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ORIGINAL ARTICLE

The Importance of Pus/Epithelial Cells Counts in Diagnosis of Urinary Tract Infection and Asymptomatic Bacteriuria

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Abstract

Background: **Asymptomatic bacteriuria (ABU) is often diagnosed incidentally, and detection of bacteria in urine can lead to unnecessary antibiotic use, may aggravate antimicrobial resistance. To our knowledge, no prior study has focused on the dual presence of pus and epithelial cells (PEDP) and its diagnostic value.**

Objective: **To evaluate the importance of Pus/Epithelial Cells Counts in diagnosis of ABU and UTI.**

Methods: **A case-control study was conducted on (140) females, divided into two groups: 70 with UTI and 70 apparently healthy controls, 28 had ABU and 42 had sterile urine cultures, with age ranging from (18 to over 58) years. Urine samples underwent general urine examination and bacteriological culture.**

Results: **Positive bacterial growth occurred in 57.1 % of UTI patients and 40 % of controls (ABU). *E. coli* was the most frequent in both groups. PEDP analysis showed that 61.4 % of UTI cases represented true infections, while 38.6 % were likely contamination (defined as presence of pus or epithelial cells alone according to culture results). *E. coli* was strongly associated with true infections, whereas *S. epidermidis* was more common in contamination. In the ABU group, 100 % of true infections showed bacteria in urine, with sensitivity, specificity, PPV, and NPV of 100.0 %, 60.0 %, 68.4 %, and 100.0 %, respectively. In the UTI group, these values were 90.6 %, 63.2 %, 67.4 %, and 88.9 %, respectively.**

Conclusion: **PEDP could be used to differentiation of true infection from contamination in patients with UTI. Combining microscopic bacterial detection with PEDP improves diagnostic accuracy for ABU and UTI in females.**

Keywords: Urinary tract infections, Asymptomatic bacteriuria, GUE, Urine culture, Pus/Epithelial dual presence

Introduction

Asymptomatic bacteriuria (ABU) is defined as the presence of bacteria in urine cultures without the typical clinical symptoms of UTI (Omar, 2022). It is a common clinical finding, with prevalence increasing with advancing age, and it occurs significantly more often in females than in males (Ali Al Youssef et al., 2020). Misdiagnosis of ABU as UTI can lead to unnecessary antibiotic use and potentially delay the identification true underlying condition. This misclassification may result in patient harm and contribute to antimicrobial resistance. Furthermore, limitations in the diagnostic definitions used by some authors may weaken the strength of their central arguments and risk diminishing their impact on healthcare practice (Johnson, 2018). One contributing factor to the overtreatment of ABU is clinicians' concern that delaying antibiotic therapy could result in adverse outcomes, such as progression to bacteremia secondary to UTI (Baghdadi et al., 2022; Korenstein et al., 2022). According to the 2019 guidelines of the Infectious Diseases Society of America (IDSA), screening for and treating ABU is recommended only for pregnant women and for patients scheduled to undergo invasive urologic procedures. There is no evidence to support treatment in other populations, including patients with diabetes, elderly individuals, those with or without urinary catheters, and persons with spinal cord injuries (Nicolle et al., 2019).

Urinary tract infections are infections affecting any part of the urinary system, most commonly the

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bladder and urethra. UTIs are typically symptomatic, presenting with dysuria, urinary urgency, frequency, and suprapubic discomfort (Kendall & Mauer, 2022). They are highly prevalent, particularly among women, with more than 50 % experiencing at least one episode during their lifetime (Czajkowski et al., 2021). Globally, the prevalence of UTIs among older adults has been reported at 23.6 %. Moreover, both the number of deaths and the age-standardized mortality rate attributed to UTIs were found to be elevated by a factor of 17.83, highlighting a substantially increased risk in this population (Kalhori et al., 2024; Zhu et al., 2021).

Although UTIs are among the most common bacterial infections in otherwise healthy individuals, they are frequently misdiagnosed, leading to unnecessary antibiotic prescribing and related consequences such as increased diagnostic testing and follow-up healthcare visits (Watson et al., 2018). A study highlights psychological and behavioral factors may contribute to UTI misdiagnosis, including inadequate understanding of urine dipstick interpretation, age-related diagnostic bias, reliance on routine testing practices, and external pressures such as time and resource constraints, patient or peer expectations, and medico-legal concerns (O'Kelly et al., 2019).

