Original Article

Histopathological Spectrum of Endometrial Changes in Perimenopausal Women with Abnormal Uterine Bleeding: A Cross-Sectional Study

Fareeha Khaliq Khan[1], Shahnilah Zafar[2], Aneeta Tajammul[3], Fariha Arshad[4], Sadaf Khurshid[5], Sanum Asif[6]

[1-4]Department of Obstetrics & Gynaecology, Fatima Memorial Hospital, Lahore, Pakistan; [5,6]Department of Obstetrics & Gynaecology, University of Lahore Teaching Hospital/ University College of Medicine and Dentistry, University of Lahore, Lahore, Pakistan

Corresponding Author: ***Dr. Fariha Arshad***, *Senior Registrar, Department of Obstetrics & Gynaecologist, Fatima Memorial Hospital, Lahore, Pakistan* **Email:** *anjumfariha36@gmail.com*

Abstract

Background: Abnormal uterine bleeding is common during perimenopause and may reflect functional, structural, premalignant, or malignant endometrial changes. Histopathological assessment is important for identifying endometrial pathology.

Objective: To determine the histopathological spectrum of endometrial changes in perimenopausal women with abnormal uterine bleeding and assess its association with age and selected clinical and diagnostic characteristics.

Methods: This descriptive cross-sectional study included 300 consecutive women aged 40–55 years at Fatima Memorial Hospital, Lahore, from 20thJanuary 2026 to 20th July 2026. Clinical assessment, complete blood count, coagulation profile, pelvic ultrasonography, and endometrial sampling by dilatation and curettage, Pipelle biopsy, or hysteroscopy-guided biopsy were performed. Histopathological findings were analyzed using IBM SPSS Statistics version 26.0; $p<0.05$ was considered significant.

Results: Mean age was 48.31±4.89 years; 217 (72.3%) women were older than 45 years. Irregular bleeding occurred in 141 (47.0%) and heavy menstrual bleeding in 113 (37.7%). Secretory endometrium was the commonest diagnosis (99, 33.0%), followed by endometrial polyp (60, 20.0%), disordered proliferative endometrium (45, 15.0%), chronic endometritis (44, 14.7%), hyperplasia without atypia (29, 9.7%), and carcinoma (12, 4.0%). Histopathological patterns were not significantly associated with age group ($p=0.539$), but were associated with ultrasonographic findings and biopsy method (both $p<0.001$).

Conclusion: Benign and functional endometrial changes predominated, although hyperplasia and carcinoma were also identified. Histopathological evaluation remains important in perimenopausal abnormal uterine bleeding.

Keywords: Endometrial hyperplasia, endometrial neoplasms, endometrium, perimenopause, bleeding

Received: 18-07-2026 1st Revision: 15-09-2026 2nd Revision: 25-09-2026 Accepted: 30-09-2026

How to cite: Khan FK, Zafar S, Tajammul A, Arshad F, Khurshid S, Asif S. Histopathological Spectrum of Endometrial Changes in Perimenopausal Women with Abnormal Uterine Bleeding: A Cross-Sectional Study. Avicenna J Health Sci. 2026;03(03): 115-122 **Doi:** https://doi.org/10.71158/ajhs.v3i3.213

Introduction

Abnormal uterine bleeding (AUB) is bleeding that differs from the expected menstrual pattern in frequency, regularity, duration, or volume. During perimenopause, variable ovarian function and anovulatory cycles can disturb normal endometrial proliferation and shedding, while reproductive endocrine and metabolic disturbances may further contribute to AUB.[1] The causes of AUB may be structural or non-structural and are classified by the International Fedration of Gynecology and Obstetrics (FIGO) using the Polyp, Adenomyosis, Leiomyoma, Malignancy and hyperplasia–Coagulopathy, Ovulatory dysfunction, Endometrial, Iatrogenic, and Not otherwise classified (PALM-COEIN) system. Structural causes are assessed mainly through imaging and, where appropriate, histopathology, whereas non-structural causes such as coagulopathy, ovulatory dysfunction, and iatrogenic factors require clinical and laboratory evaluation. Histopathology therefore complements rather than replaces the broader assessment of AUB.[1,2]

Histopathological findings in perimenopausal AUB include physiological endometrial patterns, inflammatory lesions, polyps, hyperplasia, and malignancy. Pakistani studies have reported considerable variation in their frequencies. Zubair et al. reported irregular bleeding in 48.6% and carcinoma in 5.5%, with secretory endometrium as the commonest pattern,[3] while another Pakistani biopsy series also demonstrated age-related variation in endometrial pathology.[4] Ultrasonography helps identify endometrial thickening and focal lesions before sampling.

