1971

Year Book OF UROLOGY

GRAYHACK

THE YEAR BOOK

of

UROLOGY

1971

EDITED BY

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Printed in U.S.A.

Library of Congress Catalog Card Number: CD 38-103

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INTRODUCTION

As work on this YEAR BOOK nears completion, the recurrent annual desire to delete the majority of the editorial comments is strong. Most of the articles present a summation of an effort involving years of hard work. It seems injudicious to read this summation a few times and then make a biased, oracle-like pronouncement. The urge to withdraw these comments, however, is countered by a number of factors: (1) the sophistication and background of information of the reader assure a critical evaluation of the relative merits of the comment and the article; (2) occasionally the comments have stimulated a worthwhile interchange; (3) I have reacted favorably to the comments by the contributing editors, Doctors Belman, Boyce, King and Stamey; and (4) I am reluctant at this stage to discard an established custom that has required considerable effort and has been well accepted. In the introductory remarks to the 1963-1964 YEAR BOOK (my first), your agreement, disagreement or additions to the comments were solicited. A few of you have responded to this request. It is my hope that more of you will undertake to educate your editor and his colleagues.

The article by Berci and Kont comparing various cystoscopic lens systems (Brit. J. Urol. 41:564, 1969), presented in this YEAR BOOK in the section on Urography, Instruments and Appliances, focuses attention on another problem that concerns me, and almost certainly troubles you. The criticisms by Wappler that there is some evidence of bias in this presentation and that this type of endeavor is hardly appropriate to a learned journal has some merit. Last year, a similar assessment of urinary drainage systems was presented by Finkelberg and Kunin (see the 1970 YEAR BOOK, p. 76). We are being overwhelmed by a variety of catheters, drainage bags, disposable sets, endoscopic instruments, etc., so that an individual, objective evaluation of these becomes almost impossible. Some new products almost certainly represent an improvement over those we now use. How do we identify these new products of potential merit? It seems that we need to establish an organization to test products objectively as they become available. The results of these tests should then

be made available to all of us to be utilized or discarded as we see fit. Publication of these reports would be limited to a specific section of the journals. Those of us without special skill in product evaluation need help. A mechanism should be designed to assist us with exchange of information in this area just as in others that are important to the science and art of medicine.

You will undoubtedly be pleased, as I am, to note the return of the chapter on Selected References to the YEAR BOOK. Doctors Bush and Javadpour have undertaken this task. If some of you will join me in conveying your thanks and encouragement to them, we may hopefully anticipate their continued participation in this effort.

Again, I am most grateful to Dr. William Boyce of the Bowman Gray School of Medicine, Dr. Thomas A. Stamey of Stanford University and Drs. Lowell R. King and A. Barry Belman of our institution for their generous contributions of time and effort in making comments on the various selected articles in this YEAR BOOK. My task also was made considerably easier this year because Dr. John Nanninga of our staff contributed a number of abstracts.

JOHN T. GRAYHACK

GENERAL CONSIDERATIONS

Examination of Urine

Amino Acid Excretion in Infancy and Early Childhood: Survey of 100,000 Infants. Brian Turner and D. A. Brown[1] (Sydney, Australia) screened urine samples from 100,000 infants for abnormal amino acid excretion by a simple paper chromatographic method. The survey covers a period of 20 months, starting in 1966. Infants were tested at age 6 weeks or at the time of their first visit; there was no upper age limit. No infant with a suspected or known abnormality was included in the series. Parents were instructed to place a piece of absorbent paper in the infant's diaper and, after allowing it to dry, returned it by mail to the clinic. The specimen was eluted on Whatman No. 1 chromatography paper, using a standard amino acid mixture. Chromatograms were run overnight in butanol-acetic acid-water (120:30:50) solvent and the amino acids visualized with ninhydrin. Abnormal patterns were investigated by thin-layer chromatography, electrolytic desalting and concentration or high-voltage electrophoresis.

