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Horsley H[1], Weissler A[1], Kupelian A[1], Gill K[1], Sathiananthamoorthy S[2], Brackenridge L[1], Malone-Lee J[1]
1. *University College London, UK,* ***2.*** *Royal Veterinary College, UK*

PLANKTONIC URINARY EPITHELIAL CELL COUNTS AS DISEASE INDICATORS IN OAB

Hypothesis / aims of study

The urothelium has been found to be inflamed and infected in a proportion of patients with OAB. Recent studies have shown that the innate immune system dominates the defence of the bladder to such infection. Bacterial components bind to Toll-like receptors (TLR) and thereby activate innate responses. Animal studies identify surface cell shedding as an important component of this immunity. It has already been observed that urothelial hypertrophy and metaplasia are exhibited by patients with OAB in contrast to controls (1)(2).

If OAB is associated with bacterial infection, it must feature increased urothelial cell shedding. It has long been demonstrated that urothelial cells can be seen floating in the urine when microscopy is used to examine fresh, unspun specimens for pyuria. They have usually been dismissed as contaminants and annoyances, but far from being irrelevant, the immune reaction confers potential significance. Outside of cytology, data on the pathological implications of urinary urothelial cells are sparse.

This was a blinded, prospective, comparative, observational cohort study of patients presenting with, and without, Overactive Bladder (OAB) symptoms. The purpose was to compare urinary planktonic epithelial cell counts with other disease markers, and between patient groups.

Study design, materials and methods

Patients attending an incontinence clinic had their symptoms assessed by blinded clinicians. Meticulous MSU samples were analysed and a microscopic epithelial cell count and white blood cell count (cells ul^{-1}) conducted with a haemocytometer. The samples were submitted for routine culture.

Results

228 adults with OAB (F=208; M=20; mean age=54; sd=18) (pure OAB=71%; mixed incontinence 29%) and 63 matched patients without OAB were included in the analysis. Data was collected over a 12 month period between 2010 and 2011. At presentation, 13% of patients demonstrated bacteriuria. The data were positively skewed and did not respond to logarithmic transformation; non-parametric analytical methods were used. There was a marked difference between those patients with OAB and pyuria ≥10 wbc ul^{-1} ($H=13.10$; $df=2$, $p=0.000$; see figure). No difference was demonstrated between those patients with pyuria 1-9 wbc ul^{-1}, which contrasts with data relating to cytokine responses. There was no difference in cell counts between patients with or without OAB ($H=2.59$; $df=1$; $p=0.107$), or patients with or without bacteriuria ($H=1.25$, $df=1$; $p=0.264$).

The study had a power of greater than 80% to detect a significant between group difference ($\alpha=.05$).

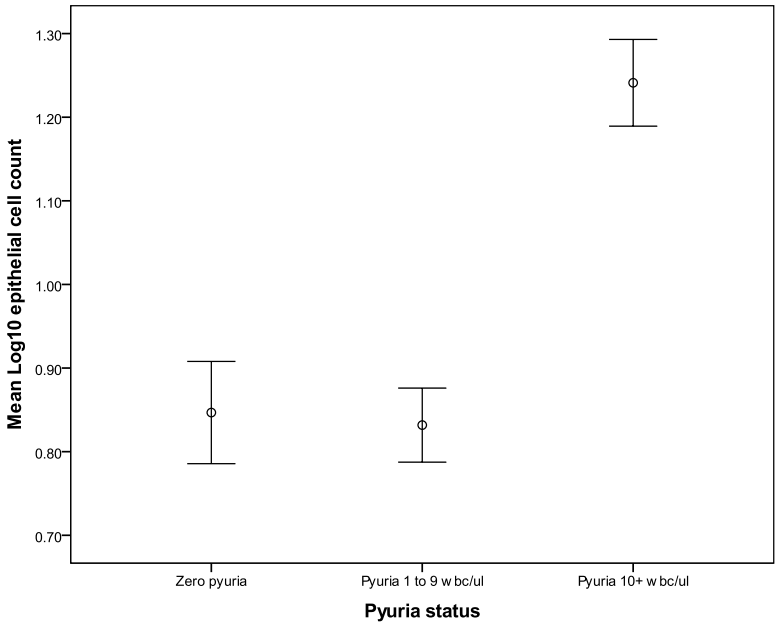
Interpretation of results

Unlike cytokines, the cell counts proved responsive when more significant inflammatory signals were present (≥10 wbc ul^{-1}). During follow-up, it was noted that elevation in the epithelial cell counts persisted long after other markers of inflammation and infection had settled. Perhaps increased urothelial cell shedding is a later manifestation of the disease process.

Concluding message

These neglected cells may prove to be important beacons of bladder pathology, particularly in relation to the later phases of bladder inflammatory disease processes. Their numbers are elevated in the presence of OAB symptoms, but only if an overt urinary inflammatory exudate is detectable.

Figure: 95% confidence interval plots of the Log10 epithelial cell counts.



References
1. Neurourol Urodyn. 2009; 28: 776-77.
2. Neurourol Urodyn. 2009; 28: 754-55.

Specify source of funding or grant	**Whittington and Moorfields Research Ethics Committee**
Is this a clinical trial?	**No**
What were the subjects in the study?	**HUMAN**
Was this study approved by an ethics committee?	**Yes**
Specify Name of Ethics Committee	**Whittington and Moorfields Research Ethics Committee**
Was the Declaration of Helsinki followed?	**Yes**
Was informed consent obtained from the patients?	**Yes**