THE YEAR BOOK *of* UROLOGY

(1960-1961 YEAR BOOK *Series)*

EDITED BY

WILLIAM WALLACE SCOTT, M.D., PH.D.

Director, James Buchanan Brady Urological Institute, The Johns Hopkins Hospital; Urologist-in-Charge, The Johns Hopkins Hospital; Professor of Urology, The Johns Hopkins University School of Medicine

---

YEAR BOOK MEDICAL PUBLISHERS

INCORPORATED

200 EAST ILLINOIS STREET

CHICAGO 11

THE PRACTICAL MEDICINE YEAR BOOKS

This volume is one of the 15 comprising the Practical Medicine Series of Year Books founded in 1900 by G. P. Head, M.D., and C. J. Head, and published continuously since then. The complete list follows:

Medicine: *Infections*, edited by PAUL B. BEESON, M.D.; *The Chest*, by CARL MUSCHENHEIM, M.D.; *The Blood and Blood-Forming Organs*, by WILLIAM B. CASTLE, M.D.; *The Heart and Blood Vessels and Kidney*, by TINSLEY R. HARRISON, M.D.; *The Digestive System*, by FRANZ J. INGELFINGER, M.D.; *Metabolism*, by PHILIP K. BONDY, M.D.

General Surgery edited by MICHAEL E. DE BAKEY, M.D., with a section on *Anesthesia*, by STUART C. CULLEN, M.D.

Drug Therapy edited by HARRY BECKMAN, M.D.

Obstetrics & Gynecology edited by J. P. GREENHILL, M.D.

Pediatrics edited by SYDNEY S. GELLIS, M.D.

Radiology: *Diagnosis*, edited by JOHN FLOYD HOLT, M.D., and WALTER M. WHITEHOUSE, M.D.; *Therapy*, edited by HAROLD W. JACOX, M.D., and MORTON M. KLIGERMAN, M.D.

Ophthalmology edited by WILLIAM F. HUGHES, M.D.

Ear, Nose & Throat edited by JOHN R. LINDSAY, M.D., with a section on *Maxillofacial Surgery*, by DEAN M. LIERLE, M.D., and WILLIAM C. HUFFMAN, M.D.

Neurology, Psychiatry & Neurosurgery: *Neurology*, edited by ROLAND P. MACKAY, M.D.; *Psychiatry*, by S. BERNARD WORTIS, M.D.; *Neurosurgery*, by OSCAR SUGAR, M.D.

Dermatology edited by RUDOLF L. BAER, M.D., and VICTOR H. WITTEN, M.D.

Urology edited by WILLIAM W. SCOTT, M.D.

Orthopedics and Traumatic Surgery edited by H. H. YOUNG, M.D., with a section on *Plastic Surgery*, by NEAL OWENS, M.D.

Endocrinology edited by GILBERT S. GORDAN, M.D.

Pathology and Clinical Pathology edited by WILLIAM B. WARTMAN, M.D.

Cancer edited by RANDOLPH LEE CLARK, JR., M.D., and RUSSELL W. CUMLEY, Ph.D.

Dentistry

TABLE OF CONTENTS

The designation (1960-1961 Series) used on the cover and title page of this volume is to indicate its publication during the "series year" which begins in September 1960.

INTRODUCTION

In a brief introduction to last year's YEAR BOOK, I described how your YEAR BOOK was produced. In addition, I described how difficult it was for one person to comment intelligently on all articles and solicited the help of urologists and physicians with special interests. The response was gratifying indeed. In this initial cooperative venture, 12 authorities were asked to write an introduction to a chapter and to comment on any or all articles within it; all complied. I know you will agree with me that their thoughts are most informative and well expressed. In each instance their contribution is acknowledged; they have my thanks and I'm sure the thanks of our readers.

During the coming year an effort will be made to expand the number of "Editorial Associates," again with the simple purpose of making *your* YEAR BOOK a better one.

