THE TWO major problems in bacterial infections facing us today are the control of staphylococcal infections, and the control of cases of bacillary sepsis. Infections due to staphylococci that are resistant to almost all existing chemotherapeutic and antibiotic agents are prevalent in hospital patients and are especially common in wound infections. Bacillary sepsis, on the other hand, makes its greatest impact in urinary tract infections and they, too, are common in hospital patients. Keefer has stated, "pyelonephritis, whether acute or chronic, active or healed or healing, is the number one problem in infectious disease due to bacteria today, and demands continuing attention and intensive study... it is a problem calling for a high priority of investigation."

The morbidity from urinary tract infections generally is not well appreciated. Few data are available that accurately reflect the prevalence of bacteriuria and true pyuria. However, such infections perhaps rank second only to respiratory infections in frequency among patients; they probably outrank all other bacterial disease in children under 2 years of age. It is well, then, to concentrate attention on urinary tract infection in infancy and childhood, for it is not only one of the most important and most frequent bacterial infections occurring in this age group, but it is in this age period that chronic disease begins, and demands continuing attention and intensive study. That urinary tract infection is frequently associated with congenital abnormalities of the urinary tract is well known. The infection may be acute or chronic, unilateral or bilateral. Patients with urinary tract infection during this age period may recover with no impairment of renal function, or they may die during the acute phase of their illness. They may recover and have latent pyelonephritis with impairment of function and a decreased renal reserve, or they may have an intermittent or recurrent or progressive infection with a healing or healed pyelonephritis and renal insufficiency that frequently leads to uremia, hypertension, renal dwarfism, or all three.

The lack of clear understanding of the pathogenesis, diagnosis and treatment of infections of the urinary tract is well recognized. It is equally well known that the classic syndrome of fever, flank pain, dysuria, frequency and pyuria may be absent in pyelonephritis, and that such disease may occur as a smoldering chronic infection in which diagnosis is often overlooked until too late. Thus, if the serious consequences of pyelonephritis are to be averted, early and more precise recognition of the presence of such infections is necessary. It is important, therefore, that criteria be established that may prove helpful to the clinician in making an early diagnosis of infection of the urinary tract.

The development of many new antimicrobial agents has emphasized the importance of studying the bacterial flora found in urinary tract infections with great care, because the selection of therapy will depend in part on the species of organisms present in the urine. The two commonest organisms isolated from single-type infections are Escherichia coli and Staphylococcus aureus. The other common Gram-negative organisms that cause urinary tract
infection in declining frequency are Aerobacter aerogenes, Pseudomonas aeruginosa and Proteus vulgaris. Aside from staphylococci, enterococci are the commonest Gram-positive organisms found in urine.\textsuperscript{10-12} General experience with adult patients indicates that 75 to 80\% of urinary tract infections are bacillary in origin, and 20 to 25\% are coccal in origin. Our own experience with children indicates that only 6 to 8\% of infections are coccal in origin, the remainder bacillary. In the experience of several clinics, including our own, roughly three-fourths of acute bacillary infections were caused by a single organism in the acute phase of the disease. Once a patient, however, has been treated with an antimicrobial agent or has required an indwelling catheter or an operation on the urinary tract, the infection is likely to become mixed. A mixed infection may also be present in a complicated urinary tract lesion, i.e., with some anatomic or functional anomaly.\textsuperscript{10, 12}

The evaluation of organisms in cultures of urine has received scant attention. The significance of any given bacterial strain has been usually determined by the demonstration of its constancy in the urine in the absence of specific therapy. This method has the obvious disadvantage of requiring multiple cultures before therapy, each taken with meticulous care; even then, the significance of the findings may remain in doubt. It should be emphasized that the mere presence (or absence) of any given microorganism is not an adequate basis for ruling it in or out as a cause of clinical urologic disease. It is absolutely necessary that a distinction be made between true bacteriuria, i.e., the presence of bacteria in the urine of the urinary tract, and contamination of the urine during the procedure of collection. The bacterial count of the urine has offered a means of resolving the problem.\textsuperscript{13}