Conventional diagnostic methods, such as urine culture, remain the gold standard for UTI diagnosis. However, culture results typically require 2–3 days, potentially delaying targeted treatment. In contrast, dipstick tests provide rapid, point-of-care results but lack accuracy and do not offer microbiological identification (Davenport et al., 2017).

The adoption of improved diagnostic strategies can promote more rational antibiotic use, aiding in the fight against multidrug resistance and reducing healthcare costs by minimizing unnecessary treatments and hospitalizations (Grey et al., 2023; Mathew, 2017). The current study hypothesis that the dual presence of both pus/epithelial cells counts may serve as a strong indicator of true infection, whereas the presence of only one of these parameters could suggest contamination. Thus, the aim of this study is to evaluate the diagnostic value of quantitative assessment of pus and epithelial cell counts in differentiating ABU from UTIs.

Material and method

Study design and setting

A case-control study was conducted involving 140 female participants, comprising 70 patients diagnosed with UTIs and 70 apparently healthy individuals, among control group of whom 28 had ABU and 42 had sterile urine cultures. Data collection took place from September to December 2024 at the Urology Consultant Clinic in Imam Hussein Hospital, located in the holy city of Karbala.

Participants selection

Participant information was obtained through a structured questionnaire. Inclusion criteria involve female with age range from (18 to over 58) years. Matching criteria between the two groups include age and residency. Whereas, exclusion criteria included females with comorbidities such as COVID-19, asthma, cardiovascular diseases, cancer, diabetes, autoimmune disorders, chronic kidney disease, urinary tract abnormalities (including nephrolithiasis), and pregnancy.

Collection samples

Urine samples were collected from both female patients with UTI following diagnosis by urologist and apparently healthy female. A disposable sterile plastic container was used for collecting urine. About 5 ml "midstream" of urine was collected from each female and samples were centrifuged. Centrifuged samples were used for GUE and culture on standard culture media, including MacConkey and blood agar. Upon receiving the urine sample, 5 mL was centrifuged at 1700 g for 5 min. The supernatant was removed and the sediment was resuspended and by examined at low power (10× objective) and high power (40× objective) using light microscope (Palsson et al., 2020). The samples were then incubated under aerobic conditions at (37 °C) for a period of 24–48 h and identification was performed using the VITEK® 2 system (Pławińska-Czarnak et al., 2023).

Identification of bacteria

The bacterial identification was done through the use of automated devise. The VITEK2 system has become the backbone of diagnostic microbiology labs even in developing countries (Khurana et al., 2020). The integrated VITEK 2 system is a closed system comprises the filler-sealer unit, reader-incubator, computer control module, data terminal, and multi-copy printer. This devise facilitates the identification of chemical reactions and bacterial proliferation within the microwells of thin plastic cards (El-Ameir et al., 2024). It employs 64-well cards including a barcode that encodes the card

type, expiration date, lot number, and unique identification number. Available test kits comprise ID-GN (identification of gram-negative) and ID-GP (identifying of gram-positive) (Duraye et al., 2024).

Pus/Epithelial Cells Dual Presence (PEDP)

The PEDP was calculated as the dual presence of high number of pus (>5 cells/HPF) and epithelial cells (>20 cells/HPF) might be considered as strong indicator of true infection while if one of them present might possibly regarded as contamination. There wasn't previous study that focused on dual presence of both pus and epithelial cells. Also, to facilitate the results interpretation of positive bacterial growth and exclude contamination using GUE, this study investigated the pus/epithelial cell dual presence (PEDP) and study their impact on diagnosis of UTI based on urine culture.

Ethical approval

The study protocol was approved by the Ethical Committee at the College of Applied Medical Sciences, University of Kerbala (No. IQ.UOK.CAMS.DCL.REC.7, 2024/9/1) and the Ethical Committee at Imam Hussein Medical City at Kerbala. All patients included in this study were informed and verbal agreement was obtained prior to sample collection. The ethics approval number has been updated to [Ref.: CLAMSKU/8].

