*Year Book*

OF

UROLOGY

SCOTT

1962–1963

SERIES

# THE YEAR BOOK *of* UROLOGY

*(1962-1963* YEAR BOOK *Series)*

EDITED BY

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# INTRODUCTION

Beginning with the 1960-1961 Series, I have enlisted the help of a number of our medical colleagues in the preparation of the YEAR BOOK and I want to express my sincere thanks to them for their assistance. Lowell R. King, Instructor in Urology, Johns Hopkins University School of Medicine, and Urologist, Johns Hopkins Hospital, has been of tremendous help with the current volume. He not only helped to select articles and to correct abstracts, but wrote many editorial comments. Each of his comments bears his signature.

I want to thank the following physicians who have contributed introductions to certain sections of this book: Paul B. Beeson, Ensign Professor of Medicine and Chairman of the Department of Internal Medicine, Yale University School of Medicine; Wilhelmina F. Dunning, Professor of Experimental Pathology, Cancer Research Laboratory, University of Miami; Willard E. Goodwin, Professor of Urology, University of California School of Medicine at Los Angeles; Donald F. McDonald, Professor of Urology, University of Rochester School of Medicine and Dentistry; Albert J. Paquin, Jr., Professor of Urology, University of Virginia School of Medicine; Jorgen U. Schlegel, Professor and Chairman, Department of Surgery (Division of Urology), Tulane University School of Medicine; Baxter A. Smith, Minneapolis; Howard I. Suby, Visiting Urologist, Massachusetts General Hospital; and John D. Young, Jr., Professor of Urology, University of Maryland School of Medicine. Their contributions are acknowledged as presented.

Because of increasingly heavy commitments and a desire to devote more time to my research, I have decided I must relinquish my editorship of this YEAR BOOK. It has been a happy and rewarding experience for me, and it is with sincere regret that I break the pleasant relationship which I have enjoyed with the Publisher over the past 12 years.

I am happy to announce that my successor will be Dr. John T. Grayhack, Professor of Urology, Northwestern University of Medicine, whose knowledge of clinical and experimental medicine makes him admirably suited for the work.

Under his editorship, the YEAR BOOK OF UROLOGY should continue to provide the medical profession with the very best of the literature and to serve its purpose as a valuable source of information to the practitioner and the investigator.

WILLIAM WALLACE SCOTT

## GENERAL CONSIDERATIONS

### Examination of Urine

**Nonglucose Melituria**s were studied by J. B. Sidbury[1] (Duke Univ.). The recent upsurge of interest in genetics has focused attention on these conditions, since most of them are inheritable disorders. Paper chromatography for detection of urinary sugars has established an easy and rapid method for discovery and identification of urinary sugars which has led to the recognition of new syndromes associated with melituria.

For routine screening, the author prefers the standard qualitative Benedict reaction, a nonspecific test for all reducing sugars. If the Benedict reaction is positive but the glucose oxidase stick reaction negative, nonglucose melituria is likely, and paper chromatography must be done for further identification.

In normal persons, presence of a disaccharide (lactose, maltose, sucrose) in the urine is due to its ingestion, except for lactose in the urine of the pregnant and lactating female. The trace amounts of glucose and fructose in normal urine can be considered of endogenous origin, but galactose is probably always exogenous. Ribose, desoxyribose, xylulose and ribulose are endogenous, whereas xylose and arabinose are from plant sources. These have all been found in the urine of normal persons.

Melituria often is associated with hepatic disease due to the failure of the liver to metabolize the ingested sugar rapidly. Renal disease can also result in melituria from failure of reabsorption by the tubules. Gastrointestinal disturbances, the neonatal state and prematurity may be associated with melituria.

Sucrose and lactose have been found frequently in the urine of infants with hiatus hernia. Fructose intolerance has been reported to have many symptoms and findings in common with galactosemia, except cataract formation.

The familial disaccharidurias follow a similar clinical pattern. The young infants show hyperchloremic acidosis,

(1) J. M. A. Alabama 31:112-114, October, 1961.

chronic intractable diarrhea, frequent vomiting and marked failure to thrive. Death follows if the diagnosis and proper treatment are not effected. It should be noted that the melituria is not marked.

► [In 1945, Thaddeus Mann (Biochem. J. 39:451, 1945) discovered and identified fructose in the seminal vesicular component of seminal plasma. In man, its concentration is of the order of 315 mg./100 ml., and it is entirely possible that small amounts of fructose found in the urine actually come from the seminal vesicles.—Ed.]