**GENERAL CONSIDERATIONS**

Prior to a discussion of the validity of bacterial counts in urine in relation to the diagnosis of urinary tract infection, it may be useful to advance the following generalizations based on our own experience and that of others:

**Urine as a Culture Medium**

Urine is usually an excellent culture medium for the common pathogens of the urinary tract. Pasteur was the first to direct attention to this important fact. Thus, if small numbers of these bacteria were to be discharged into the urine from a urinary tract lesion, they would multiply rapidly to reach a concentration of many thousands of bacteria per milliliter of urine.\textsuperscript{14} Further, it has been noted by us and others\textsuperscript{14} that storage of urine at room temperatures for 2 hours or longer leads to a distinct increase in the number of bacteria; on the other hand, storage of a specimen of urine at usual refrigerator temperatures (4-5°C) up to 1 week will not alter significantly the number of organisms present. These considerations must be kept in mind at all times in the examination of urine specimens.

**Definition of Pyuria**

Pyuria is said to be the hallmark of pyelonephritis but it alone is not satisfactory for making a diagnosis of urinary tract infection. In the first place, there is no general agreement as to what constitutes pyuria. Wilson and Schloss\textsuperscript{15} used the term to designate “the presence of sufficient pus to cause definite cloudiness of the urine.” They further restricted the term to cases in which the pus cells were not only very numerous on microscopic examination, but were present in definite clumps. Campbell\textsuperscript{16} considers three to five cells per low-power microscopic field in an uncentrifuged catheter specimen to be within normal limits; Helmholtz (cited by Campbell\textsuperscript{16}) has stated that two to eight cells per low-power field are normal. It is of no moment if the leukocytes are single or clumped, especially in girls where vaginal mucus may be the cause of clumping. Stevenson\textsuperscript{17} considers more than
two to four leukocytes per low-power field, from an uncentrifuged specimen, as abnormal.

Others have defined pyuria as the presence of five or more leukocytes per high-power microscopic field in a centrifuged specimen of urine. Kass has shown that pyuria defined in this way occurs in one-third to one-half of patients with a true bacteriuria (i.e., with more than 100,000 organisms/ml of urine), but in only 2% of those with less than 100,000 organisms/ml of urine. Even if the criteria of pyuria were lowered to three leukocytes per high-power field, the incidence in those with true bacteriuria rose by but 10%. In the patients in whom the house staff of the Harvard Medical Service at the Boston City Hospital had diagnosed pyelonephritis on clinical grounds, pyuria was found in only about one-half; 95% of the same patients had bacterial counts greater than 100,000 organisms/ml of urine.

Jackson and associates found that 22% of 41 adult patients with pyelonephritis (as determined by histopathologic findings in kidneys removed at surgery) had no pus cells in their urine. Of the patients without pyelonephritis, 20% showed 2 to 10 leukocytes per high-power microscopic field and 33% showed more than 10. The importance of extra-renal infections in causing, or being associated with, pyuria is pointed up by the report of Beeler and Helmholtz who found pyuria present in 9 out of 18 infants (less than 2 years of age), and in 7 out of 18 children (over 2 years of age) with extra-renal infections.

It is of further interest that in the early work on "pyelitis," findings indicated that the disease affected almost exclusively female babies. As Chown has indicated, it seems that little or no attempt was made to be sure that the urine, upon which the diagnosis was based, was uncontaminated. The error is continued up to the present time. There are three main sources of error here: a) That pyuria may be due to catarrhal vaginitis, itself secondary to some acute febrile condition such as pneumonia, tonsillitis, appendicitis, or one of the exanthemata; or b) to a specific vaginitis, which is frequently associated with urethritis; or c) to contamination from the stool in acute enteritides. Chown, in addition, reported four children with marked pyuria, but with no source for the pyuria detectable at careful post-mortem examination; deaths were due to extra-renal infection in all cases. While sterile pyuria may be uncommon, it may occur in 1) the extreme dehydration of pyloric obstruction, low fluid intake, or acute toxemia; 2) in trauma caused by instruments or calculi; 3) when infection has disappeared but an irritating agent remains; 4) in chemical inflammation; and 5) in acute glomerulonephritis. We have encountered a fair degree of pyuria in several patients with the last-mentioned disorder. Unless all these sources are ruled out, no case can be considered one of true pyuria. It is clearly evident, then, that pyuria may be of diagnostic value only when it is clearly present; its absence from any single specimen cannot be taken as evidence of the absence of bacteriuria. It is equally clear that pyuria may frequently be found in the presence of extra-renal infections, and in the absence of urinary tract infection.

