

Pyuria in institutionalized elderly subjects

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K RODGERS, LE NICOLLE, M MCINTYRE, GKM HARDING, D HOBAN, D MURRAY. Pyuria in institutionalized elderly subjects. *Can J Infect Dis* 1991;2(4):142-146. Two hundred and forty-three urine specimens from 76 elderly institutionalized residents were obtained for urine culture, quantitative leukocyte count and urinalysis. Significant bacteriuria was present in 153 specimens (63%), including 33 (22%) with more than one organism. Pyuria (greater than or equal to 10 leukocytes/mm³) was present in 214 specimens (88%), including 116 (97%) with single organism bacteriuria, 27 (82%) with multiple organism bacteriuria, and 71 (80%) without significant bacteriuria. The leukocyte esterase test had a positive predictive value of 99% for pyuria but a negative predictive value of only 30%. The quantitative level of pyuria was associated with the level of proteinuria and inversely with pH. A relatively constant level of pyuria tended to persist over months to years in a given individual if bacteriuria persisted. Pyuria is significantly associated with bacteriuria in the institutionalized elderly, but is also common in the nonbacteriuric. The clinical significance of pyuria requires further assessment.

Key Words: Elderly, Pyuria, Urinalysis, Urinary infection

La pyurie et la personne âgée hospitalisée

RESUME: Deux cent quarante-trois échantillons d'urine recueillis chez 76 personnes âgées hospitalisées ont fait l'objet d'urocultures, de numérations leucocytaires et d'examen des urines. Une bactériurie significative était présente dans 153 (63 %) échantillons, dont 33 (22 %) à plus d'un organisme. Une pyurie égale ou supérieure à 10 leucocytes par millimètre cube était présente dans 214 (88 %) échantillons, dont 116 (97 %) présentaient des bactériuries à un seul germe, 27 (82 %) des bactériuries à germes multiples, et 71 (80 %) étaient sans bactériurie significative. Le dosage des estérases leucocytaires avait une valeur prédictive positive de 99 % pour la pyurie mais une valeur prédictive négative de seulement 30 %. La concentration quantitative de pyurie était associée au niveau de protéinurie et inversement au pH. Un niveau relativement constant de pyurie avait tendance à persister sur plusieurs mois et jusqu'à plusieurs années chez un sujet donné si la bactériurie se prolongeait. La pyurie présente une association significative avec la bactériurie chez les personnes âgées hospitalisées, mais elle est aussi courante chez les non-bactériuriques. L'importance clinique de la pyurie requiert qu'on poursuive l'évaluation.

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Received for publication August 22, 1990. Accepted October 16, 1990.

AS MANY AS 30 TO 50% OF ELDERLY INSTITUTIONALIZED individuals have persistent bacteriuria (1-4). The prevalence of bacteriuria correlates with the level of functional disability (3,5,6), and is highest in the most disabled. In the absence of a chronic indwelling catheter, bacteriuria is associated with relatively low morbidity, and treatment with antibiotics is followed by early recurrence (1,2). It has been suggested, however, that the presence of pyuria in individuals with bacteriuria is an indicator of infection of the urinary tract rather than 'colonization', and that pyuria is an indication for therapy. The validity of treatment decisions based on the presence or absence of pyuria has not been reported.

This study was undertaken to determine some of the characteristics of pyuria in a group of institutionalized elderly subjects. The association of pyuria with bacteriuria and other urinary characteristics including pH, protein and glucose measurements, type of infecting organism, and the leukocyte esterase test were examined. Some observations on the natural history of pyuria are also reported, including degree of variability in the same individual over time.

PATIENTS AND METHODS

Patient population: The population studied included 57 males and 19 females, 32% of the 239 permanent residents of the Deer Lodge Centre, an extended care facility in Winnipeg, Manitoba. The mean age was 80 years (range 50 to 95). All participants had a high level of functional disability. Urine specimens were collected from a convenience sample of residents for a study characterizing some features of asymptomatic bacteriuria in this population. Nursing staff collected specimens from one individual whom they felt had bacteriuria based on a subjective assessment of smell and cloudiness, and from a second individual on the same ward whom they thought did not have infection. Residents with symptomatic bacteriuria characterized by symptoms of dysuria, frequency, urgency, hematuria, acute alteration in continence status, suprapubic discomfort, or signs of epididymo-orchitis or bacteremia, were excluded.

Microbiological and biochemical methods: Urine specimens were obtained by 'clean catch' technique at the first morning void. Patients who were unable to control bladder function and required condom drainage had the first urine voided and leg-bag collected after the application of a clean condom (7). Six individuals with chronic indwelling catheters had specimens collected by aspiration from the catheter port.