Statistical analysis

The statistical package for the social sciences (SPSS), version 25 software (IBM Corp., NY, and USA), was used to analyze data. Descriptive statistics were used to determine frequencies, mean and standard error, and cross-tabulation. Numerical data was tested for normality. Categorical variables were tested using chi-square test. The statistical significance level was established at $P \leq 0.05$.

Result

The study population was divided into two main groups: 70 patients with diagnosed UTI and 70 apparently healthy controls (women without symptoms and sign of UTI). Within the control group, 28 participants were identified as having ABU (women screened and found to have bacteria in urine culture results), while 42 had sterile urine cultures. The mean age of UTI patients and ABU were (39.36 ± 14.28) and (39.10 ± 14.38), respectively. Based on history of recurrent UTI (rUTI), significant higher percentage of UTI patients had rUTI, whereas the higher percentage of ABU female were without rUTI, as shown in Table (1).

Highly significant differences according to the pH categories were observed between the two groups. However, no other significant differences were observed concerning epithelial cells, RBC or the presence of pus cells, as shown in Table 2. Moderate to low sensitivity, specificity, PPV and NPV were observed for each variable alone.

Forty (57.1 %) patients from UTI and 28 (40 %) individuals from the total number of control group (they were referred to as ABU) showed positive bacterial growth. The most common pathogen isolated was *E. coli* in both groups, accounting for (30.0 %) of UTI cases and (46.4 %) of ABU cases. This was followed by *S. saprophyticus* (18.6 % in UTI and 32.1 % in ABU) and *S. epidermidis* (5.7 % in UTI and 14.3 % in ABU), as shown in Table 3.

There wasn't previous study that focused on dual presence of both pus and epithelial cells and their diagnostic utility. PEDP was calculated as the dual presence of high number of pus (>5 cells/HPF) and epithelial cells (>20 cells/HPF).

As shown in Table 4, approximately (67.9 %) and (61.4 %) of ABU females and UTI patients were considered true infection. The PPV and NPV were (69.4 %) and (25.0 %), respectively.

Further analysis was carried on to gather the results of PEDP with the results of culture which revealed that (30 %) of UTI patients with positive bacterial growth were considered as contamination, as shown in Table 5.

In the Table 6, cross tabulation was made between the PEDP variable and microscopic presences of bacteria in urine between two groups. Thirty-two from UTI patients had bacteria seen in urine microscopically, among them 29 (90.6 %) had true infection while 3 (9.4 %) was considered as contamination. Sensitivity, specificity, PPV and NPV were (90.6 %), (63.2 %), (67.4 %), and (88.95) for UTI patients, respectively.

In Table 7, 13 (100.0 %) of ABU from those seen bacteria in urine had true infection and about

Table 1. Demography of UTI patients and asymptomatic bacteriuria.

Variable	UTI Patients N (%)	ABU N (%)	P-value
Mean age ±SD	39.36 ± 14.28	39.10 ± 14.38	
History of rUTI			
With	59 (84.3)	10 (35.7)	0.000[a]
Without	11 (15.7)	18 (64.3)	
Total Number N (%)	70 (100.0)	28 (100.0)	

N, Number; rUTI, Recurrent Urinary Tract Infection; ABU, Asymptomatic Bacteriuria; SD, Standard Division.
[a] Significant at 0.05 level.

Table 2. Urinalysis parameters between UTI patients and asymptomatic bacteriuria.

Variable	Category	UTI Patients N (%)	ABU N (%)	Chi-Square	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
PH	From 4–6	65 (92.9)	15 (53.6)	0.000[a]	7.1	53.6	27.8	18.8
	From 7–9	5 (7.1)	13 (46.4)					
Pus Cell	≤ 5	26 (37.1)	9 (32.1)	NS	62.9	32.1	69.8	25.7
	> 5	44 (62.9)	19 (67.9)					
RBC	≤ 5	36 (51.4)	17 (60.7)	NS	48.6	60.7	75.6	32.1
	> 5	34 (48.6)	11 (39.3)					
Epithelial Cell	< 20	38 (54.3)	12 (42.9)	NS	45.7	42.9	66.7	24.0
	≥ 20	32 (45.7)	16 (57.1)					

N, Number; NS, Not Significant at 0.05 level; UTI, Urinary Tract Infection; RBC, Red Blood Cell; ABU, Asymptomatic Bacteriuria; PPV, Positive Predictive Value; NPV, Negative Predictive Value.
[a] Significant at 0.05 level.