## Infections, Including Urethritis

**Diagnosis of Urinary Tract Infection: Value of Clean-Voided Noncatheter Urines with Quantitative Bacterial Counts** was investigated by R. N. Howie, J. R. Little, J. Z. Montgomerie and J. D. K. North[2] (Auckland Hosp.). Clean-voided midstream specimens were taken for examination from both men and women. In women, chlorhexidine cream was applied by the nurse to the labia and urethral orifice; it was removed after 15 minutes by swabbing with sterile normal saline. The patient then urinated standing astride a toilet, with the labia separated by hand; the mid-urinary flow was collected directly into a wide-mouthed sterile jar. In males, the penis was first cleansed with chlorhexidine cream and a midstream specimen was collected similarly.

Examinations were carried out on 373 urine specimens from 157 patients. Of 24 with infected urine, 21 were females. No patient had symptoms of acute urinary tract infection. Quantitative bacterial counts were found to be the most consistent and reliable means of detecting urinary tract infections. Positive results were obtained, with over 10,000 bacteria per ml. of freshly voided urine, in 92% of urine specimens from patients with untreated urinary tract infections; 78% of these had bacterial counts over 100,000/ml. In contrast, pyuria defined as more than 5 leukocytes per high-power field in the urinary sediments was present in only 65% of the urine specimens. The Sternheimer stain was positive in 51% of patients with urinary tract infections.

To assess the value of the clean-voiding midstream method of obtaining urine specimens from women, results of bacterial counts from male and female patients with uninfected urines were compared. The degree of contamination in fe-

(2) New Zealand M. J. 60:481-484, October, 1961.

males was almost identical with that in males, with 74% of urines from each sex sterile on culture for bacterial counts. Contamination with bacterial count over 10,000 occurred in only 3% of males and 4% of females.

In the 24 patients with urinary tract infection, the infecting organism was obtained in the first urine specimen in 85% and in the second in 89% of specimens examined. Both first and second specimens grew the responsible organism in 74% of cases.

► [As Dr. Paul Beeson points out in his introduction to the section Pyelonephritis and Renal Infections in this YEAR BOOK "There is no practical method of obtaining urine specimens for culture without the risk of contaminating the specimen with a few bacteria lying in the urethral canal." Hence, the *number* of bacteria cultured is most important in distinguishing contaminants from pathogens —Ed.]

**Simple Test for Significant Bacteriuria** was devised by N. A. Simmons and J. D. Williams,[3] based on the fact that bacteria can reduce the colorless compound triphenyltetrazolium chloride to a red insoluble dye in an alkaline medium.

TECHNIC.—The reagent was made up by dissolving 750 mg. triphenyltetrazolium chloride (T.T.C.) in 100 ml. saturated solution of disodium hydrogen phosphate ($Na_2HPO_4$). A working solution was prepared by taking 4 ml. of this solution and diluting it to 100 ml. with saturated $Na_2HPO_4$. Both stock and working solutions were sterilized by Seitz filtration and stored in the dark. Stock solution was stable for at least 2 months and working solution for 2 weeks. The test was performed by measuring 2 ml. of well-mixed urine into a clean test tube and adding 0.5 ml. T.T.C. working solution with a sterile pipet. The tube was incubated for 4 hours at 37 C., after which the deposit was examined with the naked eye. A positive result was shown by a red precipitate of triphenylformazan. A concave mirror was helpful in reading the result. Whenever blood cells were present in excess, after incubation the deposit was removed and examined on a slide with the naked eye. Though triphenylformazan could still be seen clearly, red cells were no longer visible. Highly colored urines were centrifuged after incubation and the urine was replaced by water; results were then easy to read.

Results of T.T.C. tests in 480 consecutive urine specimens were compared with quantitative bacterial counts. In 113 urines containing over 100,000 organisms per ml., 106 (94%) gave positive results with the T.T.C. test. All 83 urines infected with gram-negative bacilli in pure culture gave a positive result. When other organisms were present, correlation with bacterial counts was less precise (table). Of 17 urines containing streptococci, 14 gave a positive test, as did 8 of 12 urines containing more than one organism. Only 2% of posi-

(3) Lancet 1:1377-1378, June 30, 1962.