WILLIAM WALLACE SCOTT

Clinical Value of Indirect Methods for Determination of Residual Urine Volume were assessed by Stanley D. Chovnick, Saul Boyarsky and Harry R. Newman[1] (Albert Einstein College of Medicine). Symptoms correlate poorly with amount of residual urine. Suprapubic percussion to discover dullness is usually of value in demonstrating residual urine of 150 cc. or more and does not rule out lesser amounts. The fractional 2-hour phenolsulfonphthalein test is accurate in determining residual urine only when renal function is normal. Its chief value is in demonstration of absence of residual urine. Even then, individual variations from optimal excretions may simulate small amounts of residual urine.

X-ray methods are useful in ruling out the presence or estimating the amount of residual urine with fair accuracy after experience with the method. A postvoiding cystogram should be routine in all excretory urograms. The authors confirmed the finding of previous investigators that bladder volume does not bear a constant mathematical relationship to the area of the bladder shadow.

The choice of any particular method depends on the entire clinical picture. The most accurate and reliable determination is still the direct approach by catheterization. However, if conditions allow, all patients should be screened by indirect methods first to reduce the number of catheterizations and thereby the septic hazards. The clinical value of indirect methods is highest in patients with very small or very large residual urines, in whom catheterization can be entirely avoided in diagnosis.

► [As Cotran and Kass pointed out 2 years ago (New England J. Med. 259:337, Aug. 14, 1958), it is possible to determine the volume of residual urine without catheterization and in patients with a reduction in renal function by the following procedure: "The well-hydrated patient empties the bladder, is given 3 mg. dye (0.5 ml. standard solution) intravenously and voids again 3 hours later. This specimen is labeled urine 1. The patient is given 2 glassfuls of water to drink and voids an hour after the previous voiding. The second specimen is labeled urine 2. The volumes and phenolsulfonphthalein concentrations of both specimens are determined and the volume of residual urine is calculated from the formula

$$V_r = \frac{U_2 \times V_2}{U_1 - U_2}$$

(1) New York J. Med 60:259-264, Jan. 15, 1960.

in which V_r is the volume of residual urine in milliliters, U_1 a..d U_2 are the concentrations of phenolsulfonphthalein in milligrams/milliliters in the first and second specimens, respectively; and V_2 is the volume of the second urine in milliliters."—Ed.]

Simple Rapid Method for Determination of Specific Gravity of Small Samples of Urine is presented by Allen S. Goldman[2] (Yale Univ.). The method requires only a few drops of urine and is similar in principle to determination of specific gravity of blood by the copper sulfate method.

PROCEDURE.—For use with urine, mixtures are used of two relatively nonvolatile liquids, immiscible with water and with specific gravities nearly equally above and below the range in urine. The two solutions selected were dibutyl-n-phthalate (Eastman), specific gravity $1.048^{20°}$, and kerosene, specific gravity $0.82^{20°}$. Similar results were obtained by substituting California mineral oil, specific gravity $0.842\text{-}0.884^{20°}$ for kerosene.

The specific gravity of urine is determined by allowing 1 drop to fall into each of a series of tubes containing a mixture of the two liquids made up to various specific gravities ranging from 1.005 to 1.030. That mixture in which the drop of urine comes most nearly to remain still, neither rising nor falling after coming to rest, approximates the specific gravity of the urine. The total sample of only a few drops can be quite small if a dropper with a small opening (2 mm.) is used. The determination takes only a few minutes, and a year's supply of the mixtures can be made in an afternoon at a cost of under $6.00.

► [The method described is a simplification of the falling drop method of determining specific gravity introduced by Barbour and Hamilton years ago (J. Biol. Chem. 69:625, 1926).—Ed.]