**Technique of Gram Staining**

It has been known for many years that bacteria can usually be found in stained specimens of urine if infection is present. This has been subjected to quantitative evaluation with one group finding that Gram-stained smears of uncentrifuged urines were positive in 80% of adults with counts of 100,000 microorganisms or more per milliliter of urine, and in 20% of specimens with counts between 100 and 100,000. Sanford and his associates, studying methylene blue stains of urinary sediments in adults, found organisms in 6 of 34 patients (17%) with urinary bacterial counts between 1 and 1,000/ml, in 5 of 18 (27%) with counts between 1,000 and 10,000/ml, and in all
of 91 patients with counts greater than 100,000 organisms/ml of urine. Gram stains of uncentrifuged specimens of urine in a large group of children showed organisms in 95% when the bacterial count was 100,000/ml or more. No organisms were found when the colony count was less than 1,000/ml, except in one specimen (a random voided one) in which Gram-positive cocci were seen in association with epithelial cells. The use of the Gram stain as a clinical guide to the presence of infection (as distinguished from contamination) appears amply justified by these observations. The intrinsic error in the procedure varies from 5 to 27%.

BACTERIAL COUNTS

Early Studies

Helmholz and Milleken in 1922 were among the first to point out the fact that chances for contamination during the collection of specimens were so great that the presence of organisms in the urine did not prove, without further control, that they came from the urinary tract. Some two decades later, Marple, studying adult women, again called attention to the necessity of performing quantitative bacterial counts in urine specimens. In 1940, Rantz and Keefer, in a quantitative study of microorganisms in the urine of patients with pyelonephritis, found that $10^5$-6 (100,000-1 million) or more organisms per milliliter of freshly voided and promptly cultured urine were always present during acute infections.

Criteria for Contamination versus Infection

In the only published account in the English literature of a study relating to children, Masters reported semi-quantitative findings in five children from whom catheter and non-catheter specimens were obtained on the same day, and six others for whom the interval between the two types of specimens was 1 or 2 days. The bacterial contamination varied from 0 to more than 100 colonies/3-mm micromelope (3 to 5 mm) of well-shaken urine, i.e., from 0 to approximately 100,000 organisms/ml of urine. Interestingly, he found less contamination in the non-catheter specimens than in those obtained by catheter. Linneweh, in an evaluation of catheter specimens in children, found the zone between contamination and infection to be approximately 1,000 organisms/ml of urine. Others reported findings in 21 adult women from whom both clean-voided and catheterized specimens were taken. Five of this group had more than 10,000 organisms/ml of urine in clean-voided culture, and in each case the catheterized specimen confirmed this. The other 16 patients had 900 or fewer organisms/ml of urine in both clean-voided and catheterized specimens. Jackson et al. compared 50 pairs of voided and catheter specimens of urine from a group of adult women with hypertension attending an outpatient department, and found that the voided specimen was comparable to the catheter specimen in 96% of cases in which the growth from the catheter sample was greater than 100,000 colonies/ml of urine. Among 11 catheter specimens that yielded a positive culture but less than 100,000 colonies/ml of urine, the voided specimen produced the same result in 10 of the 11, or 95% of the observations.