Table 3. Urine cultures of UTI patients and asymptomatic bacteriuria.

Variable	UTI Patients N (%)	ABU N (%)	Chi-Square
Isolated organism			
Escherichia coli	21 (30.0)	13 (46.4)	0.001[a]
Staphylococcus saprophyticus	13 (18.6)	9 (32.1)	
Staphylococcus epidermidis	4 (5.7)	4 (14.3)	
Other Bacteria	2 (2.9)	2 (7.1)	
None Growth	30 (42.9)	0 (0.0)	
Total Number	40 (100.0)	28 (100.0)	

N, Number; UTI, Urinary Tract Infection; ABU, Asymptomatic Bacteriuria; Other Bacteria, Bacteria Species Others Than *E. coli, S. saprophyticus* and *S. epidermidis.*
[a] Significant at 0.05 level.

(40 %) of ABU whom they haven't bacteria in urine might considered to have true infection. Sensitivity, specificity, PPV and NPV were (100.0 %), (60.0 %), (68.4 %), and (100.0) for ABU females, respectively.

Cross tabulation between the PEDP and the type of isolated bacteria from UTI patients and ABU females revealed that the *E. coli* isolates were associated with true infection whereas the presence of *S. epidermidis* most commonly could be regarded as contamination, as shown in Table 8.

Discussion

Although the pathophysiology and microbiology are well understood, the connection between ABU and UTI remains incompletely defined. The occurrence of ABU is notably less frequent than that of UTI (Murri et al., 2018).

The presence of pyuria (pus cell in urine) aids in confirming the diagnosis of UTI in patients presenting with typical clinical symptoms and signs. Additionally, urinalysis has been found to be an effective "rule-out" test for UTI (Advani et al., 2024). A presence of ≥5 pus cells per HPF is typically regarded as UTI (Thyagaraju et al., 2024). Epithelial cells can be further divided into squamous and transitional types. While these sub-classifications are clinically significant, they are rarely included in routine urine diagnostic reports. The normal range for epithelial cells is 0–15 per HPF. An elevated count suggests inflammation in the urinary tract (Goswami et al., 2021).

The study showed that (84.3 %) of UTI patients had rUTI, whereas, (35.7 %) of ABU had rUTI (Table 1). Similarly, Al-Musawi and Al-Husseini (2021)

Table 5. Pus/Epithelial cells dual presence in UTI patients with and without bacterial growth.

Variables	With Growth N (%)	Without Growth N (%)	Chi-Square
PEDP			
True Infection	28 (70.0)	15 (50.0)	NS
Contamination	12 (30.0)	15 (50.0)	
Total Number	40 (100.0)	30 (100.0)	

N, Number; NS, Not Significant at 0.05 level; PEDP, Pus/Epithelial cell dual presence; UTI, Urinary Tract Infection.

Table 4. Pus/Epithelial cells dual presence of UTI patients and asymptomatic bacteriuria.

Variables	UTI Patients N (%)	ABU N (%)	Chi-Square	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
PEDP							
True Infection	43 (61.4)	19 (67.9)	NS	61.4	32.1	69.4	25.0
Contamination	27 (38.6)	9 (32.1)					
Total Number	70 (100.0)	28 (100.0)					

N, Number; NS, Not Significant at 0.05 level; PEDP, Pus/Epithelial cell dual presence; UTI, Urinary Tract Infection; ABU, Asymptomatic Bacteriuria; PPV, Positive Predictive Value; NPV, Negative Predictive Value; Contamination, The Presence Normal Flora Bacteria in Urine Samples.

Table 6. Pus/epithelial cells dual presence in UTI patients according to bacteria in urine.