Acute Intermittent Porphyria: Family Study by D. H. Curnow, E. H. Morgan and G. A. Sarfaty[3] (Perth) was prompted by death of a woman, 27, due to acute intermittent porphyria. It was later found that her father excreted significant amounts of porphobilinogen. A medical history was obtained, and estimation of porphyrins in urine and feces was carried out in most of the 54 members of the family. Five males and 6 females definitely had porphyria. Five had "acute porphyria," i.e., they had clinical and chemical stigmas of acute intermittent porphyria, and 6 had "latent porphyria," i.e., they excreted abnormal quantities of porphobilinogen and porphyrins but had no symptoms attributable to porphyria.

The incidence of porphyria in this family is compatible with inheritance by a non-sex-linked dominant gene. The disorder was found in 3 successive generations, was trans-

(2) Pediatrics 24 (pt. 1):814-818, November, 1959.
(3) Australasian Ann. Med. 8:267-271, November, 1959.

mitted from father to daughter and mother to son, and its incidence was high in the 3d generation, 9 of 16 persons being affected. In the 4th and 5th generations, in which only 1 member was affected, only 4 persons were over age 15 years. The low incidence of biochemical or clinical signs of porphyria in children is well known.

In every case in which porphobilinogen was detected in the urine by the Watson and Schwartz test, urinary porphyrin excretion was also increased. It is apparent that a positive response to the Watson and Schwartz test is highly specific for this disease and that this simple procedure is just as valuable for making the diagnosis as estimation of urinary porphyrin excretion.

Screening Test for Aminoaciduria, based on horizontal paper chromatography, was devised by H. Ghadimi and H. Shwachman[4] (Harvard Med. School).

PROCEDURE.—Necessary equipment and reagents include scissors, twine, 15-cm. Petri dishes, Whatman no. 1 circular, 18.5-cm. filter paper, a hair drier, micropipets, pyridine, ethanol, acetic acid, acetone and ninhydrin. The circular filter paper is cut into a cross to speed migration of the solvent. Four specimens can be run simultaneously. Samples are placed 0.6 cm. from the center of the filter paper, and 5 ml. native urine specimen is applied in amounts of 1 or 2 ml. and dried after each application by a hair drier. The four spots on each paper should be of equal size. One spot is a known normal urine and serves as a control. Urine with excess of amino acids is recommended as a second control. When urine of infants is examined, the control should be from an infant of about the same age.

The twine, previously boiled in 10% pyridine for 10 minutes and dried, serves as a wick and is threaded through the center of the prepared filter paper, leaving a free end 5-8 cm. long. To the bottom of the Petri dish is added about 20-30 ml. solvent, consisting of glacial acetic acid, water and 90% ethanol in the proportion of 1:3:16. The prepared filter paper is centered over the top of the bottom half of the Petri dish, with cotton wick well immersed in the solvent. The dish is then closed, with filter paper intervening. Migration of solvent begins as soon as the wick is immersed and spreads rapidly from the center of the filter paper, reaching the end of the paper in 40 minutes at room temperature. The top of the Petri dish is removed, the wick discarded and the paper dried at room temperature for a few minutes and stained by immersion in 0.25% ninhydrin in acetone. The paper is dried at room temperature and hung in an oven at 150 F. for 3 minutes. If an oven is not available, development of full color may require over an hour at room temperature.

The papers are graded according to number and intensity of stained bands. Normal urine produces four bands with cystine close to point

(4) New England J. Med. 261:998-1001, Nov. 12, 1959.

of origin, followed by a band with histidine and methyl histidine. The third band is wide and most intense and is due to glutamic acid, glutamine, taurine, serine and glycine. The band at the periphery is due to alpha alanine, and in some instances leucine, valine and isoleucine contribute. Visual comparison is made of the known and unknown. Normal urine is scored 2. When bands are less intense and fewer, the score is 1. A score of 3 or 4 indicates abnormal excretion of amino acids. For a borderline case with a rating between 2 and 3, repetition with a new sample is recommended. Increase in one specific amino acid is shown by an unusually intense or distinct band.