A wide range of abnormalities was found, totaling 144, for an incidence of 1.44 per 1,000 infants tested. There were 46 cases of incomplete cystinuria, 53 of prolinuria and 21 of generalized aminoaciduria. Less common abnormalities included 7 cases of phenylketonuria, 9 of complete cystinuria, 3 of histidinuria, 2 of Hartnup disease and 1 each of hyperglycinuria, hydroxyprolinuria, and β-aminoisobutyric aciduria. Cystinuria was initially suspected in 73 infants, who excreted over 100 mg. creatinine per Gm. and also excessive lysine. Proline-glycinuria was initially found in 79 infants, 53 of whom were confirmed at 3-6 months. Three of 14 infants studied, with persistent aminoaciduria, had elevated serum proline levels. Of 23 infants initially found to have generalized aminoaciduria which persisted beyond the first test, 4 had persistent aminoaciduria when retested at 6-12 months. Indole excretion was grossly abnormal in 2 of these infants, suggesting the diagnosis of Hartnup disease.

This study, envisaged initially as a survey of the infant

(1) M. J. Australia 1:11-14, Jan. 3, 1970.

population for phenylketonuria, has revealed an unexpectedly high return of abnormal results. More recently, Levy *et al.* obtained similar results while screening 15,000 specimens in Massachusetts.

►[This type of routine testing seems simple to do (it was carried out on 100,000 infants) and would be desirable in that the early detection of cystinuria and xanthinuria should permit prevention of calculi in such children by urine alkalinization alone.—Lowell R. King.]

Immunoreactive Basement Membrane Antigens in Normal Human Urine and Serum. J. J. McPhaul, Jr., and Frank J. Dixon[2] (Scripps Clinic, La Jolla, Calif.) investigated soluble antigens in the urine of normal people and their isolation and characterization. Sheep antiserum to human glomerular basement membrane was used to show 2 cross-reactive antigens. These antigens were purified partially by preparative electrophoresis and electrofocusing and were separated on G-200; both appeared to be acidic, of high molecular weight and carbohydrate rich. They are immunologically related to soluble extracts of human glomerular basement membranes. The indication of immunologic identity between these urinary antigens and normal human glomerular basement membrane (GBM) is inferred from double diffusion analyses of individual and pooled concentrates of urinary fractions next to extracts of human GBM. This inference is strengthened by two lines of evidence. First, absorption experiments performed with the antigens from normal human urine demonstrated their capacity to block fixation of homologous anti-GBM antibody to human kidney sections as detected by direct immunofluorescence. Secondly, immunization with a mixture of these urinary antigens was capable of evoking production of anti-GBM antibodies, with fixation of autologous IgG on the host animals' kidneys in the characteristic linear pattern demonstrated by direct immunofluorescence.

Despite the established immunologic relationship between native GBM and urinary basement membrane antigens, the structure (or structures) from which they are derived is not clear. Further experiments were done to find basement membrane antigens in normal human serum. Fractionation of different pools of bank blood serum consistently indicated the presence of trace amounts of antigenic material. Moreover, there appeared to be two such antigens, separable on

(2) J. Exper. Med. 130:1395-1409, December, 1969.

G-200, which showed a reaction of identity with the urinary basement membranes in gel diffusion.

Studies in Urinary Tract Infections: IV. Urinary Leukocyte Excretion in Bacteriuria was studied by C. E. Mabeck[3] (Roskilde, Denmark) in 152 women.

METHOD—At 4 P.M. 5 I.U. of Pitressin tannate in oil was given subcutaneously. The exact time of the first voiding the next morning was noted. During the next voiding a midstream specimen was collected. Estimation of the diureses per hour was based on the total volume of the second voiding and the time interval between the first and second voidings. A specimen from each was saved for later determination of osmolality.

The midstream specimen from the second voiding was used for urine culture and leukocyte count. After stirring of the specimen, 1 drop of Sternheimer-Malbin or Prescott's stain was added to 1 ml. urine. Leukocytes were counted in a Fuchs-Rosenthal counting chamber. Two hundred leukocytes were counted.