PROPORTION OF POSITIVE T.T.C. TESTS ACCORDING TO BACTERIAL SPECIES ISOLATED*

| Bacterial species | No. of isolations | No. of positive T.T.C. tests | % |
|---|---|---|---|
| *Escherichia coli* .. .. | 48 | 48 | 100 |
| *Paracolon* spp. .. .. | 7 | 7 | 100 |
| *Proteus mirabilis* .. .. | 17 | 17 | 100 |
| *Proteus rettgeri* .. .. | 3 | 3 | 100 |
| Unidentified *Proteus* spp... | 5 | 5 | 100 |
| *Bacterium aerogenes* .. | 2 | 2 | 100 |
| *Pseudomonas pyocyanea* .. | 1 | 1 | 100 |
| Monilia .. .. .. | 1 | 1 | 100 |
| *Streptococcus fæcalis* .. | 17 | 14 | 78 |
| More than one organism .. | 12 | 8 | 66 |

*Present in numbers exceeding 100,000/ml.

tive results were obtained in urines containing less than 100,000 organisms.

It is suggested that this simple test can be used (1) as a screening test for detecting urinary tract infections in patients without symptoms referable to the urinary tract and (2) as an adjunct to routine bacteriologic examination of urine for rapid assessment of the significance of growth occurring on routine culture.

► [The correlation between high bacterial counts and positive T.T.C. tests is good, especially when the organisms are gram-negative bacilli, and certainly suggests that this test could provide a screen for detecting urinary tract infections.—Ed.]

**Urinary Tract Infections in Schoolchildren.**—*I. Prevalence of bacteriuria and associated urologic findings.*—Calvin M. Kunin, Elizabeth Zacha and Albert J. Paquin, Jr.[4] (Univ. of Virginia) made a community-wide survey of urinary tract infections among 9,878 schoolchildren in Charlottesville-Albemarle County, Va., which resulted in detection of 56 cases, 54 (1.1%) in girls and 2(0.026%) in boys. All but 2 of these children were unaware of the infection. Four other cases were detected among 222 girls enrolled at the University of Virginia; none was found among 1,116 male college students. Prevalence of infection in girls was independent of age, race or rural-urban residence.

Urologic investigations in 65 cases discovered in this program and in a pilot study in Waynesboro, Va., revealed abnormalities on intravenous pyelography in 22% and on cystography in 44%. Six girls had abnormalities consistent with the megacystis syndrome. Recent symptoms, past his-

(4) New England J. Med. 266:1287-1296, June 21, 1962.

RELATION OF AGE TO SYMPTOMS, HISTORY, PYURIA AND UROLOGIC FINDINGS

| POSITIVE FINDINGS | 5-9 YR. OF AGE | | 10-14 YR. OF AGE | | 15-19 YR. OF AGE | | 20-24 YR. OF AGE | | TOTALS | |
|---|---|---|---|---|---|---|---|---|---|---|
| | no. | % | no. | % | no. | % | no. | % | no. | % |
| Recent symptoms | 8/23 | 34.8 | 17/32 | 53.1 | 5/17 | 29.4 | 2/2 | 100.0 | 32/74 | 43.2 |
| Past history of infection | 8/23 | 34.8 | 7/32 | 21.9 | 2/17 | 11.8 | 0/2 | 0.0 | 17/74 | 23.0 |
| Pyuria | 9/23 | 39.1 | 8/32 | 25.0 | 7/17 | 41.2 | 2/2 | 100.0 | 26/74 | 35.1 |
| On intravenous pyelography | 5/22 | 22.7 | 8/27 | 29.6 | 1/14 | 7.1 | 0/1 | 0.0 | 14/64 | 21.9 |
| On cystography | 11/21 | 52.4 | 11/27 | 40.7 | 6/14 | 42.9 | 0/1 | 0.0 | 28/63 | 44.4 |
| On intravenous pyelography & cystography | 4/21 | 19.0 | 6/26 | 23.1 | 1/14 | 7.1 | 0/1 | 0.0 | 11/62 | 17.7 |
| On intravenous pyelography or cystography | 12/22 | 54.5 | 12/28 | 42.9 | 6/14 | 42.9 | 0/1 | 0.0 | 30/64 | 46.2 |

tory of infection, pyuria, age and race were of little aid in predicting extent of structural involvement (table). Mothers and sisters of persons with infections were often found to have had urinary tract infections in the past (33 and 18%, respectively), but rates almost as high were found in relatives of noninfected paired control children. Nonetheless, clustering of cases in families was frequently observed, and in 4, dual active cases were detected in siblings. Proteinuria was more frequent in children with bacteriuria than in the base population but too rare (7.4%) to be of diagnostic value. Significant glycosuria was found in 7 children (0.07%) and in 1 student nurse; all were known to have diabetes.