Kass studied a group of unselected women in a medical outpatient department who presumably were free of clinical infection of the urinary tract. All specimens of urine were obtained by catheterization. He found that bacterial counts fell into two separate but overlapping population groups: one group with bacterial counts between 0 and 10,000, and a second group with more than 100,000 organisms/ml of urine; this latter group was presumed to represent patients with infection of the urinary tract. The two population groups overlapped at 10,000 organisms/ml. On the basis of these data, Kass arbitrarily designated a count of $10^5$ (100,000) or more organisms/ml of urine as the dividing line between true bacteriuria and contamination. He found that 5% of patients with known
infection of the urinary tract had colony counts less than 100,000/ml of urine. In over half (55%) of the group of patients with more than 100,000 organisms/ml of urine, there was a history of past urinary tract infections, instrumentation, or inlying catheterization. These patients were repeatedly found to have bacterial counts greater than 100,000/ml of urine, and the organisms found were almost always the common pathogens of the urinary tract. These patients were therefore considered to have true bacteriuria and infection. If the patients have fever, flank pain, dysuria, and pyuria, then more than 100,000 organisms/ml of urine and a Gram stain positive for bacteria are almost always found. In fact, the failure to find large numbers of bacteria in the presence of the classic syndrome of urinary tract infection should raise the question of ureteral obstruction.

Validity of Clean Voided Specimens

It has been long-standing medical, pediatric, and urologic teaching that in girls catheterized urine specimens alone can be relied upon for the diagnosis of urinary tract infection. We recently completed an investigation designed to determine the validity of a clean-voided specimen in a group of 170 young girls (all but 17 were free of clinical urinary tract infection), ranging in age from 3 to 12 years. From 58 of the girls, paired (catheter and clean voided) specimens of urine were obtained; the time interval between these two collections of urine specimens was less than 1 hour. There was a 96.5% positive correlation between catheter and clean voided specimens.

Of the group of 17 children with clinical evidence of infection of the urinary tract, three had colony counts less than 100,000, but more than 1,000/ml of urine in a clean voided specimen; the remaining 14 children had colony counts greater than 100,000 organisms/ml of urine. Thus, 17% of this small group of patients with clinical infection of the urinary tract had colony counts less than 100,000/ml of urine in the initial specimen of urine. However, all of these patients showed colony counts greater than 100,000/ml of urine in subsequent specimens. Conversely, only 2 of 100 clean voided specimens from patients without clinical urinary tract infection showed colony counts of more than 1,000/ml. Subsequent specimens from these two patients, however, had lower counts.

Thus, it can be seen that colony counts provide a valid means of differentiating infection from contamination in a given specimen of urine. The data in children suggest that urines containing less than 1,000 colonies/ml are indicative of contamination; urines containing between 1,000 and 100,000 colonies/ml are to be suspected of infection and studies repeated, and urines containing more than 100,000 colonies/ml are indicative of infection.

Catheterization has not eliminated the possibility of contamination during collection. In addition, the procedure is unpleasant for the child, may be difficult to perform in young children, and is inconvenient in outpatient clinics and in general practice. The demonstrated validity of properly collected clean voided specimens in relation to the diagnosis of urinary tract infection is important in view of the considerable concern expressed recently regarding the possibility of initiation of urinary tract infection during catheterization, especially repeated catheterization. Marple reported that 4 out of 100 women developed a urinary tract infection following a single catheterization. Kass has reported a 2% incidence of urinary tract infection following a single catheterization in a group of 200 adults seen in medical outpatient clinics. Guze and Beeson studied a group of 12 women free from urinary tract infection, from each of whom they obtained a specimen of urine by direct needle aspiration of the bladder at laparotomy, and by urethral catheterization. All 12 aspiration specimens were sterile, but four of the catheter specimens showed organisms on culture. One of the patients developed signs and symptoms of infection 36 hours after
carried out a similar study; in their results, 27 of 34 collected by catheter were sterile. One of the 34 patients developed an acute prostatitis 1 day following the procedure.