Variables	True Infection N (%)	contamination N (%)	Total Number	Chi-Square	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
Bacteria in Urine								
Bacteria Seen	29 (90.6)	3 (9.4)	32 (100.0)	0.000[a]	90.6	63.2	67.4	88.9
Bacteria Not Seen	14 (36.8)	24 (63.2)	38 (100.0)					

N, Number; PEDP, Pus/Epithelial cell dual presence; UTI, Urinary Tract Infection; PPV, Positive Predictive Value; NPV, Negative Predictive Value.
[a] Significant at 0.05 level.

Table 7. Pus/Epithelial cells dual presence in asymptomatic bacteriuria according to bacteria in urine.

Variables	True Infection N (%)	contamination N (%)	Total Number	Chi-Square	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
Bacteria in Urine								
Bacteria Seen	13 (100.0)	0 (0.0)	13 (100.0)	0.000[a]	100.0	60.0	68.4	100.0
Bacteria Not Seen	6 (40.0)	9 (60.0)	15 (100.0)					

N, Number; PEDP, Pus/Epithelial cell dual presence; ABU, Asymptomatic Bacteriuria; PPV, Positive Predictive Value; NPV, Negative Predictive Value.
[a] Significant at 0.05 level.

Table 8. Pus/Epithelial cells dual presence in UTI patients and asymptomatic bacteriuria according to isolated organism.

Variable	UTI Patients		Total Number N (%)	ABU		Total Number N (%)	*P*- value
	True infection N (%)	Contamination N (%)		True infection N (%)	Contamination N (%)		
Isolated organism							
Escherichia coli	19 (90.5)	2 (9.5)	21 (100.0)	9 (69.2)	4 (30.8)	13 (100.0)	0.000[a]
Staphylococcus saprophyticus	6 (46.2)	7 (53.8)	13 (100.0)	7 (77.8)	2 (22.2)	9 (100.0)	
Staphylococcus epidermidis	1 (25.0)	3 (75.0)	4 (100.0)	2 (50.0)	2 (50.0)	4 (100.0)	
Other bacteria	2 (100.0)	0 (0.0)	2 (100.0)	1 (50.0)	1 (50.0)	2 (100.0)	
None	15 (50.0)	15 (50.0)	30 (100.0)	–	–	–	

N, Number; Other Bacteria, Bacteria Species Others Than *E. coli, S. saprophyticus* and *S. epidermidis.*
[a] Significant at 0.05 level.

documented that more than three-quarters of the patients (82.4) experience rUTIs. The rUTI are typically defined as culture-confirmed UTIs that occur at least twice within six months or three times within a year (Aslam et al., 2020). One potential factor contributing to the risk of rUTIs is the insufficient characterization of empirical treatment regimens. Moreover, UTIs are frequently managed with inappropriate therapeutic approaches (Hamilton & Fishman, 2014).

Highly significant differences according to the pH categories were observed between the two groups (Table 2). Hattah et al. (2022) found no significant correlation between urine pH and the occurrence of UTIs. It has been documented that urine pH during UTIs is affected by multiple factors, including the virulence traits of the causative pathogen as well as the host's immune response and physiological state (Lai et al., 2021).

Urine culture revealed *E. coli* as the most common isolate in both groups (Table 3). Sharmin et al. (2022) *E. coli* was identified as the predominant isolate, accounting for (65.84 %) of cases. According to findings by Ali and Aljanaby (2023), *E. coli* was the most commonly isolated bacterium at (48 %), followed by *K. pneumoniae* at (17.4 %), and *S. saprophyticus* at (10 %).

To the best of our knowledge this is the first study focused on dual presence of both pus and epithelial cells (PEDP). Approximately (67.9 %) and (61.4 %) of ABU females and UTI patients were considered true infection (Table 4). Urinary symptoms alone have limited accuracy in identifying culture-positive UTIs; however, diagnostic reliability increases when urine microscopy reveals pyuria and/or a high bacterial count (Tan et al., 2019). PPV and NPV are affected by disease prevalence, with higher prevalence generally resulting in increased PPV and NPV (Gogtay & Thatte, 2017).

Thirty percent of UTI patients with bacterial growth positive were considered as contamination, whereas, (67.9 %) of ABU females were considered

to have true infection (Table 5). Urine culture is complex and prone to contamination by various bacteria (Xie et al., 2022). Urine sample contamination may be influenced by factors such as BMI, the interval since the last shower, and the degree of intimate hair removal (Pernille et al., 2019). Individuals with ABU may carry these bacteria for extended periods months or even years without showing any symptoms. Studies have shown that ABU can offer protective effects against the development of symptomatic UTIs (Wullt & Svanborg, 2016).

