THE MAJORITY of the concern in pediatric urology is centered around infections and anomalies, the former occupying the greater portion of the practicing pediatrician's problem in this field. Therefore, discussion was aimed mainly at pyelonephritis, with queries on other facets of genito-urinary pathology being mentioned.

A review of the literature reveals that pyelonephritis is the commonest cause of death in uremia. While it kills twice as many patients as glomerulonephritis, it occupies only about a third of the literature given to these two problems. The statistics of a number of widely accepted authorities reveals that of all the patients admitted to hospitals, 1% have a urinary tract infection and 5% of all patients treated by pediatric services have a urinary tract infection. Pyelonephritis is more common in the female than in the male in the ratio of 9:1. In the female it is more common in the years from 0-12 and from 25-70 years of age. Very few males have pyelonephritis except those with congenital anomalies, and in the older age group those with gonorrheal obstructions and prostatic enlargement. The manifestations of congenital obstructions to urine flow usually present themselves in the ages from 0-6 years.

CAUSES OF PYELONEPHRITIS

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Natural Causes

THE SHORT URETHRA OF THE FEMALE: In females under 8 or 9 years of age, the urethra is about 1 cm long and some females have such a short urethra that it is essentially only a urethral sphincter. In 10 females less than 10 years of age, all 10 had dye in their bladders, after they sat down and stood up 20 times in 6 inches of dyed water. What is not understood is why more females do not get infection, if this is the answer to more frequent infections in females than in males.

OVERDISTENTION OF THE BLADDER: Marked overdistention of the bladder causes vesicoureteral reflux. This condition is more common in adolescents who do not have enough social experience, i.e. those who would not feel free to excuse themselves from company in order to urinate.

INVOLUNTARY RESIDUAL URINE: In the male patient who has severe paraphimosis and dysuria, an increase in residual urine is often found. Also following circumcision, the skin of the glans penis often exfoliates, leading to urethral meatal ulceration causing dysuria which is followed by a residual urine.

VOLUNTARY RESIDUAL URINE: In females, excessive masturbation causes reddening and ulceration of the labia and dysuria, which in turn causes retention of urine in the bladder. In contradistinction, in females with congenital anomalies and urinary infections vulval irritation is rarely seen. This may be a clue in distinguishing between the etiologic factors.

CONGENITAL OBSTRUCTIONS: (In the order of frequency in the author's practice.)

1. Atonic cord bladder.
2. Ureteropelvic and ureterovesical stricture.
3. Foreign body in the urethra or bladder.
4. Urethral valves.
5. Ureteral compression due to tumor, mostly due to metastatic nodes in the periureteral area.

Iatrogenic Causes

An indwelling catheter for 24 hours will lead to an infection. Following vaginal hysterectomy, it was found that in patients who had catheters inserted for 3 days, infection invariably followed. Treatment was needed for 3 months regularly, and often it was 18 months before sterile cultures were obtained. Without the indwelling catheter, and by forcing the patient to void, which was painful, infections usually did not follow vaginal hysterectomy.

This brought up the question of how dangerous was instrumentation into the bladder. By 1893, the Germans had shown in executed convicts that, if urethral samples at various levels were cultured, in females the cultures were positive to the urethral sphincter, and in males to the voluntary sphincter. Therefore it seems impossible not to carry organisms into the bladder by transurethral instrumentation. It has also been shown that if bladders are aspirated by means of sterile puncture through the skin of the abdominal wall, that normal patients will have a sterile urine. Following bladder catheterization, about 70 to 80% of these patients have a positive culture from urine aspirated from the bladder through the sterile skin.

This raised the question of the dangers of infection following cystoscopy and retrograde pyelography. The danger of infection from intravenous pyelography is nil. On many occasions, because of minimal hematuria and minor flaws in the intravenous urogram, cystoscopy is regularly done. When intravenous pyelography was repeated within 30 hours of cystoscopy, 4 out of 13 girls had hydrourerteres. (In 22% of a series of adults who underwent ureteral catheterization, renal function was affected also.) The hydrourerter and hydronephrosis following retrograde pyelography is completely reversible. It seems that the trauma of ureteral catheterization produces edema of the mucosa leading to obstruction and predisposing to infection. Besides contamination of the bladder by the cystoscope, the hydrourerteres are susceptible to invasion by bacteria periodically carried in the bloodstream. Others have found that 30 minutes after patients with carious teeth had chewed beefsteak, the organisms cultured from the dental cavities could be found in the arterial blood. This is a transient asymptomatic phenomenon, but may be an etiologic factor since bacteria go through the glomerular filters. Interestingly enough, this phenomenon has not been tested with chewing gum.

PATHOLOGY

Focal collections of inflammatory cells destroy tubules and surround glomeruli and blood vessels, eventually leading to periglomerular and perivascular fibrosis. Different parts of the same kidney are not damaged equally, and rarely are two infected kidneys in the same patient damaged equally. In chronic renal infection the inflammatory cells infiltrate between, and destroy muscle bundles of the infundibulum, renal pelvis and ureter. The resultant muscular inefficiency leads to faulty peristalsis, dilatation and urinary stasis.