In a retrospective study of 77 specimens previously investigated for amino acid content, results of the screening test were compared with values for $\frac{\text{alpha amino nitrogen}}{\text{total urine nitrogen}} \times 100$ and the milligrams of alpha amino nitrogen/100 ml. urine. When the score on the screening test is 1, mean value is 0.62; with score 2, it is 0.88 and with score 3 or 4, the ratio is as high as 3. There was little overlapping in values when specimens scoring 2 were compared with those scoring 3 or 4. Two-dimensional chromatographic findings also supported the correlation.

In another study in which 81 random urine specimens were examined, 72 were scored 1 or 2 and were considered normal. Further investigation showed that 2 patients with a score of 3 were receiving methionine. One was retested a month after discontinuance of methionine, and the urine showed a normal pattern. One of the 9 patients with scores of 3 or 4 is known to have phenylketonuria, and 3 others merit special study because of neurologic symptoms associated with aminoaciduria. It was impossible to obtain 24-hour urine collections in the other 3 patients.

The screening test may be used as a guide to select specimens for further, more elaborate studies.

► [It should be emphasized that in cystinuria, with or without stones, cystine crystals appearing as perfect hexagons can be seen in the urine, except if the patient is taking a medicine to make the urine alkaline.

Fuller Albright (J.A.M.A. 113:2049, 1939) devised a simple qualitative test for cystine in urine. Equipment and reagents include test tubes, concentrated ammonia water solution (28% NH_3), sodium cyanide solution (5%) and sodium nitroprusside powder (reagent grade powdered).

Method.—To 5 cc. freshly voided urine (preferably a.m. specimen), made alkaline with 2-5 drops of concentrated ammonia solution, add 2 cc. of 5% sodium cyanide solution, mix and allow to stand 10 minutes. This is the unknown tube. To another 5 cc. of the same urine, made alkaline with the same amount of ammonia solution, add 2 cc. of water and allow to stand 10 minutes. This is the control tube. Prepare a fresh 5% solution of sodium nitroprusside (dissolve about 0.25 Gm. powder in 5 cc. water in a small tube), add 8 drops of this reagent to the control tube and then immediately

add 8 drops of the reagent to the urine-cyanide tube. Mix each. In the presence of cystine a permanent wine color will develop. If the color is no deeper than the control, the result shows a trace or less. If the color is deeper than the control, report in grades of deepness of color as 1+, 2+, 3+ and 4+ positive. Normal urines will show a *positive trace or less.* Abnormal urines will show a positive wine color. Old urine specimens which may contain hydrogen sulfide may give a false positive result. *Do not use old urine for the test.* If the control tube gives a positive result, the test is worthless and another freshly voided urine should be examined. Also, this test has been modified to permit quantitative estimation.—Ed.]

Total Nondialyzable Solids (TNDS) in Human Urine: V. Subfractionation of Ultrafiltrate (UF-O) Fraction. J. Stanton King, Jr., and William H. Boyce[5] (Bowman Gray School of Medicine) found that the nondialyzable solids of normal human serum can be separated into three primary fractions, the most abundant of which is the ultrafiltrate fraction. They devised a method for separating this fraction of the total nondialyzable solids of normal urine into six arbitrary but reproducible subfractions. Daily excretion of each of the subfractions is fairly constant for normal subjects. There are no apparent significant differences between older and younger, male and female or white and Negro subjects. Excretion seems to be less during December and January and more during September. There is almost no information concerning the origin of the subfractions, how many components are present in each and their natural chemical state in urine.

► [Those of you who are interested in the stone problem will find the original article to be most informative, containing carefully collected data on the urinary concentration and partial characterization of such classes of substances as the glucides, peptides and certain inorganic constituents.—Ed.]

Infections, Including Gonorrhea

► Dr. Leighton E. Cluff, Associate Professor of Medicine, Johns Hopkins University School of Medicine, and Head, Division of Allergy and Infectious Diseases of the Department of Medicine, kindly agreed to write a brief introduction to this chapter. His remarks follow and include comments on several of the 15 articles on infection.