Increased endometrial thickness has been associated with premalignant and malignant pathology in perimenopausal women.[5,6] Clinical assessment and ultrasonography can therefore guide tissue sampling, while histopathology establishes the final endometrial diagnosis.[5] Recent Pakistani studies have reported variable histopathological findings in perimenopausal women with AUB, but evidence from tertiary-care populations in Lahore remains limited.[3,7] Differences in referral patterns, patient characteristics, and diagnostic practices may influence the observed spectrum. Defining the local histopathological pattern therefore provides directly applicable evidence for this population.

It was hypothesized that benign and functional patterns would predominate, with fewer structural, premalignant, or malignant lesions. The objective was to determine the histopathological spectrum and assess its association with age and selected clinical and diagnostic characteristics.

Methods

This descriptive cross-sectional study was conducted from 20th January to 20th July 2026 in the Departments of Obstetrics & Gynaecology and Pathology, Fatima Memorial Hospital, Lahore. Ethical approval was obtained from the Institutional Review Board/ Ethical Review Committee (ERC ID: FMH-ERC-2026/PROG-014; Ref. No. FMH/ERC/2026/01-0941; approval 03 January 2026). All subjects provided written informed consent and granted their permission before enrolment and sampling. Sample size was calculated in OpenEpi for estimation of a single population proportion. Tabassum et al. reported endometrial hyperplasia in 25.9% of perimenopausal women with AUB.[7] Using an anticipated frequency of 25.9%, 95% confidence level, 5% absolute precision, and design effect of 1.0, the minimum sample size was 295. It was increased to 300 participants to ensure the required analyzable sample.

A total of 300 consecutive women aged 40–55 years with AUB were included by non-probability consecutive sampling. For this study, perimenopause was operationally defined as menstrual irregularity or amenorrhea for at least six but less than 12 months; the six-month minimum identified sustained menstrual transition, while amenorrhea ≥12 months represented established menopause. Women with known uterine fibroids, coagulopathy, liver disease, thyroid dysfunction, diabetes mellitus, current hormonal therapy or anticoagulant use, cervical or vaginal pathology, pregnancy, or recent obstetric complications were excluded to reduce recognized structural, systemic, endocrine, pharmacological, and pregnancy-related causes of AUB. IUCD use was not an exclusion criterion because the study described the histopathological spectrum of perimenopausal AUB rather than a single etiological category. Parity was recorded as nulliparous, multiparous, or grand multiparous. Socioeconomic status was operationally classified from self-reported monthly household income as low (<25,000 PKR), middle (25,000–50,000 PKR), or high (>50,000 PKR) for descriptive stratification. Participant selection is summarized in Figure 1.

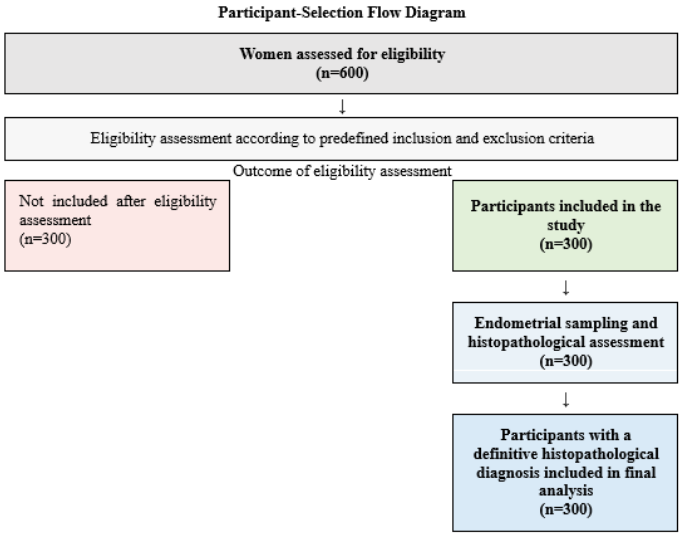


Figure 1: *Flow Diagram of Participant Selection and Inclusion in the Final Analysis*