SYMPTOMS

Symptoms were absent in 60% of the author’s patients. Dysuria, urgency and terminal hematuria occurred in about 30-40% of the patients; chills and fever, in about 20-30%. Backache, abdominal and flank pain occurred in less than 5% of the patients.

DIAGNOSTIC CRITERIA FOR PYELONEPHRITIS

1. Pyuria is defined as more than 20 leukocytes in a field of high power magnification of a centrifuged specimen (many patients with this number of leukocytes only have cystitis). In an uncentrifuged specimen, 5-8 leukocytes with clumps indicate an infection is usually present.

2. If pyuria is associated with chills, fever, nausea and vomiting, the diagnosis of pyel-
onelitis is usually certain. In the author's clinic, a child with these two criteria has also been found to have an abnormal intravenous urogram.

3. The presence of calyceal changes (distortion) and two positive urine cultures showing the same organism, were originally used to make the diagnosis, but are not considered necessary now. The chills and fever are probably caused by septicemia secondary to a blocked ureter or collecting tubule.

**URINE CULTURES**

How can a satisfactory urine culture be obtained? In males and females, the initial portion of the urine will contain saprophytic urethral bacteria. In the male, if the prepuce is retracted and the glans penis cleansed, and in the female, if the labia are spread and the urethral meatus cleansed, satisfactory cultures from mid-stream urine can be obtained if the *flow* of urine is *constant*. In hydrodynamics it is well known that when a liquid flows through a pipe at a constant velocity, only the central core moves, and the layer of fluid next to the wall of the pipe does not move. Likewise, when the flow of urine from the urethral meatus is variable, turbulence occurs within the urethra and again saprophytic urethral bacteria appear in the voided urine. To obtain satisfactory urine specimens from the female, it is necessary to have her squat, spread the labia well, and urinate without contamination from the adjacent structures. Frequently this causes psychic problems and most of the girls are catheterized. When the catheter is inserted, the eye of the catheter scrapes saprophytic urethral bacteria into the lumen and contaminates it. Accordingly, when a catheter is used to obtain a urine culture, it is also necessary to catch the urine sample from a urine stream flowing at a constant rate.

**TREATMENT**

Because of the fact that a culture of the urine and roentgenographic visualization of the urinary tract cannot be performed in the pediatrician's office, a plan of therapy, which was successfully tried in 60 patients with pyuria, is given. It is designed to treat patients efficiently in the face of the increasing costs of medical care and will enable the pediatrician to group his patients into four categories.

Patients with pyuria are treated first with a soluble sulfonamide, using a dosage of 100 mg/lb/day. This is divided into three equal doses, each separated by an 8 hour interval. The patient is treated for 4 weeks in this fashion. At the end of the 4 weeks, urinalysis and culture of the urine are obtained. The patients are then divided into four groups:

1. Those who have no pyuria and a negative culture. Approximately 80% of the patients fall into this group. The rapid cure indicates that these patients had a cystitis or a minimal pyelonephritis. To avoid recurrence, the same individual dose of sulfonamide is given at 12-hour intervals, i.e. two-thirds of the original dose, for 3 months. The urine culture is then repeated, and, if negative, a cure has been performed. The additional 3 months of treatment reduces the recurrence rate to 1-2%.

2. Those who have pyuria and a positive culture. About 99% of this group will have surgical problems, and the patient should be referred to a urologist. It is suggested that intravenous pyelography not be performed before consultation is made, because the great majority of such urograms are not satisfactory to the consultant.

3. Those who have pyuria and a negative culture. With the exception of those patients with glomerulonephritis, these patients have unusual renal diseases, e.g., toxic nephritis, renal tuberculosis, disseminated lupus erythematos, leukemia, etc.

4. Those who have no pyuria, but a positive culture. At this time, therapy with sulfonamide is continued until another culture can be obtained. If these two cultures show identical organism the patient has chronic pyelonephritis. Then the sulfonamide is stopped and the type of antibiotic therapy is adjusted on the basis of adequate bac-
terial-sensitivity studies. Penicillin excepted, we usually give 20 mg/lb/day, in three divided doses at 8-hour intervals. This therapy is continued for 2 weeks. At this time, the urine is again cultured. The patient will then fall in one of two categories:

A. The urine will be sterile in about 80% of the patients treated. To avoid recurrence, the antibiotic therapy is stopped and sulfonamide treatment, 100 mg/lb/day in three divided doses at 8-hour intervals, is begun and continued for 6 months. At this point the sulfonamide is given at 12-hour intervals for 6 months. Then the sulfonamide dosage is reduced one-half, but the drug is still given at 12-hour intervals for the succeeding 6 months. A culture is usually obtained about 1 month after the drug dosage is reduced. After 1½ years, the therapy is stopped if the intervening urine cultures are sterile. Two follow-up urine cultures are obtained 3 and 6 months after termination of treatment, before discharging the patient.

