URINARY TRACT DISEASES

Infections of the Urinary Tract I—Diagnosis

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Symptoms suggesting infection of the urinary tract are common. In domiciliary practice they are encountered in 12 to 20 of every 1,000 consultations. During the past fifteen years quantitative bacteriology has shown the important role of bacteria in causing these symptoms. At a time when considerable medical resources are being invested in treating terminal renal failure, interest in a preventable cause of progressive renal disease is appropriate.

The article this week considers some of the present problems of the diagnosis of infections of the urinary tract; the inadequacies of a purely symptomatic approach; the significance of recent developments in bacteriological techniques; and the enigma of pyelonephritis. A second article, appearing next week, will be devoted to the management of patients with infections of the urinary tract.

Symptomatic Infections

When a patient complains of frequency, painful micturition, and foul-smelling urine a diagnosis of "cystitis" is usually made. Nevertheless, recent studies in domiciliary practice in England, New Zealand, and Denmark indicate that these symptoms must be interpreted with more reserve, for only about half of those patients who complained of symptoms suggesting urinary tract infection were found to have infected urine. Patients who have the syndrome of dysuria, frequency, and urgency in the absence of an infected urine are said to have the "urethral syndrome." This syndrome may have a variety of causes. It is sometimes associated with chronic infection of the prostate in men and of the paraurethral glands in women. A history of precipitating factors such as cold weather, sexual activity, contraceptive devices, and sensitivity to deodorants and bubble baths is occasionally obtained. It is not always easy to relieve these symptoms.

When lower urinary tract symptoms are combined with fever, and tenderness in the loin is found on examination, it is usual to assume that the renal parenchyma has become infected, and acute pyelonephritis is then diagnosed. This concept is supported by finding a positive blood culture in some cases and raised antibody titres against the O antigen of Escherichia coli in many patients infected with this organism. Nevertheless, it is not only in those patients who develop loin pain and rigors that evidence of renal infection may be found.

Infections of the upper urinary tract may be present without causing any symptoms. This possibility was first disclosed by the surprisingly high incidence of chronic pyelonephritis found at necropsy, which had been undiagnosed during life. Though the histological criteria of some of the earlier necropsy studies are now questioned, these studies did serve to highlight the problem. Subsequent population surveys have shown that significant bacteriuria occurs frequently in the absence of symptoms, while further inves-

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† The stringent requirements for rapid transmission of samples have limited the application of quantitative bacteriology in domiciliary practice, where most of these infections occur and are treated. The introduction of the dip-inoculum technique, however, meets the needs of the busy general practitioner. The inoculum is presented on a plastic spoon or plate or glass slide (see Figure); it is dipped into the sample of "clean" freshly passed midstream urine, and then replaced in its sterile container and posted to the laboratory. A colony count can be made after overnight incubation in the laboratory. When significant bacteriuria is found subculture is often necessary to complete identification and always when sensitivity tests are required. This technique is simple and rapid, both for the clinician and the laboratory, and is in routine use in several clinics at St. Thomas's.

Pyuria reflects inflammation in the urinary tract. Urine should not be centrifuged to count the white cells, for this gives an unreliable estimation of the white cell excretion rate,
bacteriuria in non-pregnant women has not been so intensively studied, it is probably similar to that found at the antenatal clinic. The incidence of symptomatic infections among these patients is also similar, but the infections are much less severe. The value of treating asymptomatic bacteriuria in non-pregnant women has been questioned. Reinfections with different organisms appear to be more likely to be associated with symptomatic infections than is the original untreated bacteriuria. Sponaneous remission of the bacteriuria occurs in patients in whom there are no radiological abnormalities.

Asymptomatic bacteriuria is found in 1 to 2% of schoolgirls. Further questioning of the parents of these children may show that the significance of symptoms of enuresis, frequency or urgency of micturition, or of obscure fevers had not been appreciated. The intravenous pyelogram shows pyelonephritic scarring in at least one in ten, and hence radiological pyelonephritis is likely to be present in one out of every 500 schoolgirls, which makes it the most common renal disease of children. Nevertheless, long-term antimicrobial prophylaxis in children with known vesico-ureteric reflex may permit normal renal growth and prevent the development of renal scars.

The risks associated with finding bacteriuria in various situations will be better defined when the results of long-term prospective studies are available. Bacteriuria cannot be equated with infection of the host. Pathogenic organisms may be carried in the throats and colons of certain people without causing disease; possibly an analogous situation exists among persons with bacteriuria, but, unlike the throat and colon, urine does not have a normal flora.

Localization of Infections
Quantitative bacteriology allows the precise diagnosis of significant bacteriuria but does not indicate whether the infection is confined to the lower urinary tract or involves the kidneys. There is a great need for a simple and reliable test which will permit this differentiation to be made, for proof of renal involvement has a profound influence on the management of individual patients. At present various interesting approaches are being used to investigate this problem.