A structured proforma recorded age, parity, socioeconomic status, bleeding pattern, laboratory findings, ultrasound findings, biopsy method, and histopathological diagnosis. Bleeding was categorized from the presenting history as irregular vaginal bleeding, heavy menstrual bleeding, or intermenstrual bleeding. Baseline investigations included complete blood count (CBC), coagulation profile, and transvaginal ultrasonography. Hemoglobin concentration was classified using WHO thresholds for non-pregnant adult women: normal ≥12.0 g/dL, mild anemia 11.0–11.9 g/dL, moderate anemia 8.0–10.9 g/dL, and severe anemia <8.0 g/dL. Coagulation profile was recorded as normal or abnormal according to the institutional laboratory reference range.

Transvaginal ultrasonography was performed before endometrial sampling to assess the uterus, endometrium, and focal intrauterine lesions. Endometrial thickness was measured in the sagittal plane at its thickest portion as the maximum double-layer thickness, excluding intracavitary fluid. For analysis, ultrasonographic findings were recorded as normal endometrium, thickened endometrium, endometrial polyp, or suspected fibroid. These investigations were performed before tissue sampling so that the sampling approach could reflect the clinical presentation and imaging pattern rather than the subsequent histopathological result.

Endometrial sampling was selected according to clinical and ultrasonographic findings. D&C was performed in the operating room under general anesthesia when definitive uterine evacuation was required or outpatient sampling was unsuitable or unsuccessful. Pipelle biopsy was performed as an outpatient suction-sampling procedure without routine cervical dilatation or general anesthesia. Hysteroscopy-guided biopsy was used when ultrasonography demonstrated a focal intrauterine lesion or when direct visualization was required so that tissue could be obtained from the identified lesion. These procedures reflected routine clinical decision-making rather than randomized allocation. No investigational drug, injection, or study-specific therapeutic intervention was administered.

Each specimen was placed immediately in 10% neutral buffered formalin and transferred to the pathology department. Tissue was routinely processed, paraffin embedded, sectioned, and stained with hematoxylin and eosin. Only final reports verified and authorized by consultant histopathologists were used for data collection; reports initially reviewed by trainees required consultant verification. Specimen adequacy was assessed before interpretation, and all 300 participants included in the final analysis had sufficient endometrial tissue for a definitive diagnosis. Diagnoses followed the WHO framework and were recorded as secretory endometrium, disordered proliferative endometrium, atrophic endometrium, chronic endometritis, endometrial polyp, endometrial hyperplasia without atypia, or endometrial carcinoma. Premalignant or malignant diagnoses were independently reviewed by a second consultant histopathologist before the final report was accepted for the study.

Because this was a descriptive cross-sectional study, no longitudinal research follow-up was planned. Each participant contributed one clinical assessment and one endometrial-sampling episode to the study dataset. Histopathology reports were subsequently managed through routine clinical care, and no scheduled research follow-up after tissue acquisition contributed additional outcome data.

Statistical Analysis

IBM SPSS Statistics version 26.0 was used for analysis. Categorical variables were summarized as frequencies and percentages; age was reported as mean±SD and median (IQR). Normality of age was assessed with the Shapiro–Wilk test. For secondary age-stratified analyses, participants were categorized as ≤45 and >45 years; the 45-year cut-off provided clinically interpretable younger and older strata within the predefined 40–55-year study population. Associations between histopathology and age group, bleeding pattern, ultrasound findings, and biopsy method, and between bleeding pattern and hematological variables, were evaluated using Pearson chi-square; an exact test was to be used when assumptions were not met. Cramer's V quantified effect size. Because age was not normally distributed across bleeding-pattern groups, Kruskal–Wallis was used for that comparison. For inferential analyses, histopathological diagnoses were grouped as functional/non-neoplastic (secretory, disordered proliferative, and atrophic), endometrial polyp, chronic endometritis, and hyperplasia/carcinoma. All tests were two-sided and $p<0.05$ was considered significant.