Hospital records of known cases of urinary tract infection among the population of schoolchildren failed to reveal a tendency of those with known cases to avoid voluntary participation in the program. As many cases of megacystis syndrome were detected in the present study as had previously been found in the population by investigation of symptomatic patients referred to the hospital by local physicians.

Point-prevalence data, i.e., 1.1% incidence of active cases in girls, provides only a limited view of the over-all problem of urinary tract infection in schoolchildren. Incidence of new cases, as a rate per year, has not been established, nor is the rate of spontaneous recovery (if it does occur) known. Rate of appearance of symptomatic disease, results of treatment and rate of relapse or reinfection must be measured. It is hoped that a second survey of the study population after one academic year will permit a more dynamic concept of the natural history of urinary tract infections in schoolchildren.

Mass detection of urinary tract infections among children of school age is practical and productive, obviously much more so than the search for glycosuria in this age group. Long-term study is required to demonstrate whether or not

significant prevention of pyelonephritis can be achieved by this approach.

► [Studies such as these certainly suggest that a significant number of children, especially girls, have urinary tract infections which go unrecognized, often for a long time, and that these infections are often associated with significant abnormalities of the urinary tract. Furthermore, they suggest that as a public health measure, mass quantitative urine cultures will detect more children with disease processes than will mass tests for urinary sugar.—Ed.]

*II. Characterization of invading organisms.*—Kunin and Norma E. Halmagyi[5] identified according to species bacteria isolated in 74 cases of urinary tract infection detected in surveys among 13,000 healthy schoolchildren in Waynesboro and Charlottesville-Albemarle County, Va. In the case of Escherichia coli, O and H antigens were also identified.

Organisms of the E. coli group accounted for 84% of the infections. Infections with other species were more frequently associated with previously known infection. Identification by the O antigen was possible for 77% of the E. coli strains. More than half belonged to group 1A, and multiple cases were observed with O antigen groups 01, 2, 4, 6, 7, 30 and 75. One third of the E. coli strains were motile; 14% were hemolytic.

Studies in 43 untreated cases in which multiple cultures were obtained indicated a marked tendency for the same organism to persist for weeks to months in most children. Studies of multiple cases in 5 families failed to indicate the same type in members of the same family.

Serologic characterization of E. coli strains should prove helpful in an understanding of the pathogenesis of urinary tract infections in man. Studies to be reported indicate that persistent bacteriuria may occur in the presence of specific antibody, and relapse after successful sulfonamide therapy is usually due to reinfection with a new E. coli serotype or another bacterial species. Serologic typing of E. coli, as with bacteriophage typing of Staphylococcus aureus, permits detailed epidemiologic study and may have the added advantage of permitting correlations to be made with specific antibody defense mechanisms of the host.

**Incidence of Bacteriuria with Indwelling Catheter in Normal Bladders** was investigated by Clair E. Cox and Frank Hinman, Jr.[6] (Univ. of California) in 80 urologically normal patients. A relatively low incidence of infection was found,

(5) New England J. Med. 266:1297-1301, June 21, 1962.
(6) J.A.M.A. 178:919-921, Dec. 2, 1961.

contrary to the current assumption that infection always exists with retention catheterization. The lower infection rate is even more significant, since in this study bacteriuria was defined as 500 or more bacteria per ml. urine, whereas 100,000 bacteria per ml. is usually taken as an indication of true bacteriuria.

Of 30 patients with catheter drainage for 18-24 hours, only 2 acquired bacteriuria. Of 30 with catheter drainage for 36 hours, 6 became infected. Among 20 with catheter drainage for 36-72 hours, bacteriuria developed in 9.

These results suggest that the factor that influences subsequent incidence of bacteriuria with retention catheterization is the condition of the bladder at the time of catheterization. The normal bladder, because of a strong defense mechanism, not only delays onset of bacteriuria, but can clear itself of infection, since 12 patients who became infected during bladder drainage were later determined to be free from bacteria.

It appears that if defense mechanisms are strong (a normal bladder that empties completely), considerable contamination with bacteria will be tolerated. If the bladder is obstructed or congested, or if residual urine is present, minimal contamination will establish infection.