A comparative quantitative bacteriologic study of urine obtained by catheter and by percutaneous suprapubic aspiration was carried out recently in our clinic in a group of 42 children who were presumed free from clinical urinary tract infection, and who were undergoing elective surgery for conditions that did not involve urinary tract manipulation. All but two of the aspiration specimens were sterile, and in these the bacterial count was well below the critical figure of $10^8$ (1,000) colonies/ml of urine; therefore, on the basis of these findings, the suprapubic specimens showed complete correlation with our clinical impression of the patients. The first portion of the catheter samples ($C_1$) were sterile in 25 (59.5%) of the cases; if the 14 additional patients showing counts of non-pathogenic organisms below the critical figure of $10^8$ and assumed to represent contamination, are added to the 25 sterile cases, there is a 92.8% diagnostic correlation between the suprapubic and $C_1$ specimens. There was a 97.5% diagnostic correlation between the second few milliliters of catheter urine ($C_2$) and the suprapubic specimens. Three of the patients in our series had significant bacterial counts in the specimens obtained by catheter, but the $C_2$ specimens showed a significant count in only one of these three patients, pointing up the well-known importance of discarding the initial few milliliters of urine obtained by catheterization. In this one patient the suprapubic specimen was sterile, and a subsequent clean voided specimen did not exhibit significant growth.

In view of the reported danger of introducing infection during the process of obtaining urine specimens by catheter, the course of this group of children subsequent to their catheterization was followed closely. All patients in the study were free from urinary tract infection within a period of 4 to 6 months following catheterization. Thus, while organisms were introduced into the urine of the children during catheterization and in apparently significant quantities, infection was not a complication. It is our belief that while properly collected clean voided specimens may be used in most instances for making the diagnosis of true bacteriuria in children, catheterization, when properly done, should not be withheld in the fear of producing urinary tract infection. While in some quarters it is thought that the best way to correct abuses of a procedure is to do away with the procedure entirely, our experience with Prohibition would show this not to be a solution. In our view, while all physicians should be alert to the importance of catheterization in occasionally initiating infection, catheterization must remain a necessary procedure in the diagnosis and management of urinary tract infections in certain cases, notably the following: 1) where there is urinary retention; 2) where repeated study of clean voided specimens yields borderline or doubtful results; 3) where the patient is so acutely ill that there is a need for immediate antimicrobial therapy, and no time for multiple specimens to be obtained; and 4) where the patient is unable or unwilling to co-operate.

It is imperative, however, that if a proper specimen for a valid bacterial count is to be obtained, it must be collected by the physician in charge or under his direct supervision; the collection cannot be entrusted to a clinical clerk or student nurse.

**Bacteriuria and Pyelonephritis**

While it appears clear from all studies to date that bacteriuria is associated with urinary tract infection, bacteriuria is not synonymous with pyelonephritis. That bacteriuria is indeed frequently associated with pyelonephritis has been shown by the investigation of MacDonald et al. who studied bacterial counts of the bladder urine obtained by needle aspiration in 100 unselected necropsies and correlated the counts with histopathologic findings. Fifty-

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**URINARY TRACT INFECTION**

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the single catheterization. Monzon et al. carried out a similar study; in their results, 27 of 34 collected by catheter were sterile. One of the 34 patients developed an acute prostatitis 1 day following the procedure.
three per cent of the urines obtained at necropsy by needle aspiration of the bladder contained no bacteria, 7% contained between 10 and 10,000 bacteria/ml of urine, and 40% of the urines contained more than 100,000 organisms/ml. Active pyelonephritis was found in 14 of the 40 patients with 100,000 or more bacteria/ml of urine (who were considered to have true bacteriuria) and occurred in but 3 of 60 patients with no or relatively few bacteria; two of these latter patients had received antibiotics prior to death, and the third patient was admitted in a terminal state from out of town and her history was not available. Three additional patients with counts greater than 100,000 organisms/ml of urine had evidence of acute cystitis without pyelonephritis. It is of great interest that a clinical diagnosis of active infection of the urinary tract was not made in 70% of the cases in which active pyelonephritis was found at necropsy. Reliable clinical means for determining which of the patients with true bacteriuria have renal involvement are not presently available, but, as MacDonald rightfully states, it would appear prudent in the meantime, in view of the association of bacteriuria with pyelonephritis, to regard each case of bacteriuria as being associated with or likely to become associated with active pyelonephritis and managed accordingly.