Specimens were refrigerated at 4°C immedi-

ately following collection until transfer to the laboratory. Urine was inoculated quantitatively onto a split plate containing MacConkey agar and blood agar, and incubated at 37°C for 24 to 48 h. Quantitation, isolation and identification of organisms was done using standard microbiological methods (8). Routine urinalysis was performed to identify glucose, protein and pH. The leukocyte esterase test was performed using a Chemstrip 6L R (Mannheim Co), and the quantitative leukocyte count determined on uncentrifuged urine by the hemocytometer method. For a subset of 89 specimens the quantitative leukocyte count was performed three times on the same specimen to determine variability in the test for the same specimen.

Definitions and analysis: Pyuria was defined as greater than or equal to 10 leukocytes/mm³ urine (10x10⁶/L). Significant bacteriuria was defined as greater than or equal to 10⁵ colony forming units (cfu) of one or more organisms/mL urine (equivalent to 10⁸ cfu/L). For studies of the variability of pyuria in the same specimen or over time, the leukocyte count was expressed as the log₁₀. Statistical analysis used standard hypothesis tests, including the χ^2 test for proportions and *t* test and analysis of variance for comparison of means, and was performed on a personal computer with the Microstat computer package (Ecosoft Inc, Indiana).

RESULTS

Pyuria: Two hundred and forty-three specimens from 76 individuals were studied. Fifty-four residents had more than one urine specimen collected at intervals from three weeks to 30 months. Bacteriuria was identified in 225 specimens (93%), but only 153 (63%) had significant growth. For specimens with significant growth, 120 (49% of total specimens and 78% of those with significant growth) had a single organism, while 33 (13% of total and 22% of those with significant growth) had more than one organism isolated. For one specimen a quantitative bacterial count was not available.

Two hundred and fourteen specimens (88%) had greater than or equal to 10 leukocytes/mm³. These included 70 (29% of total) with 11 to 100 leukocytes/mm³; 99 (40%) with 101 to 1000 leukocytes/mm³; and 45 (19%) with greater than 1000 leukocytes/mm³. The mean coefficient of variation for the quantitative leukocyte count was 0.146 for three examinations on the same specimen, indicating approximately 15% laboratory variation among readings.

Relationship to bacteriuria: One hundred and sixteen of 120 specimens (97%) with significant

TABLE 1

The association of urine pH and protein with level of pyuria in urine specimens from the institutionalized elderly

Leukocyte count/mm ³	pH	Protein
0-10	6.6±0.8	0.16±0.52
11-100	7.1±1.4	0.81±1.19
100-1000	7.0±1.2	1.34±1.79
>1000	6.7±1.1	2.10±1.59

Values are given as mean ± SD

TABLE 2

Associations of urinalysis variables with cell count and with infecting organism

Organism (≥10 ⁵ cfu/mL)	pH	Protein	log ₁₀ WBC
<i>Escherichia coli</i> (n=33)	6.2±0.9	0.74±1.58	2.5±0.9
<i>Proteus mirabilis</i> (n=31)	8.1±1.0	2.26±1.91	2.6±0.6
<i>Providencia stuartii</i> (n=18)	7.4±1.2	1.28±1.56	2.5±0.7
Other pure cultures (n=38)*	7.4±1.3	2.04±1.59	2.6±0.8

Values given are mean ± SD. *Ten different species are included in this group. cfu Colony forming units; WBC White blood cell count

TABLE 3

The relationship of pH to quantitative leukocyte count stratified by infecting organism

	Quantitative leukocyte count			P
	10-100	100-1000	>1000	
<i>Providencia stuartii</i> (n=18)	8.4 (5)	7.3 (7)	6.8 (6)	0.04 *
<i>Proteus mirabilis</i> (n=30)	8.8 (5)	8.3 (8)	7.4 (7)	0.04*
<i>Escherichia coli</i> (n=33)	6.3 (6)	6.2 (19)	6.4 (8)	0.84*

Numbers in brackets are numbers of specimens. *Analysis of variance

bacteriuria with a single organism, and 27 of 33 multiple organism bacteriuria specimens (82%), had pyuria. However, 10 of 17 specimens (59%) with no growth and 61 of 72 (85%) with lower quantitative counts of bacteria also had pyuria. Eighteen of the 243 specimens were collected while the patient was receiving or within seven days following antibiotic treatment for various infections. Eleven of these specimens (61%) still showed bacteriuria, and 16 (89%) had pyuria.