"The emphasis during recent years on improved methods of diagnostic bacteriology useful in the recognition of urinary tract infections is indicated by the articles selected for publication in this Year Book. Much more can be learned but there is no apparent short cut to the cultural identification of the micro-organisms responsible for infection in the individual patient. Although slide smears of urine may aid in recognizing the presence of gram-negative bacilli or gram-positive cocci and may be useful as a crude index of the numbers of bacteria per milliliter of urine they do not by themselves greatly assist in selection of the appropriate therapeutic agent. Quantitative enumeration of the bacteria in freshly collected urine

(5) J. Clin. Invest. 38:1927-1934, November, 1959.

has been the only means of reliably identifying asymptomatic urinary tract infections. In addition, attention to the numbers of bacteria has reduced the necessity for analysis of midstream as compared with initial stream urine cultures. The number of bacteria contaminating the anterior urethra that might be eliminated by collection of a midstream specimen is usually small so that it should not confuse the recognition of micro-organisms associated with cystitis or pyelonephritis.

"Studies of therapeutic agents often fail to differentiate acute from chronic urinary tract infection. When such a distinction is made, as in the study of Petersdorf and Hook on colistin, it is apparent that an antibacterial drug capable of eradicating a specific micro-organism from the urine may have little effect in curing the infection, as recrudescence may occur after cessation of therapy or there may be superimposed infections by entirely different bacteria. On the other hand, acute urinary infection that is uncomplicated by structural abnormalities of the urinary tract so often subsides spontaneously that the efficacy of an antibacterial drug can be evaluated only by carefully conducted controls. Bacteriologic documentation of the effect of chemotherapy is the only possible means of evaluating the results of treatment.

"Although in time there will be a reorientation of thinking about the implication of the catheter as an instrument inducing urinary tract infection, the importance of the ascending route as a source of infection has been established and the pathogenetic effects of indwelling catheters are clear. The importance of nonindwelling catheters in inducing infections has been discussed in some of the articles abstracted here, and although they may not induce infection commonly their potential for doing so is indicated and instrumentation that is not absolutely necessary should be avoided.

"The article by Beeson and Rowley is the first real effort to explore and explain some of the reasons for the localization of infection in the kidney by organisms almost unable to establish infection elsewhere. These brilliantly conceived studies, in addition to the studies previously done by Beeson and his colleagues, will go far in directing investigations to further our understanding of the pathogenesis of urinary tract infection and thereby enabling a more rational therapeutic approach."—Ed.

Comparative Bacteriologic Study of Urine Obtained from Children by Percutaneous Suprapubic Aspiration of Bladder and by Catheter is reported by Charles V. Pryles, Mark D. Atkin, Thomas S. Morse and Kenneth J. Welch[6] (Boston City Hosp.). The 42 children were free from clinical evidence of infection of the urinary tract. There was complete diagnostic correlation between urine obtained by suprapubic aspiration and clinical impression. In 40 children the specimens were sterile; in 2, growth occurred but the count was well below the critical figure of 10,000 colonies/ml. urine. There was a 92.8% diagnostic correlation between the first few milliliters of urine obtained by catheter (C_1) and the specimens obtained by suprapubic aspiration and a 97.5% correlation between the second few milliliters of urine obtained by catheter (C_2) and the suprapubic specimens.

Three patients had significant bacterial counts in catheter

(6) Pediatrics 24:983-991, December, 1959.

specimens. On this basis alone, diagnosis of pyelonephritis might have been made erroneously, but C_2 specimens showed a significant count in only 1 of the 3, pointing up the importance of discarding the initial few milliliters of urine obtained by catheterization. In this patient, the suprapubic specimen was sterile, the C_2 specimen grew 3,100 colonies of Escherichia coli/ml. urine, while a subsequent clean-voided specimen did not show significant growth. The patient remained in good health. Apparently, the organisms grown in the C_2 specimen were caused by contamination.