► [These data also clearly indicate that the incidence of bacteriuria is distinctly related to the length of time the catheter is left indwelling. Thus, 9 of 20 patients (45%) with catheter drainage for 36-72 hours developed bacteriuria. Such findings admonish us all not to leave an indwelling catheter any longer than is absolutely necessary, as well as to consider intermittent catheterization when feasible.—Ed.]

**Initiation of Urinary Tract Infection Following a Single Bladder Catherization** is reported by Michael Kaye, J. de Vries and K. T. MacFarlane[7] (Montreal Gen'l Hosp.). The incidence of pyuria and bacteriuria in clean-voided specimens from 353 women within 24 hours of delivery was compared with that 5 days after delivery. A single catherization had been performed on 168 of the 353 at delivery.

On admission, the catheterized and noncatheterized groups were comparable at each level of bacteriuria (Table 1.) On discharge, fewer catheterized patients showed sterile urine, mainly because of the increase in the number of patients with a count of $10^{10}$ or more. It is considered that bacterial counts in the range of $10^{1}$-$10^{8}$ represent predominantly contamination, whereas counts of $10^{10}$ or over are due to

(7) Canad. M. A. J. 86:9-14, Jan. 6, 1962.

TABLE 1.—BACTERIURIA IN 353 PATIENTS

| Log. numbers of bacteria | Admission | | Discharge | | Total of present series 353 patients 706 cultures | All specimens 1678 cultures |
|---|---|---|---|---|---|---|
| | Catheterized % | Not catheterized % | Catheterized % | Not catheterized % | % | % |
| Sterile | 44.6 | 46.4 | 34.5 | 49.7 | 44.0 | 39.4 |
| $10^1$ | 1.1 | 2.7 | 0 | 0 | 0.9 | 5.5 |
| $10^2$ | 14.2 | 13.5 | 11.9 | 11.4 | 12.7 | 12.9 |
| $10^3$ | 23.2 | 19.4 | 20.2 | 16.8 | 19.8 | 18.0 |
| $10^4$ | 5.3 | 8.1 | 5.3 | 6.4 | 6.3 | 6.7 |
| $10^5$ | 3.5 | 3.2 | 5.3 | 3.2 | 3.8 | 3.9 |
| $10^6$ | 3.5 | 0.5 | 0.5 | 3.2 | 1.9 | 2.8 |
| $10^7$ | 0 | 1.6 | 4.1 | 2.1 | 1.9 | 1.4 |
| $10^8$ | 0 | 0.5 | 0 | 0.5 | 0.2 | 0.2 |
| $10^9$ | 0 | 0 | 0 | 0 | 0 | 0 |
| $10^{10}$ or more | 4.0 | 3.7 | 17.8 | 6.4 | 7.9 | 8.7 |

TABLE 2.—RELATION BETWEEN BACTERIURIA AND PYURIA

| LOG. NO. BACTERIA | % WITH PYURIA |
|---|---|
| Sterile | 19 |
| $10^1$ - $10^2$ | 27 |
| $10^3$ - $10^4$ | 23 |
| $10^5$ - $10^8$ | 33 |
| $10^{10}$ or more | 50 |

TABLE 3.—BACTERIAL COUNTS 6 WEEKS AFTER DELIVERY

| | DISCHARGE CULTURE $> 10^{10}$ (12)* | DISCHARGE CULTURE $> 10^5$ (22)* |
|---|---|---|
| Sterile | 25% | 36% |
| $10^1$ - $10^2$ | 8% | 9% |
| $10^3$ - $10^4$ | 50% | 32% |
| $10^5$ - $10^6$ | 8% | 18% |
| $10^{10}$ | 8% | 4% |

*No. patients.

active multiplication of organisms within the urinary tract before voiding. A definite increase of pyuria was noted with counts of $10^{10}$ or more (Table 2).

Findings on admission and at discharge revealed a 10% and 15% increase in leukocytes and bacteria, respectively, in the catheterized, as compared with the noncatheterized, group. Because only 16% of the patients admitted with counts under $10^{10}$ bacteria per ml. urine and discharged with counts over $10^{10}$ were discharged with the same organism that was present on admission and because half had had sterile urine on admission, it is apparent that most of them acquired infection and a new bacterial flora while in the hospital. In 75% of patients the responsible organism was Escherichia coli.

Among 36 women with counts over $10^{10}$ at discharge,

only 1 of 12 who had repeat cultures after 6 weeks had a count of this order (Table 3).