Sternheimer and Malbin in 1951 renewed interest in certain characteristics of the leukocytes excreted in pyelonephritis. Through the use of the stain recommended by these authors, Poirier and Jackson have found a good correlation between pyelonephritis and the presence of pale-staining leukocytes in the urine. When the urine has a low specific gravity, these cells also show Brownian movement of the cytoplasmic granules. Poirier believes the staining characteristics of the cells are the important feature and granular motion incidental. The supravitai staining technique is especially helpful among patients with low degrees of pyuria and chronic pyelonephritis. Apparently, in patients with cystitis or urethritis the leukocytes do not show such staining characteristics. This deserves further study.

Under certain conditions, the bacterial count in a given sample of urine from a patient with clinical evidence of urinary tract infection may be low; this may happen when 1) the rate of urine flow is rapid and the number of bacteria discharged into the urine is small; 2) the pH of the urine is below 5.0, and the specific gravity is less than 1.003; 3) a bacteriostatic agent is in the urine; and 4) there is complete obstruction of the ureter preventing the entrance of organisms into the urine. Rarely, fastidious organisms that grow poorly in urine may be present in but small numbers during active infection. Should such an organism be isolated from cultures of urine in a patient thought to have active infection on clinical grounds, the organism can be inoculated into a specimen of sterile urine and its growth characteristic studied. Should the microorganism grow poorly in such a urine, one would be justified in incriminating it as a possible pathogen in the patient under observation.

Special consideration must be given to those patients with chronic or recurrent urinary tract infection who frequently, in the presence or absence of symptoms, may show counts well below the range considered to be significant (i.e., less than 1,000 microorganisms/ml of urine). They are less likely to show low counts in the presence of symptoms. Relman reported that 14 out of 23 adult patients with chronic active pyelonephritis, as shown by histopathologic studies (at nephrectomy or necropsy), repeatedly showed bacterial counts in urine samples of less than 1,000 bacteria/ml. Others have reported similar findings. We have frequently encountered children with persisting low bacterial counts in the urine after treatment, and have, perhaps erroneously, considered these to represent contamination, rather than evidence of a continuing infection. Suprapubic aspiration of bladder urine may be one means of resolving this problem of low bacterial counts.
in patients with chronic urinary tract infection, but this and other means remain to be explored.

BIOPSY OF THE KIDNEY

Twenty years ago Iversen and Roholm introduced a safe technique for percutaneous needle biopsy of the liver. Since then, the clinical and histologic spectrum of the most important diseases of the liver have been defined. In 1951, Iversen and Brun published a technique for aspiration biopsy of the kidney and subsequently reported their experience in the use of biopsies to study certain diseases involving the kidney. The value of percutaneous renal biopsies has been shown to be no less than that for the liver, and its potentialities have been investigated by several groups. In discussing the clinical value of renal biopsy, Kark et al. state: "Renal biopsy appears to be a more accurate method than culture of the urine in determining exactly the organism responsible for infection within the kidney." General experience, including our own limited one, has failed to live up to this optimistic appraisal.

Other workers found that bacteriologic cultures of a fragment of renal tissue obtained from needle biopsy, in contrast to the urine obtained nearly simultaneously, were negative in 11 out of 13 cases. In the two biopsy specimens, the organism from the kidney was the same species as that recovered from the urine. Iversen and Brun performed kidney biopsies upon eight patients with infected urine and a clinical diagnosis of pyelonephritis and the biopsy supported the diagnosis in only one of the eight patients. In the six patients in whom we have carried out needle biopsies during an acute urinary tract infection, all cultures were negative, and histopathologic studies supported the diagnosis in only one.

While culture of renal tissue obtained by needle biopsy has not been rewarding, histopathologic examination of such tissue has been somewhat more fruitful. A criticism of the renal biopsy technique by needle has been that tissue obtained is not adequate or reliably representative for interpretation in view of the local nature of pyelonephritis. In the report by Kipnis et al., the correlation between the kidney morphology, as seen in the biopsy, and kidney function was relatively good, although the degree and type of functional impairment of the kidney could not be judged reliably from the microscopic examination of the biopsy specimen. Kipnis cites unpublished data from Pironi and Dallenbach regarding the general reliability of the biopsy in reflecting the diffuse morphology of the kidney when five or more glomeruli are examined. Open biopsy technique, permitting visualization of most of the kidney and selection of sites for biopsy, may be more rewarding than the blind needle technique, but adequate comparative data are lacking.