Results

The mean age was 48.31±4.89 years (median 49; IQR 44–53), and 217 (72.3%) women were >45 years. Multiparity was most frequent (164, 54.7%), while 92 (30.7%) were grand multiparous and 44 (14.7%) nulliparous. Low socioeconomic status was recorded in 130 (43.3%), 271 (90.3%) had a normal coagulation profile, 103 (34.3%) had thickened endometrium, and hysteroscopy-guided biopsy was used in 129 (43.0%). Parity differed significantly by age group ($\chi^2=151.463$, df=2, $p<0.001$; Cramer's V=0.711), while socioeconomic status, CBC category, coagulation profile, ultrasound findings, and biopsy method showed no significant age-group association (all $p>0.05$) (Table-1).

Table 1: *Baseline Demographic, Laboratory and Diagnostic Characteristics According to Age Group*

Characteristic	Category	Overall (n=300)	≤45 years (n=83)	>45 years (n=217)	χ^2 (df)	p-value	Cramer's V
Age, years	Mean ± SD	48.31 ± 4.89	41.75 ± 1.61	50.82 ± 3.04	–	–	–
	Median (IQR)	49 (44–53)	41 (40–43)	51 (48–54)	–	–	–
Age group	≤45 years	83 (27.7)	83 (100.0)	0 (0.0)	–	–	–
Age group	>45 years	217 (72.3)	0 (0.0)	217 (100.0)	–	–	–
Parity	Nulliparous	44 (14.7)	44 (53.0)	0 (0.0)	151.463 (2)	<0.001	0.711
	Multiparous	164 (54.7)	39 (47.0)	125 (57.6)			
	Grand Multiparous	92 (30.7)	0 (0.0)	92 (42.4)			
Socioeconomic status	Low (<25000 PKR)	130 (43.3)	35 (42.2)	95 (43.8)	0.444 (2)	0.801	0.038
	Middle (25000-50000 PKR)	126 (42.0)	34 (41.0)	92 (42.4)			
	High (>50000 PKR)	44 (14.7)	14 (16.9)	30 (13.8)			
Complete blood count	Normal	117 (39.0)	29 (34.9)	88 (40.6)	1.167 (3)	0.761	0.062
	Mild Anemia	106 (35.3)	30 (36.1)	76 (35.0)			
	Moderate Anemia	62 (20.7)	20 (24.1)	42 (19.4)			
	Severe Anemia	15 (5.0)	4 (4.8)	11 (5.1)			
Coagulation profile	Normal	271 (90.3)	76 (91.6)	195 (89.9)	0.200 (1)	0.655	0.026
	Abnormal	29 (9.7)	7 (8.4)	22 (10.1)			
Pelvic ultrasound finding	Normal	79 (26.3)	20 (24.1)	59 (27.2)	0.319 (3)	0.956	0.033
	Thickened Endometrium	103 (34.3)	29 (34.9)	74 (34.1)			
	Endometrial Polyp	72 (24.0)	21 (25.3)	51 (23.5)			
	Fibroid Suspected	46 (15.3)	13 (15.7)	33 (15.2)			
Biopsy method	Dilation and Curettage (D&C)	95 (31.7)	26 (31.3)	69 (31.8)	0.140 (2)	0.932	0.022
	Pipelle Biopsy	76 (25.3)	20 (24.1)	56 (25.8)			
	Hysteroscopy-guided Biopsy	129 (43.0)	37 (44.6)	92 (42.4)			

Irregular vaginal bleeding was the commonest presentation (141, 47.0%), followed by heavy menstrual bleeding (113, 37.7%) and intermenstrual bleeding (46, 15.3%). Age did not differ across bleeding patterns (H=2.096, p=0.351), and neither age group nor grouped histopathology was associated with bleeding pattern (p=0.147 and p=0.125). CBC category was strongly associated with bleeding pattern (χ^2=327.571, df=6, p<0.001; Cramer's V=0.739); all moderate and severe anemia occurred with heavy menstrual bleeding. Coagulation profile was also associated with bleeding pattern (χ^2=53.127, df=2, p<0.001; Cramer's V=0.421), with all 29 abnormal profiles in the heavy-menstrual-bleeding group (Table-2). These associations describe the distribution within the study population and were not intended to establish causality.