Pyuria had a sensitivity of 97%, a specificity of 72%, a positive predictive value of 70% and a negative predictive value of 83% for bacteriuria. Conversely, bacteriuria had a sensitivity of 71%, a specificity of 82%, a positive predictive value of 97%, and a negative predictive value of 27% for pyuria. Thus, only 27% of specimens with no significant bacterial growth also had less than 10 leukocytes/μL.

Urinalysis variables and infecting organisms: Table 1 shows the observed associations of pyuria

with other urinalysis variables. Glycosuria was identified in only eight urine specimens, and no analysis with glycosuria was undertaken. Proteinuria was expressed on a scale of 0 to 6, representing a range of protein from 0 to more than 3 g/L. The level of pyuria correlated with the level of proteinuria (analysis of variance $P<0.001$) and urine pH ($P=0.009$). This association remained significant when specimens without pyuria, and thus presumably without bacteriuria, were removed, with higher white cell counts at a lower urine pH.

The most common infecting organisms were *Proteus mirabilis*, *Escherichia coli* and *Providencia stuartii*. When specimens with pure cultures in significant quantities were studied, there was a significant association with both urine pH (analysis of variance $P<0.001$) and proteinuria (analysis of variance $P<0.001$), and organism isolated (Table 2). The level of pyuria was not significantly associated with the type of organism. As it has been previously reported that leukocytes disintegrate rapidly at elevated pH, the pH values with specimens stratified by infecting organism and leukocyte count were examined (Table 3). There was an inverse correlation between quantitative leukocyte count and urinary pH for the urease-producing organisms, but not for *E. coli*.

The level of pyuria may have been influenced by factors specific to the individual subjects studied, particularly if one individual contributed a number of urine specimens to the study. To control for this potential confounding factor, the analysis was repeated using only the first specimen collected from each of the 76 individuals. The results obtained for all associations were similar to those when all 243 urine specimens were examined. The relationships were statistically significant in this 'first specimen group' except for the relationship between the level of pyuria and pH and protein. For that analysis the trends were consistent with the observed associations for all specimens, but did not reach statistical significance.

Leukocyte esterase test: The leukocyte esterase test was positive (1+ or greater) for 153 of 215 specimens (71%) with pyuria, and two of 28 (7%) without pyuria. The test was positive for 116 of 153 (76%) with significant bacteriuria, 32 of 72 (44%) with low count bacteriuria, and five of 17 (29%) without bacteriuria.

The positive predictive value of the leukocyte esterase test for pyuria was 99%. However, when negative, the leukocyte esterase test was associated with the absence of pyuria in only 30% of specimens. For specimens with pyuria and a negative leukocyte esterase test, 14 had less than or equal to 10 leukocytes/mm³, 31 had 11 to 100

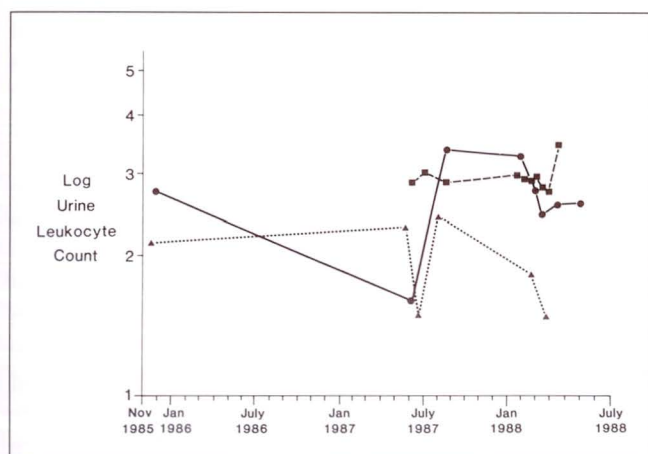


Figure 1) Variation in quantitative urinary leukocyte count with time in three individuals with multiple specimens obtained

leukocytes/mm³, 16 had 101 to 1000 leukocytes/mm³, and one had over 1000 leukocytes/mm³.

Variation of pyuria with time: The 54 patients with multiple urine specimens collected over extended times were analyzed to determine the variation in pyuria with time. Figure 1 illustrates three representative individuals. While some fluctuations in the level of pyuria are seen, these tended to be less than one log variation, with the level of pyuria relatively constant over even extended periods. The mean coefficient of variation expressed as the log of the leukocyte count was 0.57 ± 0.57 for all individuals. When only pure cultures with significant bacterial growth were examined, the mean coefficient of variation of the quantitative leukocyte count was 0.27 ± 0.20 . Thus, there may be as much as 57% of one log variation in the white count of each individual over the study months, with even less variation in individuals with persistent single organism infection.