B. The urine culture will be positive. Therapy is then continued for 2 more weeks and the urine again cultured. If negative, the sulfonamide therapy is continued as above already described in 4A for 18 months. If the urine is still positive for organisms, further investigation of the urinary tract is indicated.

The reason for protracted antibacterial therapy is based on unpublished work of others. When serial renal biopsies were obtained from patients with pyelonephritis and hypertension, it took almost 18 months of continued treatment before most of the inflammatory cells disappeared from the tissue sections. Unfortunately no cultures of the tissue were done with these specimens. Perhaps dormant bacteria live in the center of the areas of focal inflammation, where they may be visualized by Gram staining. Since these central areas of inflammation have a poor blood supply, the antibacterial drugs can only reach the peripheral segment. As these areas of focal peripheral segment diminish, the dormant bacteria are destroyed.

**QUERIES AND DISCUSSION**

A question was asked regarding specific drugs for specific infections. Our first approach to therapy is to use a soluble sulfonamide. Nitrofurazone will usually take care of proteus and aerogenes infections, but it frequently causes vomiting in children. Sulfamethoxypridazine is a useful drug, but we found that 60-70% of patients developed a recurrence of the urinary infection within 3 to 4 weeks in spite of continued administration of this drug. Also in 14% of patients receiving these poorly-excreted sulfonamides, a scarlatiniform rash developed and lasted for 4 to 10 days in spite of cessation of treatment. The long-acting type of sulfonamide is especially useful in resistant proteus infections. However, we usually try first a combination of chloramphenicol and a sulfonamide; this cures 60% of patients with a proteus infection. With pseudomonas infections we first make sure that no foreign body is present in the urinary system, and then only use sulfonamide therapy.

How should patients be managed who have symptoms of pyelonephritis and do not respond in 3 to 4 days to the prescribed therapy? Place the patient in a hospital and undertake roentgenographic visualization of the urinary tract, and give appropriate antibiotic therapy.

How should trigonitis and urethritis be treated? It should be treated as a cystitis. If there is residual urine with cystitis, the residual urine will disappear with long-term therapy when bladder function improves. In emotionally-insecure male adolescents with urethritis, a urogram will usually show bilobar prostatic enlargement. Then you know that the patient is masturbating, that a prostatic infection is present, and that while the infection may be controlled it is rarely cured.

Should all males be circumcised? The
incidence of carcinoma of the penis is about 1% of all genito-urinary tract tumors. There are only sporadic reports of cases of its occurrence, if circumcision has been done before 6 months of age. There seems to be no prophylaxis when circumcision is performed after 6 years of age.

What is the treatment of bilaterally undescended testes? The answer depends on accepting the fact that a male is sterile if he does not have 240 million motile sperm in a minimum of 4 ml of ejaculum. In one study, none of the patients who had bilateral undescended testes brought down after 1 year of life, met this criterion. If there are slightly less than 240 million motile sperm present, the chances of a pregnancy are one in a lifetime. If the operation is done under 1 year of life, most of these patients will produce more than 240 million motile sperm per ejaculum. In regards to malignant tumors of the undescended testis, it seems that the incidence of seminoma may be higher in the cases of undescended testis. However, x-ray irradiation alone will cure 60-80% of the patients with seminoma of the testis.

When is meatotomy necessary? If the urethra will admit a No. 3 or 4 French catheter, the urethra can be dilated. But if the urethra accepts only a smaller size catheter, then meatotomy is indicated.

If there is a complaint that a female voids frequently, what should be done? The bladder capacity of the normal female is three times that of the male. Urinary frequency may be due to psychologic problems, cystitis or residual urine.

In the treatment of pyelonephritis, are shower baths only recommended? Yes; tub baths will increase the rate of recurrent infections to 20-30%.

CIRCULATORY CHANGES IN ACUTE GLомерULONEPHRITIS, Valentino DeFazio et al. (Circulation, 20: 190, August, 1959.)

Conflicting opinions have been expressed as to the mechanism of pulmonary and peripheral congestion frequently observed in the oliguric stage of acute glomerulonephritis. The factors that have received major consideration as responsible for the circulatory complications are hypertension, myocardial damage, and hypervolemia.

Hemodynamic studies utilizing the technic of cardiac catheterization were carried out in 7 hypertensive and edematous patients in the early phase of acute glomerulonephritis to secure information regarding circulatory changes in this disease. The observations were made in the resting state and indicated a high cardiac output and stroke volume, an elevated left ventricular filling pressure and a normal total peripheral arteriolar resistance.

It is suggested that water retention and consequent hypervolemia per se could explain the elevation of the cardiac output. In the presence of hypertension, it is also postulated that the elevated left ventricular filling pressure (pulmonary "capillary" pressure) may be secondary to the increased work load. The authors themselves, however, point out that in the absence of hemodynamic studies during exercise it is not possible to exclude myocardial failure as a contributing factor in circulatory congestion and that further studies in this direction are needed.

S.G.
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