINS, M.D.
LISA KAPLOWITZ, M.D.
RONALD POLK, Pharm.D.
Medical College of Virginia
Virginia Commonwealth University
Richmond, Virginia 23298

1. Armstrong D, Gold JWM, Dryjanski J, et al: Treatment of infections in patients with the acquired immunodeficiency syndrome. Ann Intern Med 1985; 103: 738–743.
2. Fox CL, Jensen OJ, Mudge GH: The prevention of renal obstruction during sulfadiazine therapy. JAMA 1943; 121: 1147–1150.
3. Barnes RW, Kawaichi GK: Factors affecting the formation of sulfonamide urinary concretions. J Urol 1943; 49: 324–333.
4. Buchanan N: Sulphamethoxazole, hypoalbuminaemia, crystalluria and renal failure. Br Med J 1978; 2: 172.
5. Kotler DP, Gaetz HP, Lange M, et al: Enteropathy associated with the acquired immunodeficiency syndrome. Ann Intern Med 1984; 101: 421–428.
6. Goadsby PJ, Donaghy AJ, Lloyd AR, Wakefield D: Acquired immunodeficiency syndrome (AIDS) and sulfadiazine-associated acute renal failure. Ann Intern Med 1987; 107: 783–784.

Submitted January 4, 1988, and accepted January 15, 1988

TURNER'S SYNDROME WITH ANOREXIA NERVOSA

To the Editor:

The rare concurrence of Turner's syndrome and anorexia nervosa has some interesting aspects from the standpoints of psychiatrics and endocrinology, and about 10 such cases have been reported [1,2]. This rare association may provide evidence to clarify changes in gonadotropin responsiveness in the concurrence of hypergonadotropic and hypogonadotropic hypogonadism. Some authors reported estrogen decreased food intake [3]. Onset of anorexia nervosa in a hypogonadal patient receiving estrogen may provide further evidence of a pathogenetic role of the hormone in anorexia nervosa.

Our Japanese patient was diagnosed as having Turner's syndrome with a karyotype of 45XO at the age of six years. She was 103.2 cm tall (mean ± SD, 114.7 ± 4.9 cm) and had some stigmata of the syndrome, that is, low hairline, a shield-like chest, and cubitus valgus. Administration of stanozolol 1 mg a day was started, and ethinyl estradiol methyl ether (0.0025 mg per day; 80 ng/kg per day) was added when she was 13 years and one month old for the purpose of promoting linear growth [4]. Her height was 129.8 cm and weight was 33 kg at the age of 13 years and six months. Breast development was in the prepubertal stage. After that, food intake decreased remarkably and she lost 8.4 kg (25.5 percent of her weight) during seven months. Her serum estradiol level was 9 pg/ml. She was diagnosed as having anorexia nervosa according to the criteria proposed by Feighner et al [5]. Gonadotropin-releasing hormone (Gn-RH) (70 $\mu g/m^2$ body surface) was injected intramuscularly at the age of six years and at 14 years of age, when she was anorectic. The estrogen therapy was discontinued five months before the second examination (**Table I**). Responses of follicle-stimulating hormone (FSH) and luteinizing hormone (LH) in the anorectc period were suppressed below the prepubertal ranges. Thyrotropin (TSH) and prolactin responses to thyrotropin-releasing hormone (TRH) were within normal limits.

It has not been completely documented yet whether elevated gonadotropin levels in primary gonadal failure remained in the supranormal ranges, were within normal limits, or suppressed below normal limits when the patient had accompanying hypogonadotropic hypogonadism. Turner's syndrome with anorexia nervosa is considered to be a good experiment in nature to study such a condition. Dissociated responses of the two gonadotropins were reported [2]. The peak LH level after Gn-RH stimulation was beneath the prepubertal control value, but the serum FSH level in the patient rose higher than in normal subjects. In the present study, hypergonadotropinemia in gonadal dysgenesis, either LH or FSH, was demonstrated for the first