Table 2: *Association of Bleeding Pattern with Age, Hematological Profile and Grouped Histopathology*

Variable	Category	Irregular bleeding (n=141)	Heavy menstrual bleeding (n=113)	Intermenstrual bleeding (n=46)	Test statistic (df)	p-value	Cramer's V
Age, years	Median (IQR)	49 (45–53)	48 (43–53)	50 (46–53)	H=2.096	0.351	–
Age group	≤45 years	36 (25.5)	38 (33.6)	9 (19.6)	χ^2=3.837 (2)	0.147	0.113
	>45 years	105 (74.5)	75 (66.4)	37 (80.4)			
Complete blood count	Normal	117 (83.0)	0 (0.0)	0 (0.0)	χ^2=327.571 (6)	<0.001	0.739
	Mild Anemia	24 (17.0)	36 (31.9)	46 (100.0)			
	Moderate Anemia	0 (0.0)	62 (54.9)	0 (0.0)			
	Severe Anemia	0 (0.0)	15 (13.3)	0 (0.0)			
Coagulation profile	Normal	141 (100.0)	84 (74.3)	46 (100.0)	χ^2=53.127 (2)	<0.001	0.421
	Abnormal	0 (0.0)	29 (25.7)	0 (0.0)			
Histopathology group	Functional endometrium	81 (57.4)	56 (49.6)	18 (39.1)	χ^2=9.987 (6)	0.125	0.129
	Endometrial polyp	24 (17.0)	21 (18.6)	15 (32.6)			
	Chronic endometritis	16 (11.3)	19 (16.8)	9 (19.6)			
	Hyperplasia/carcinoma	20 (14.2)	17 (15.0)	4 (8.7)			

Secretory endometrium was the most frequent diagnosis (99, 33.0%), followed by polyp (60, 20.0%), disordered proliferative endometrium (45, 15.0%), chronic endometritis (44, 14.7%), hyperplasia without atypia (29, 9.7%), carcinoma (12, 4.0%), and atrophic endometrium (11, 3.7%) (Figure 2). Grouped histopathology was not associated with age (χ^2=2.164, df=3, p=0.539; Cramer's V=0.085), but was associated with ultrasound findings (χ^2=368.427, df=9, p<0.001; Cramer's V=0.640) and biopsy method (χ^2=170.581, df=6, p<0.001; Cramer's V=0.533). Because biopsy method was selected according to clinical and ultrasonographic findings, the biopsy-method association is subject to confounding by indication and should be interpreted descriptively. All 60 histological polyps corresponded to an ultrasonographic polyp finding and were sampled by hysteroscopy, while all 41 hyperplasia/carcinoma cases showed thickened endometrium.

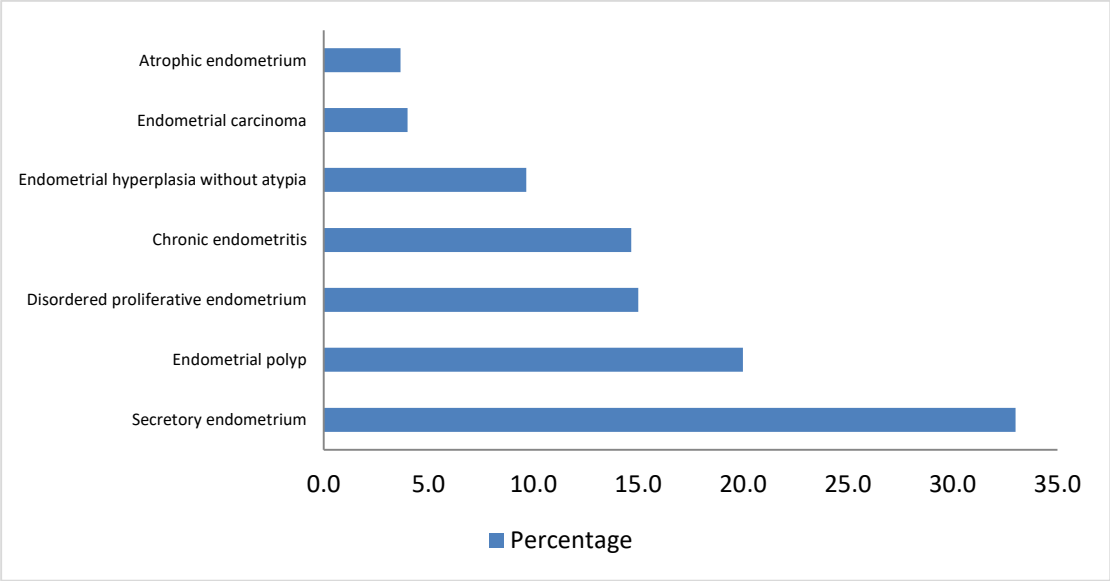


Figure 2: *Distribution of Histopathological Diagnoses among Perimenopausal Women Presenting with Abnormal Uterine Bleeding (n=300)*