DISCUSSION

This study documented a high prevalence of pyuria in an elderly institutionalized population. Urine specimens were not collected from all institutional residents, nor a randomized subset, so the proportion of institutional residents with pyuria cannot be determined. However, the data here show that for a selected group of institutionalized elderly, pyuria was present in most urine specimens. It is virtually universal in individuals with bacteriuria both with and without indwelling catheters, but also common in those without bacteriuria. In addition, the mean absolute leukocyte count in an individual tended to remain relatively constant over time.

Previous studies in ambulatory elderly men and women have also found pyuria to be common (3,4,6), but similar studies from institutionalized

populations are not, to the authors' knowledge, available. In previous studies in a small group of elderly men institutionalized in a chronic care facility and women in an acute care facility, both with asymptomatic bacteriuria, the authors observed that 90% of individuals with bacteriuria had pyuria (7,9). Pyuria was highly predictive for the presence or absence of bacteriuria in elderly asymptomatic ambulatory men (10), but was not a good predictor for bacteriuria in a group of ambulatory women, some of whom were institutionalized (6). These observations reconfirm that pyuria is universal with bacteriuria in the institutionalized elderly and would not, in the absence of symptoms, be an indication for therapy. To the authors' knowledge, no previous studies have observed the persistence of pyuria for extended periods of time.

Residents with bacteriuria with quantitative counts less than 10^5 cfu/mL may have either true bacteriuria or contaminated specimens. The proportion with pyuria in this group was similar to that observed for the group with 'significant bacteriuria'. While the observation of pyuria in these specimens is consistent with these low quantitative counts denoting true bacteriuria, it is also possible that conditions which increase the likelihood of bacterial contamination, such as vaginitis in women and urethritis in men, would also be associated with increased likelihood of contamination of voided urine specimens with leukocytes. Thus, the clinical significance of pyuria in this group requires further characterization.

Pyuria was measured using the hemocytometer counting chamber method. The hemocytometer method correlates closely with the leukocyte excretion rate, considered to be the 'gold standard' for quantitating pyuria. Greater than 10 leukocytes/mm³ has been shown to correlate with greater than 400,000 leukocytes/h determined by the excretion rate (10). The method used most commonly in clinical practice is, however, determination of leukocytes per microscopic high power field in a centrifuged urine specimen. This does not correlate well with the leukocyte excretion rate and is not reproducible due to a number of uncontrolled factors (11). Thus the observations with respect to pyuria in this study are more reliable than those based on standard urinalysis.

When the relationship of pyuria to bacteriuria was examined, the authors found that if bacteria were present in the urine, pyuria was also present in 97% of specimens. Of specimens with pyuria, 70% also had bacteriuria. Thus bacteriuria was a better predictor for pyuria than pyuria was for bacteriuria. The absence of bacterial growth in the

urine was a poor predictor for the absence of leukocytes in the urine, with a negative predictive value of only 27%. In other populations, the leukocyte esterase test has been reported to have a sensitivity of 72 to 97% (12). The leukocyte esterase test in this population had a sensitivity of 71% with a positive predictive value for pyuria of 99% but a negative predictive value of only 30%; specimens with pyuria and negative esterase tests tended, however, to have lower leukocyte counts. Thus, in this population, the leukocyte esterase dipstick method would be a poor screening tool due to the lack of sensitivity.

The level of pyuria is associated with the level of urine protein, with higher amounts of urine protein corresponding to higher leukocyte counts. As well, a trend towards higher levels of pyuria at lower pHs was also noted, which was most apparent when the analysis was stratified by organism and leukocyte level. It has previously been observed that at alkaline pH leukocytes disintegrate more rapidly, likely explaining the inverse association of pH and urine leukocytes (13). Despite the variation in urine pH and protein

levels with different infecting species, the level of pyuria did not vary with the type of organism. This observation suggests that two opposing factors may be involved: higher urine pHs and thus more leukocyte disintegration, together with an increased inflammatory reaction which is organism dependent, leading to a relatively stable leukocyte count. This observation requires further study.

The significance of the high prevalence of pyuria in institutionalized elderly individuals with asymptomatic bacteriuria is unclear. Previous studies have documented little morbidity and mortality attributable to bacteriuria in this population (1,2). As shown here, pyuria appears to be universal with asymptomatic bacteriuria in elderly institutionalized individuals. One may infer that morbidity and mortality are not influenced by the presence of pyuria, although this requires direct confirmation. Pyuria indicates inflammation in the urinary tract, but it appears that the inflammation remains subclinical and recurs with reinfection post therapy. The causes and significance of pyuria in patients without bacteriuria require further study.

ACKNOWLEDGEMENTS: This study was made possible through the support and cooperation of the nursing and laboratory staff at Deer Lodge Centre. Expert secretarial assistance was provided by Brenda Kowalczyk.

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