All patients were free from infection of the urinary tract 4-6 months after catheterization. Thus organisms introduced into the urine during catheterization were not responsible for urinary tract infection in this small group. It is imperative, however, that all specimens obtained by catheter be collected by the physician in charge, or under his direct supervision, with acceptable aseptic technics.

The authors feel that while properly collected clean-voided specimens may be used in most instances for diagnosis of true bacteriuria in children, catheterization, when properly done, should not be withheld for fear of producing infection of the urinary tract. Catheterization is necessary when (1) there is urinary retention, (2) repeated study of clean voided specimens yields borderline results, (3) the patient is so acutely ill that there is need for immediate therapy, with no time for multiple specimens to be obtained and (4) the patient is unable or unwilling to cooperate.

Clean-Voided Urine Specimens for Culture from Female Patients: Comparison with Catheterized Specimens. George F. Clabaugh, Paul S. Rhoads and Doris M. Adair[7] obtained 36 clean-voided urine specimens followed by catheterized specimens and 14 clean-voided specimens only from female hospital patients who were suspected of having urinary tract infection. On the same basis, 27 clean-voided urine specimens were obtained from male hospital patients.

The results led to the conclusion that a clean-voided specimen count from a female can be satisfactory if it is less than 10,000/ml. because subsequent catheterization yielded a specimen of less than 10,000 count in every instance. Another study revealed that other evidences of actual urinary infection seldom were present if the count was below this figure.

(7) Quart. Bull. Northwestern Univ. M. School 34:119-123, Summer, 1960.

If the count of the clean-voided specimen is over 10,000, it is safer to repeat the specimen or follow it up with a catheterized specimen before drawing conclusions regarding the presence or absence of infection.

Evaluation of Antibiotics in Urinary Infections is presented by I. Langdale Gregory and J. McDonnell[8] on the basis of a laboratory study to determine the infecting organism and relative sensitivity to various antibiotics in 219 patients with urinary infection and of clinical treatment of 25 patients. Antibiotics used were chlortetracycline, Chloromycetin, erythromycin, Furadantin, streptomycin, oxytetracycline and Tetracyn.

By far the commonest infection was due to Bacillus coli (100 cases) and next was that due to mixed B. coli and staphylococci (35). Other organisms were Staphylococcus aureus (22), Staph. albus (13), B. pyocyaneus (11), B. proteus (7) and Staph. faecalis (6). Whereas pure Staph. albus and aureus infections respond relatively well to all antibiotics and pure B. coli to all antibiotics except chlortetracycline, infection by pyocyaneus, proteus and faecalis responded only to Chloromycetin, Furadantin and streptomycin. These three drugs were superior to all the others in in vitro tests. Of particular significance is the fact that Furadantin was markedly successful in combating all infections studied.

In clinical tests in 25 patients with B. coli (17 cases) and mixed B. coli and staphylococcic (7 cases) infections, Furadantin proved superior to other antibiotics in that it was more effective in controlling the infection and urinary bacteria were less likely to become insensitive to this drug after a 5-day course. In this clinical study, Furadantin was used in 13 patients, Chloromycetin in 6, streptomycin in 3 and oxytetracycline in 3.

Although sensitivity of the infecting organism should always be determined, if drugs must be used empirically, the most useful are Furadantin, streptomycin and Chloromycetin. In proteus infections, Furadantin is superior to Chloromycetin and streptomycin. In pyocyaneus infections, streptomycin is superior to Furadantin and Chloromycetin.

Chemotherapy of Urease- and Citrase-Producing Bacteria of Urinary Tract. Harry Seneca, John K. Lattimer and Hans

(8) Central African J. Med. 5:618-622, November, 1959.