In this series, although the number of patients with bacteriuria on hospitalization was small, there was no evidence that its presence in any way prejudiced the health of the mother or infant. In the patients who showed infection after catheterization, spontaneous disappearance of the infection seemed to be the rule.

**Experiments with Induced Bacteriuria, Vesical Emptying and Bacterial Growth on the Mechanism of Bladder Defense to Infection.** According to Clair E. Cox and Frank Hinman, Jr.[8] (Univ. of California,), the natural resistance of the normal bladder to infection, which has long been known, has been overlooked in recent work on urinary infections, as is particularly evident in the recent controversy over the role of instrumentation in the etiology of infection. They therefore made an attempt to investigate this resistance, termed the "bladder defense mechanism."

The investigation showed, as was suggested by a previous study on retention catheterization, that the normal bladder is resistant to infection. This inherent resistance is provided by at least two defense mechanisms: the mechanical factor of voiding and an antibacterial factor, or factors, inherent in the bladder and not contained in urine.

The first of four experiments showed that the in vitro multiplication of bacteria in random urine is similar to the rapid bacterial multiplication that occurs in nutrient broth, and thus demonstrated that urine under ordinary circumstances is not antibacterial. The second experiment revealed that vesical emptying (voiding) reduced bacterial counts but was insufficient to rid the simulated bladder of bacteria.

The third experiment indicated that growth of bacteria in vivo was limited by an antibacterial factor, as demonstrated by comparison of the growth of bacteria introduced into the urine of a subject in vitro and the simultaneous growth of bacteria introduced into the bladder of the same subject. In 4 subjects who volunteered for this experiment, initial in vivo bacterial counts of 1,000,000/ml. calculated from assumption of a 5 ml. residual) decreased to 500,000/ml. or less, whereas initial in vitro bacterial counts increased from 50,000/ml. to over 2,000,000/ml. (Fig. 1).

(8) J. Urol. 86:739-748, December, 1961.

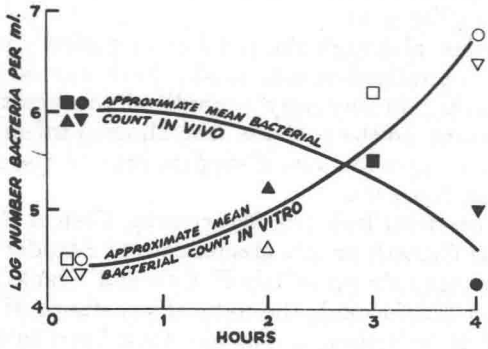


Fig. 1.—Effect of bladder antibacterial defense mechanism. Comparison of changes in in vivo and in vitro bacterial counts. Data on 4 subjects. (Courtesy of Cox, C. E., and Hinman, F., Jr.: J. Urol. 86:739-748, December, 1961.)

The last experiment showed that bacteria introduced into the normal bladder rapidly decreased in number in 6-9 hours and completely disappeared in 72 hours, demonstrating the combined effect of both bladder defense mechanisms, each increasing the effectiveness of the other. Mechanical emptying levels the normal bacterial growth curve, but the presence of an intravesical antibacterial factor is necessary to reduce the curve to zero.

► [Kass (Arch. Int. Med. 100:709, 1957) has described a "natural inhibitor" which is nonvolatile, alcohol-soluble and ether-insoluble. It is most effective at a urinary pH of 5 and loses its effectiveness as the pH of the urine rises. He, as well as others, have advocated the use of dl-methionine to lower urinary pH and to increase the effectiveness of this inhibitor.—Ed.]

**Neurotoxic and Nephrotoxic Effects of Colistin in Patients with Renal Disease.** Colistin is an antibiotic similar to polymyxin B in chemical structure and antimicrobial spectrum but which produces significantly fewer toxic reactions in man. Emanuel Wolinsky and John D. Hines[9] (Metropolitan Gen'l Hosp., Cleveland) describe potentially serious reactions to colistin in 3 adults with pyelonephritis and impaired kidney function and in a child given 10 times the recommended dosage.

Severe ataxia occurred in all 4 patients soon after colistin was administered. The 3 adults received 3.1-4.8 mg. of the drug per kg. body weight per day. Blood urea nitrogen became further elevated during treatment in 2 of these. Neurologic symptoms subsided promptly when the drug was with-

(9) New England J. Med. 266:759-762, Apr. 12, 1962.