Direct proof of upper urinary tract infection can be obtained by the following:

Bacteriological Culture

Urinary Culture.—Urinary catheterization is the only method which also permits the side the infection involves to be determined. This technique carries a risk of surgical trauma to the ureters, but more than 200 such investigations have been performed at St. Thomas's in recent years with no complications other than transient haematuria. In 35% of these investigations the infection was confined to the bladder and in 65%, the upper tract was involved. In one-third of the latter group infected urine was obtained from both ureters; in one-third from the right ureter; and in one-third from the left ureter. In two-thirds of the patients who had symptoms these were a correct pointer to the site of the infection.

K. H. Fairley and his colleagues have described a technique for obtaining ureteric urine which is less troublesome for the patient, and has the advantage that it can be used during pregnancy. By means of a Foley catheter the bladder is sterilized with a solution of neomycin and a fibrinolytic enzyme. Following a washout with sterile water the urine entering the bladder is collected at three ten-minute intervals. A rapidly rising bacterial count in these samples indicates infection of the upper tract.

Renal Biopsy.—Because of the patchy nature of pyelonephritis interpretation of the results of culture of renal biopsy material is difficult.
Indirect Evidence

Evidence of renal involvement may be sought by the following indirect approaches:

Microscopy of the Urine.—Rarely this may reveal granular or leucocyte casts, which are said to be dependable evidence of renal involvement. An increase in white cell excretion rate may be provoked by the intravenous injection of 40 mg. prednisone in patients with pyelonephritis. Unfortunately, a similar increase may also occur in patients with inflammation of other tissues, such as prostatitis. "Glitter" cells have been thought to indicate pyelonephritis, but they may be found in any case with pyuria when the urine is hypotonic. The Brownian motion in the cytoplasm of these pale, swollen leucocytes from which they get their name is related to the osmotic pressure of the urine.

Maximal Urinary Concentrating Ability.—A defect in concentrating ability has been shown in patients with both symptomatic and asymptomatic bacteruria. This may sometimes be improved after effective treatment. This test, like any which demonstrates a defect in renal function, is non-specific so far as the cause of the renal damage is concerned.

Serum Antibody Titre.—A serological approach, using a single antigen preparation from the patient's own organism as antigen, has provided a new method for diagnosing renal involvement. A close relation between infected ureretic urine and a significantly raised serum antibody titre has been shown, though infection of other tissues, such as prostatitis, may also cause a rise in antibody titre.

Pyelonephritis

In the presence of the typical clinical history, physical signs, and laboratory evidence of bacterial infection of the urine the diagnosis of acute pyelonephritis may be made with some confidence. The pathological changes in the kidney at this time probably include any of the appearances which have been described at necropsy in patients dying with acute pyelonephritis. This is a patchy disease, and appearances may range from fairly diffuse involvement of the medulla, with microabscess formation, to localized wedge-shaped lesions.

How often do multiple subclinical attacks of acute pyelonephritis occur? How often do these progress to chronic pyelonephritis, with progressive destruction of renal tissue? How often is bacterial infection the chief initiating or accelerating aetiological factor in producing the scarred, contracted "end stage" kidney? The answers to these questions are conjectural. Most pathologists regard the macroscopic appearances of calyceal distortion with overlying coarse scarring as indicative of pyelonephritis. Nevertheless, it is now widely admitted that histological findings in necropsy or in renal biopsy material are not on their own sufficient to diagnose chronic pyelonephritis if by this is meant, as is usually the case, chronic bacterial infection of the kidney. The microscopic features which have previously been interpreted as representing chronic nonobstructive pyelonephritis include the following:

1. A chronic interstitial inflammatory reaction with lymphocytes and plasma cells; tubular atrophy and dilatation with "colloid casts"; and relatively well-preserved glomeruli which often show periglomerular fibrosis and the effects of ischaemia. It has been said that the disease is "active" when polymorphonuclear leucocytes are found in the interstitium or in tubular lumina; otherwise the terms "inactive" or "healed" have usually been applied.

2. It is now clear, however, that renal disease associated with the histological appearance of "active" nonobstructive pyelonephritis according to the strictest criteria, may occur and progress in the absence of any evidence of infection of the urinary tract. Since direct evidence of bacterial infection

The Diagnostic Problem

Significant bacteriuria has precise meaning. When it is found together with symptoms suggesting infection of the urinary tract it is possible to talk in terms of diseases—cystitis and pyelonephritis. Nevertheless, important infections in the urinary tract may be asymptomatic and they can only be poorly localized from their symptomatology. Interstitial nephritis describes pathological changes in the kidney which may be wholly or partly the result of bacterial infection, but that may also be the result of noninfective injury. Proof of renal involvement in infections of the urinary tract rests at present with techniques which are not generally available. Such proof can never be construed as indicating that bacterial infection is either the primary or the only mechanism damaging an individual patient's kidneys. But it does offer a rationale for treatment and for the prevention of progressive renal damage.

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