Combining bacteria microscopic examination of urine with the presence of pus and epithelial cells, Table 6, revealed high sensitivity and NPV. High sensitivity is critical in screening tests to minimize false negatives, whereas specificity is important for reducing false positives and avoiding the incorrect diagnosis of healthy individuals (Monaghan et al., 2021).

Contamination, which can result from the presence of vaginal flora, may lead to false positives, whereas false negatives can result from errors in sample collection (Gavrusev & Raguzin, 2023). It was revealed that all of the samples that have bacteria in urine had positive pus/epithelial cells which may increase the likelihood ton be infection (Zhang et al., 2023). A high sensitivity means lower disease cases are missed. The more sensitive a test, the less likely an individual with a negative result actually has the disease, and thus the greater the negative predictive value (Advani et al., 2024; Werneburg et al., 2023).

E. coli isolates were associated with true infection whereas the presence of *S. epidermidis* most commonly could be regarded as contamination (Table 8). The association of *E. coli* isolates with true infections is primarily due to their pathogenic characteristics and genetic factors. *E. coli* is responsible for over 80 % of UTIs with specific strains exhibiting virulence traits that enhance their ability to cause infections (Delcaru et al., 2016). Most UTI patients harbor the infecting *E. coli* strain within their intestinal flora, indicating that these bacteria can migrate from the gut to the urinary tract and cause infection (Nielsen et al., 2014). However, not all strains present in the fecal flora lead to infections, highlighting the importance of specific virulence factors and host conditions in determining infection outcomes (Sarowska et al., 2019). *S. epidermidis* is often regarded as a contaminant in clinical settings due to its ubiquitous presence on human skin and mucous membranes, however, its role as a significant pathogen, especially in nosocomial infections, has gained recognition (Burke et al., 2023). In addition to serving as a commensal organism, *S. epidermidis* frequently exhibits a dual lifestyle, acting as an opportunistic pathogen. It is among the most common causes of implant-associated infections, which are often antibiotic-resistant and biofilm-related, posing significant costs to both patients and the healthcare system (Oliveira et al., 2018).

Conclusions

Significant lower percentage in the history of recurrent UTI was found in ABU in comparison to UTI patients. Significant lower percentage of ABU had urine pH ranged from (4–6) in comparison to UTI patients. *E. coli* was the most frequently identified pathogen in both groups. The findings of this study highlight the diagnostic relevance of integrating clinical and microscopic parameters, such as the presence of bacteria and pus/epithelial cell distribution patterns (PEDP), in distinguishing between UTIs and ABU. The combination of urine culture results with microscopic examination and the type of isolated bacteria appears to enhance the accuracy in differentiating true infections from possible contamination. High sensitivity and PPV of the combining results of bacterial presence and PEDP was found. Combining PEDP and the type of isolated bacteria revealed that the *E. coli* isolates were associated with true infection whereas the presence of *S. epidermidis* most commonly could be regarded as contamination. These observations support the potential value of incorporating PEDP analysis as a complementary tool in the diagnostic workup of suspected UTI cases. Further research with larger sample sizes and diverse patient populations is recommended to validate the utility of this diagnostic approach in clinical practice.

Author contributions

Saja Hadi Abdul Hamza was responsible for study concept, Definition of intellectual content, Literature search, Clinical studies, Data acquisition, Data analysis, Statistical analysis, Manuscript preparation, Manuscript editing, Manuscript review and Guarantor. Suhad Hadi Mohammed was responsible for study concept, Study design, Definition of intellectual content, Clinical studies, Data acquisition, Data analysis, Statistical analysis, Manuscript preparation, Manuscript editing, Manuscript review and Guarantor.

Presentation at a meeting

No presentation at a meeting.

Research ethics approval statement

The study protocol was approved by the Ethical Committee at the College of Applied Medical Science/University of Kerbala.

Source(s) of support

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Conflicts of interest

The authors declare no conflict of interest.

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