In 144 of 152 women with bacteriuria the leukocyte excretion rate exceeded 400,000/hour. The excretion rate was found to be the same regardless of the type of organism. In 25 patients the leukocytes in the urine aspirated by suprapubic puncture and in midstream specimens collected in connection with the puncture were counted. Good agreement was shown between the leukocyte concentration in the bladder urine and that in midstream specimens. The number of leukocytes per $mm.^3$ of urine was compared with the leukocyte excretion rate. The urine of 97% of 164 patients who excreted more than 400,000 leukocytes per hour contained more than 10 leukocytes per mm^3. Comparing microscopic examination of the urinary sediment with the leukocyte excretion rate, all patients with 3 or more leukocytes per high power field excreted more than 400,000 leukocytes per hour. If there were fewer leukocytes per high power field, pyuria could not, however, be ruled out. Simple microscopic examination of the urinary sediment is an unsatisfactory means of revealing pyuria.

In 4 patients the leukocyte excretion rate was studied during treatment. On the 2nd day of treatment all the patients had sterile urine, and the leukocyte excretion rate decreased rapidly within the next few days.

►[The physician who wants to use leukocytes as an index of bacteriuria should study this article very carefully; it may be the best on the subject.—Thomas A. Stamey.]

Assessment of Subnormal Urinary Glucose as Indicator

(3) Acta med. scandinav. 186:193-198, September, 1969.

of Bacteriuria in Population Studies: Investigation of 3,911 Subjects between Ages 4 and 65 Years. Hans Fritz, Lennart Köhler and Bengt Scherstén[4] studied the relation between urinary glucose levels and bacterial counts in the urine of 948 children, aged 4 years; 511 schoolgirls, aged 7-18 years; and 2,452 females, aged 7-65 years, comprising 80% of the total female population of this age in a small community. Urinary glucose was determined by the hexokinase and glucose-6-phosphate-dehydrogenase method and with Uriglox, a test paper sensitive to small amounts of glucose normally present in urine. The criterion of subnormal urinary glucose in adults and children was 2 mg./100 ml.

With a bladder retention time of at least 4-6 hours, urinary glucose levels below 1 mg./100 ml. were regularly associated with significant bacteriuria, indicating bacterial multiplication above the urethra. Glucose levels of 1-2 mg./100 ml. could occur in bacteriurics, and also in nonbacteriuric subjects if fluid intake during the night was not restricted. A level above 2 mg./100 ml. indicated the absence of bacteriuria, provided urine was sampled in the fasting state after retention for at least 4-6 hours. Results with the semiquantitative Uriglox paper test agreed with those of the quantitative glucose method. The latter is a useful complement to bacteriologic study in differentiating contamination and bacteriuria and offers a simple means for the mass detection of bacteriuria. The sensitivity of the glucose method was 96%, and its specificity exceeded 99%. The confidence level with a single specimen having subnormal urinary glucose in predicting significant bacteriuria was almost twice as high as that with a single specimen containing more than 100,000 organisms per ml.

►[The appealing aspect of this urinary glucose technic as a screening method for detecting bacteriuria is its independence of how the first A.M. voided urine is collected. Contaminating bacteria cannot influence the urinary glucose level provided the urine is refrigerated. For detecting bacteriuria, and fully realizing all the difficulties in attaching confidence limits to 10^5 or more bacteria per ml. of voided urine (Stamey, T. A., and Pfau, A.: Urinary Infections: A Selective Review and Some Observations, California Med. 113:16, 1970), the method of Fritz *et al.* is the way I would initially screen a population.—Thomas A. Stamey.]