Enzyme Profile, Biochemical Reactions and Resistance Pattern of Pathogenic Bacteria

Profile	Enzyme		Enzyme Media					Resistance Pattern							Carbohydrates				
	Urease	Citrase	Bacto Urea	Simmon's Citrate	Urea Citrate	Urea	Citrate	Nitrofurantoin	Sulfisoxazole	Tetracycline	Chloramphenicol	Erythromycin	Penicillin Streptomycin†	Colymycin	Lactose	Dextrose	Maltose	Mannitol	Saccharose
Profile 1																			
Proteus columbiensis	++++	+	SlB	Sl	SlB	Sl	+	R	R	R	R	R	R		–	AG	AG	–	AG
P. vulgaris								R	R	R	R	R	R		–	A/AG	–	A/AG	A
P. rettgeri								R	R	R	R	R	R		–	AG	–	–	AG
P. mirabilis								R	R	R	R	R	R		–	AG	AG	–	AG
P. OX 2																			
Profile 2																			
P. morgani	++++	–	SlB	–	Sl	Sl	–	R	S	R	R	R	R		–	AG	–	–	–
69% of Micrococcus	++	–	Sl	–	Sl	Sl	–	R	S, R	S, R	S/R	S	S, R		A	A	A	A	A
Profile 3																			
Aerobacter aerogenes	++	+	Sl	Sl	Sl	–	–	R	R	R	R	R	R		AG	AG	AG	AG	AG
Klebsiella pneumoniae								R	S	S	S	S, R	S		AG	AG	AG	AG	AG
77% of *Pseudonomas aeruginosa*								R	R	R	S, R	R	R	S	–	–	–	–	–
Profile 4																			
P. OX 19	–, +	–, +	–, Sl	–, Sl	–, Sl	–, Sl	–								–	AG	AG	–	AG
P. OX K								R	S	S, R	S	S, R	S		–	AG	–	–	A
Profile 5																			
P. inconstans	–	–, +	–	Sl	Sl	–	–								–	A/AG	–	–	A/AG
Profile 6																			
23% of *Pseudomonas aeruginosa*	–	+	+	+, Sl	Sl	+	+	R	R	R	S, R	R	R	S	–	–	–	–	–
Alcaligenes faecalis								R	S	S	R	R	S		–	–	–	–	–
Salmonella								R	S	S	S	R	S/R		–	AG	AG	AG	–
Vibrio cholerae								S/R	S	S	S	S	S		–	A	A	A	A
Escherichia (freundii, intermedia)															AG	AG	AG	AG	AG
Profile 7																			
Escherichia (coli, aurescens)	–	–	+	–	–	–	–	S/R	S/R	S	S	R	R		AG	AG	AG	AG	AG
Eberthella typhosa								R	S/R	S	S	R	S/R		–	A	A	A	–
Salmonella (paratyphi, pullorum, gallinarum)								R	R	S	S	R	S		–	AG	AG	AG	–
Vibrio El Tor															–/A	A	–/A	–/A	–/A
31% of Micrococcus								R	S/R	S/R	S/R	S	S/R		A	A	A	A	–
Enterococcus								R	R	S, R	S/R	S/R	S/R		A	A	A	–	–/A
Streptococcus pyogenes								S/R	S	S	S	S	S		A	A	A	–	A
Shigella								S/R	S	S	S	S/R	S/R		–/A	A	A	–/A	–/A
Pneumococcus																			

+ indicates growth; –, no growth reaction; A, acid; AG, acid and gas; Sl, slant; B, butt in media; S, sensitive; R, resistant.

H. Zinsser[9] (Columbia Univ.) found that organisms capable of surviving with citrate and urea as the sole substrate are peculiarly resistant to most antibacterial agents in common use at the present time.

