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"MIXED GROWTH OF DOUBTFUL SIGNIFICANCE" IS EXTREMELY SIGNIFICANT IN PATIENTS WITH LOWER URINARY TRACT SYMPTOMS.

Hypothesis / aims of study

The assessment of patients with lower urinary tract symptoms (LUTS) commences with the exclusion of urinary tract infection (UTI). This is subordinated to the culture of a clean-catch, midstream urine sample (MSU), with a threshold of 10^5 colony forming units (cfu) ml^{-1}, of a single species of a known urinary pathogen. Kass et al described this criterion in 1957 (1), but the proposition rested on a study of 74 women with acute pyelonephritis, and 337 asymptomatic controls. Nevertheless, the threshold has become ingrained as an accepted gold standard. Some have questioned the widespread adoption of a single dichotomous threshold for the diagnosis of infection, in all clinical circumstances, but they have had little influence. In recent times there has been further dissent (2, 3), and the validity of the Kass criteria is starting to look very shaky. This is more worrying given that all surrogate markers, such as urinary dipsticks, are calibrated to this standard. Kass' insistence on a single species of a known urinary pathogen has no basis in research evidence and yet it is commonplace for mixed growths to be dismissed as of "doubtful significance". A Darwinian perspective insists that the adaptability of living organisms, particularly bacteria, should cause us to expect polymicrobial infections rather than the dominance of a single species.This study re-examined the significance of a mixed growth culture result obtained from MSU samples collected from patients with non-acute LUTS, by comparison against symptoms, inflammatory markers: pyuria and uroepithelial cell shedding, and urinary dipstick.

Study design, materials and methods

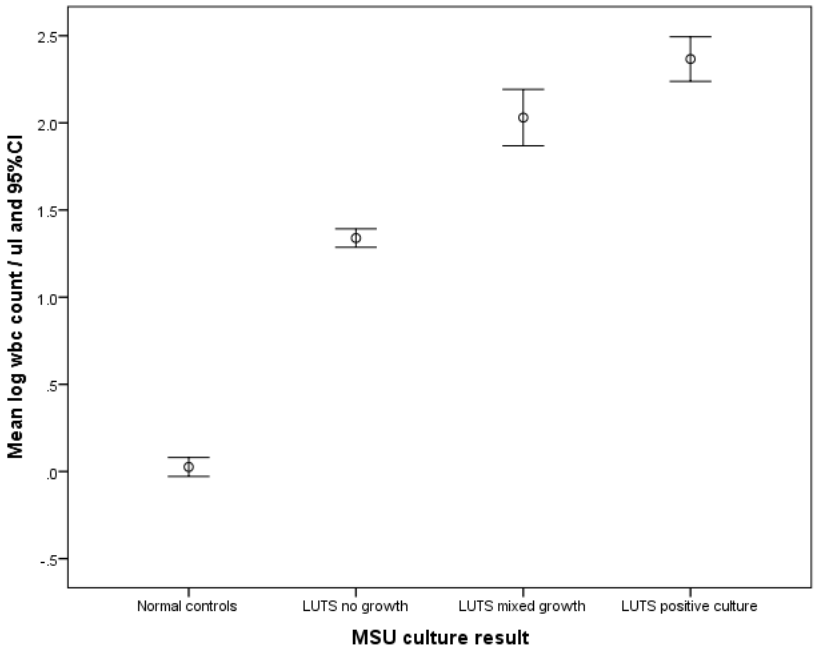
Normal controls and patients with non-acute LUTS had symptoms measured and an MSU cultured. Fresh urine specimens were examined microscopically to quantify pyuria and uroepithelial cells and analysed using a urinary dipstick. Four groups were compared: normal controls, LUTS no growth, LUTS mixed growth and LUTS positive culture.

The data were checked for normality using Q-Q plots and satisfied the criteria for parametric analysis so ANOVA was used to test the between-group differences (alpha = .05), with post-hoc analysis using Bonferroni's method (alpha = .01).

Results

43 control subjects (M=10, F=33, Mean age 41 sd=15) and 6208 LUTS patients (M=590 F=5618, Mean age 56, sd=17) provided data. The symptom distribution was as follows: storage symptoms 58% (stress urinary incontinence 16%); voiding dysfunction 20%; non-dysuric pain symptoms 28%.The log pyuria count differed markedly between: "Normal controls"; "LUTS no growth"; "LUTS mixed growth"; and LUTS positive culture" ($F=110$; $p<.0001$; $df=3$). The figure shows how "mixed growth" and "positive culture" discriminate from other groups. Similar between-group differences were identified in measures of frequency and incontinence, in symptoms of urgency, stress incontinence, voiding dysfunction and dysaesthesia, and additionally in the amount of uroepithelial cell shedding. In all cases "LUTS mixed growth" differed markedly from "normal controls" and "LUTS no growth" behaving similarly to the "LUTS positive culture" group. Urinary dipstick data were comparably distributed so that for leucocyte esterase the following proportions proved positive: "Normal controls" 4%; "LUTS no growth" 26%; "LUTS mixed growth" 40%; "LUTS positive culture" 36%, and for nitrite: "Normal controls" 0%; "LUTS no growth" 1%; "LUTS mixed growth" 11%; "LUTS positive culture" 9%.

Figure: comparison of the log pyuria count by the different MSU culture result groups



Interpretation of results

These data have scrutinised this problem from several different perspectives that have addressed the symptom complexes and examined the evidence of inflammatory reaction, urothelial reactivity and nitrite conversion. Every analysis points to a very significant pathological state coinciding with “mixed growth of doubtful significance”.

Concluding message

These data imply that it is no longer tenable to dismiss “mixed growth of doubtful significance” as implying no disease. We are going to have to re-examine many previous assumptions in order to achieve a proper perspective on the pathophysiology of all LUTS.

References

1. Arch.Intern.Med., 11-1957, 100; 709, 714.
2. N.Engl.J.Med., 19-8-1982, 307; 463, 468.
3. J.Urol., 17-3-2010, 183; 1843, 1847.

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