Fixed and Reproducible Orthostatic Proteinuria: VI. Results of 10-year Follow-up Evaluation are reported by Alfred L. Thompson, R. Robert Durrett and Roscoe R. Robin-

(4) Acta med. scandinav., supp. 504, 1969.

son.[5] Orthostatic proteinuria has long been considered a benign, transient condition of adolescence, but recent reports have suggested that this may not be the case. Study of 64 young men with this disorder was begun 10 years ago at the Medical Center, Lackland Air Force Base, Texas. Initial observations showed intact renal function and a normal renal hemodynamic response to standing, but there were glomerular alterations in most subjects. At 5 years, at least 70% still had proteinuria, but renal function was well maintained. Examination 10 years later was possible in 43 patients.

Only 7 patients (16%) had fixed orthostatic proteinuria on 10-year follow-up. Five had a transient orthostatic pattern, and 2 had persistent proteinuria. Seven others had a variable pattern, and 22 had no qualitative evidence of proteinuria. Most patients with fixed orthostatic proteinuria at 10 years showed the same pattern at 5 years; no patient with a negative urinary protein at 5 years exhibited qualitative proteinuria at 10 years.

All patients appeared healthy. Four had had dysuria in the second 5-year period. One had a single episode of gross hematuria at 5-10 years, and another had had a similar episode in the first 5 years. In the second 5-year period, 1 patient noted symptomatic urolithiasis. No patient had diabetes or hypercalcemia in the second part of the follow-up period. Only 1 patient had sustained diastolic hypertension. Only 5 patients had a creatinine clearance that approached low normal values; each had had similar low values 5 years earlier. The remaining patients had unequivocally normal clearances. One patient had ureteral reduplication at urography at 10 years, and 1 had minimal calyceal clubbing. Changes at 5 years had been similar. No patient had bacterial growth in midstream urine specimens. Eight patients (18%) had an abnormal urine sediment compared with 11% initially and 45% at 5 years. Six of the 8 had renal biopsy initially, and 4 had subtle or definite histologic changes. No apparent relation was observed between any particular pattern of proteinuria and an abnormal urinary sediment.

Fixed orthostatic proteinuria is not a transitory condition of adolescence but at least the 10-year outlook of young men whose fixed orthostatic proteinuria is first detected during

(5) Ann. Int. Med. 73:235-244, August, 1970.

early adulthood is excellent. A given group of patients may eventually exhibit a variety of clinical courses. Continued observation of the present group of patients is important.

Infections, Including Gonorrhea

Study of Childhood Urinary Tract Infection in General Practice. Current interest in screening well groups for asymptomatic urinary tract disease is related to a belief that much of the renal damage resulting from urinary tract infection originates in childhood, during which infection is often missed because of the nonspecific nature of the symptoms. N. C. Mond, R. N. Grüneberg and Jean M. Smellie[6] (London) studied the feasibility and value of detecting bacteriuria in the pediatric population of a general practice. The practice is in a residential area of London and includes some 3,200 patients, predominantly belonging to the professional, managerial and skilled working classes. Initially 247 boys and 189 girls under age 13 were registered. All children were seen 3 times within 8 months. Fifty children with fever associated with upper respiratory infection or an exanthem were screened for bacteriuria during the study, on presentation and a week later. Midstream specimens were cultured for 24 hours, and if results were uncertain or positive, the study was repeated within 48 hours.

One of 426 children had bacteriuria on the first screening, 3 of 420 on the second and none of 413 on the third. Among the 4 children with confirmed asymptomatic urinary tract infection, 1 girl had significant pyuria. A total of 41 specimens had significant pyuria. Two children had significant pyuria on two screenings but without bacteriuria. More than trace proteinuria was found in 36 children (2.9%), but no correlation with pyuria or bacteriuria was apparent. One diabetic child had glycosuria. Three children treated throughout with chemotherapy had presented earlier with symptomatic infections. One of 50 children with upper respiratory infections or exanthemas had significant bacteriuria on one screening. All 3 children who reported frequency or dysuria had negative urine cultures. A girl who had bacteriuria discovered when she presented with abdominal pain and fever had duplication of the kidneys. One of the 4 infected children discovered by

(6) Brit. M. J. 1:602-605, Mar. 7, 1970.