METHOD.—Strains of pathogenic bacteria, gram-positive and gram-negative, derived from genitourinary infections, were studied extensively by tube dilution technics for antibiotic susceptibility. In addition, their susceptibilities to enzyme inhibition and survival on a variety of simple substrates, in particular Bacto urea, Simmon's citrate, SAT medium, citrate and urea agar, were analyzed. In patients with clinical infection, the antibiotic sensitivities were initially determined, the patient was given oral doses of mercurial diuretic and bacterial sensitivities of the organisms were subsequently determined and their identification repeated. For the purposes of identification and specific species subtyping, known strains derived from United States Army and Navy medical laboratories and the National Institutes of Health were also surveyed. Organisms were subdivided on their urease and citrase capacities into seven groups that correspond roughly to their susceptibility to antibacterial agents (table).

It was found that the addition of a period of exposure to chlormerodrin, 36.6-55.8 mg./day reversed the alkalinity of the urine in patients harboring urease-positive bacteria. The persistence of this pH-reversing effect implied a profound change in the metabolism of the bacteria. Subsequent to this change in the enzymatic capacities of the bacteria, which is apparently transmitted genetically from generation to generation within the given strain, their sensitivity to a variety of antibacterial agents has changed, in some instances favorably.

Because the most resistant organisms found in the urinary tract exhibit urea- and citrate-utilizing capacity, the addition of organic mercurials to a therapeutic regimen, particularly in the presence of stone, seems justified

► [Many will recall the authors' splendid exhibit entitled "A New Method for the Classification of Bacteria from the Urinary Tract Using a 'Profile' of Their Enzyme Activity," which was awarded first prize in the category Exhibit on Laboratory Research at the Annual Meeting of the American Urological Association in Chicago, May 16-19, 1960.—Ed.]

Current Status of Anti-infective Therapy in Urology is discussed by Russell D. Herrold and Nick Karabatsos[1] (Univ. of Illinois). Acute uncomplicated infections of the urinary tract are usually caused by bacilli. The drug of first choice is a sulfonamide, if the patient is not sensitive. It should be given in maximum dosage for at least 5 days and in

(9) Ann. Int. Med. 53:468-474, September, 1960.
(1) J.A.M.A. 172:771-773, Feb. 20, 1960.

lower dosage for an additional 5 days. If this therapeutic regimen fails to cure the infection, a complete urologic examination is indicated. Occasionally, the lack of response is due to bacterial resistance. This is usually indicated by absence of subjective or objective improvement in the first 48 hours of therapy. The chief current problem is the management of chronic infections without associated uropathy or with nonremediable uropathy.

In urinary infections, the infecting organisms can be identified most accurately by cultures. If these are not available, Gram staining of the urinary sediment, which will establish whether the infection is bacillary, "coccic" or mixed, should be done. A wet cover-slip preparation is a simple method for evaluating the degree of pyuria and hematuria. Also, bacilli may often be identified microscopically under the high-power field, especially in samples from patients with acute infections.

The results of the disk method of sensitivity testing are more likely to correlate in vitro and in vivo if the primary inoculations are made from the patient's urine or prostatic secretion. There is usually enough growth so that it is seldom necessary to make subcultures into broth before making sensitivity tests. Sensitivity readings are most important when the zones of inhibition of growth show completely resistant or highly sensitive reactions to the drug. Intermediate readings between these two areas are of some importance only when two drugs are to be given in combination.

In treating chronic infections, broad-spectrum antibiotics are suggested. The authors reviewed observations on 75 patients treated with the newest broad-spectrum antibiotic, kanamycin (Kantrex). The original organism was eradicated in about 60% of this group, but other organisms emerged after or even before the treatment was ended in about 30%. Best results were obtained in patients with infections caused by Escherichia coli, Aerobacter aerogenes, paracolobactrum, intermediate coliform bacteria, klebsiella and staphylococci, although this last organism is usually found mixed with one of the gram-negative bacilli.

► [Dr. Russell D. Herrold was always a real student of urinary infections, and his many contributions have helped us all to treat our patients better. He will be sorely missed.—Ed.]

Sulfamethoxypyridazine (Kynex)—Evaluation in Urinary Tract Infections. J. D. Wargo, R. Teichner and J. H.