Discussion

Benign and functional endometrial changes predominated. Secretory endometrium was most frequent (33.0%), followed by endometrial polyp (20.0%), disordered proliferative endometrium (15.0%), and chronic endometritis (14.7%). Lahore studies reported chronic endometritis in 12.2% with carcinoma in 3.2%,[8] and disordered proliferative endometrium in 12.6% with carcinoma in 4.1%.[9] Differences in sampling indications and targeted hysteroscopy may explain some variation, but local data consistently show a predominance of benign pathology with a smaller malignant burden.[8,9]

Irregular bleeding was the commonest presentation (47.0%), followed by heavy menstrual bleeding (37.7%) and intermenstrual bleeding (15.3%). Other Pakistani studies reported heavy bleeding in 49.9%[10] and menorrhagia in 42.0%.[11] Differences may reflect bleeding terminology, referral patterns, eligibility criteria, and the restriction of the present cohort to perimenopausal women. Functional patterns remainned important. Secretory endometrium accounted for one-third of cases, whereas Indian studies reported varying proportions of proliferative and secretory endometrium.[12,13] These differences may relate to cycle phase, ovulatory dysfunction, age distribution, participant selection, and timing or indication for biopsy. Ultrasonographic findings were significantly associated with histopathology ($p<0.001$), and all women with hyperplasia or carcinoma had a thickened endometrium. Similar relationships have been reported elsewhere.[14,15] Ultrasonography therefore helps identify women requiring tissue assessment, although histopathology remains necessary for definitive diagnosis. Biopsy method was also associated with histopathology ($p<0.001$), with hysteroscopy-guided biopsy used most frequently.[16,17] However, biopsy method was selected according to clinical and ultrasonographic findings, with hysteroscopy preferentially used for suspected focal lesions. This association is therefore subject to confounding by indication and should not be interpreted as evidence of diagnostic superiority of one sampling method. Endometrial polyps occurred in 20.0%, consistent with previous studies supporting ultrasonography and hysteroscopy for focal lesions.[18,19] Hyperplasia without atypia and carcinoma occurred in 9.7% and 4.0%, respectively, broadly comparable with international reports.[20,21] Histopathological patterns were not associated with age group ($p=0.539$), suggesting that age should not be considered in isolation when deciding on tissue assessment. The study is limited by its single-center cross-sectional design, non-probability sampling, possible selection and spectrum bias, exclusion of common comorbidities, residual confounding related to IUCD use, the small number of carcinomas, and confounding by indication in biopsy selection. Although endometrial thickness was measured clinically, only categorical ultrasound findings were available for analysis, preventing quantitative threshold assessment. Long-term outcomes could not be evaluated.

Future multicenter studies should use standardized endometrial-thickness measurements, predefined biopsy-selection criteria, and broader assessment of clinical and iatrogenic risk factors.[22]

Conclusion

Benign and functional endometrial changes predominated in perimenopausal women with AUB, with secretory endometrium the most frequent pattern. Hyperplasia and carcinoma were also identified. Histopathological patterns were not significantly associated with age group, indicating that age alone may not identify women with significant endometrial pathology.

Ethical Approval: The Institutional Review Board/ Ethical Review Committee, Fatima Memorial Hospitals & Allied Institutions, Lahore, Pakistan Approved this study vide. ERC ID: FMH-ERC-2026/PROG-014; Ref. No. FMH/ERC/2026/01-0941.

Conflict of Interest / Disclosure: Nil.

Funding Source: Nil.

Authors' Contribution:

FKK: Conception and design, critical revisions for important intellectual content

SZ: Conception and design, analysis and interpretation of data, critical revisions for important intellectual content

AT: Acquisition of data, drafting of article, critical revisions for important intellectual content

FA: Acquisition of data, conception and design, drafting of article, final approval of the version to be published

SK: Analysis and interpretation of data, final approval of the version to be published

SA: Analysis and interpretation of data, drafting of article, final approval of the version to be published

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