With only indirect (leukocytes, casts, erythrocytes) and direct (bacteria) evidence of inflammation and infection, one cannot of course, localize the inflammation. Only if there are signs of functional renal damage due to the spread of inflammation to renal interstitial tissue, and to damage and destruction of the surrounding structures, can one be reasonably certain about the diagnosis of pyelonephritis, i.e., of renal involvement. Roentgenographic studies may also be helpful in showing renal involvement, but the absence of roentgenographic findings does not, of course, rule out such involvement. The performance of renal biopsy by needle is not a technically difficult procedure, and with adequate precautions little morbidity will be observed. However, until further experience and the contributions of the procedure are established, we believe that its use should be restricted.

CONCLUSIONS AND SUMMARY

The mere presence (or absence) of any given microorganism is not adequate for ruling it in or out as a cause of clinical urologic infection. A distinction between true bacteriuria and contamination of the urine during the procedure of collection
must always be made in the evaluation of a positive urine culture. The bacterial count in a given urine sample has offered a means of defining this distinction. The limited data in children, supported by more extensive data in adults, suggest that urines containing less than 1,000 colonies/ml are indicative of contamination; urines containing between 1,000 and 10,000 colonies/ml are to be suspected of infection and studies repeated, and urines containing more than 100,000 colonies/ml are indicative of infection. The proper collection and handling of specimens after collection is mandatory, and should not be entrusted to untrained personnel.

Conditions under which low bacterial counts may be encountered in the presence of active infection are discussed. Special consideration must be given to those patients with chronic or recurrent urinary tract infection who frequently, in the presence or absence of symptoms, may show bacterial counts in the urine below the range considered to be significant. Reliable clinical means for resolving this problem remain to be explored. Suprapubic aspiration of bladder urine for culture and bacterial counts may prove helpful in given cases. Pyuria, said to be the hallmark of pyelonephritis, is not of itself satisfactory for making a diagnosis of urinary tract infection. In the first place, there is a lack of general agreement as to what constitutes pyuria; secondly, pyuria may be seen with many extra-renal infections; and finally, pyuria may be absent with infection of the urinary tract. A Gram stain of an uncentrifuged specimen of urine will usually reveal bacteria if infection is present. This has been subjected to quantitative evaluation, with almost all urine specimens with bacterial counts of 100,000 or more/ml showing organisms when stained by Gram's method. Thus, the Gram stain of a smear of urine provides a useful screening technique for detecting patients with urinary tract infection.

While it has been taught, generally, that only the study of catheter specimens in girls is reliable for the diagnosis of urinary tract infection, recent studies refute this. While there is always a risk of introducing infection during the procedure of catheterization, this is minimal if proper precautions are exercised, and such fear should not interdict catheterization under certain circumstances which have been mentioned.

While bacteriuria is not to be considered synonymous with pyelonephritis, several histologic studies (at necropsy, at nephrectomy, and after renal biopsy) show that bacteriuria is frequently associated with involvement of the renal parenchyma. While reliable clinical means of determining which of the patients with true bacteriuria have renal involvement are not presently available, prudence dictates that each case of bacteriuria be regarded as being associated with active renal disease, or very likely to become so. The staining characteristics of leukocytes excreted in pyelonephritis may be helpful in determining the presence of renal involvement; the leukocytes of patients with cystitis or urethritis apparently do not show the staining characteristics of those excreted in pyelonephritis. A wider use of this supravital staining technique is needed to elucidate further its usefulness. In addition, renal function studies and roentgenographic examinations may be helpful.

Bacteriologic culture of renal tissue obtained by needle biopsy has not proved fruitful, in general. Histopathologic study of such tissue has proved more rewarding. The limitations of the renal biopsy technique by needle are in large measure due to the focal nature of pyelonephritis. While the open biopsy technique, permitting direct visualization of the kidney and selection of site(s) for biopsy, may provide more adequate tissue for examination than the blind needle technique, satisfactory comparative data are lacking.

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