Is secretory change in endometrial hyperplasia acceptable in the absence of progestin therapy? What is the appropriate way to address an endometrial biopsy with secretory glandular changes and an increase in the gland-to-stroma ratio?

Q. Is secretory change in endometrial hyperplasia acceptable in the absence of progestin therapy? What is the appropriate way to address an endometrial biopsy with secretory glandular changes and an increase in the gland-to-stroma ratio?

A.November 2022—Secretory change superimposed on endometrial hyperplasia is well recognized, as are the challenges of making this diagnosis. Although secretory change is most commonly seen in the setting of progestin therapy for previously diagnosed endometrial hyperplasia, it may also be seen de novo due to the effect of progesterone, resulting from ovulation or pregnancy, on preexisting hyperplasia.

Glandular crowding in secretory endometrium is normal and is due to the glands coiling. The pattern of crowding is more or less uniform. Hyperplasia presents as a spatially distinct lesion with abnormal glandular crowding that is distinct from the background normal secretory endometrium.[1,2] The glands show architectural abnormalities, such as dilation, crowding, and branching. Severe glandular abnormalities, such as confluent or cribriform growth and complex papillary patterns, indicate carcinoma. The secretory changes in hyperplasia are nonuniform, weak, and patchy. Pseudostratification is frequently present, if only focally. Mitotic activity may also be focal as progestins suppress proliferative activity.[3]

Two small studies suggest that the Ki-67 proliferative index may be useful for distinguishing normal secretory endometrium from hyperplastic endometrium with secretory changes.[1,4] However, there is debate about how to best measure the Ki-67 index, and there is significant overlap in the Ki-67 proliferative index between secretory endometrium and non-atypical hyperplasia with secretory change.

I take a conservative approach to borderline cases by communicating the uncertainty of the diagnosis to the clinician and recommending resampling in six months. A small study involving patients who were diagnosed with simple hyperplasia with secretory change showed that virtually all patients demonstrated normal endometrium at six months or one year.[5]

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Q. I want to inquire about verification of target mean/ranges for hematology analytes. We run a control material 20 times and calculate statistics such as mean, standard deviation, and coefficient of variation. We also calculate total analytical error based on a formula (TAE = bias + 2 SD) and compare the TAE with the allowable total error recommended by CLSI and other sources. For example, if TAE for platelets (based on reading control material 20 times) is less than 25 percent (a CLSI recommended value), we accept the target range; otherwise, we reject it. However, since low concentrations of analytes are prone to a higher degree of variation, the aforementioned target range verification process frequently fails.

Is it necessary to accept or reject established target values based on total analytical error? Or is there an alternative way to do that?

A.It is not necessary to calculate total analytical error when establishing or verifying control ranges when implementing a new lot of control material. Repetitive analysis of the new lot to determine mean, standard deviation, and coefficient of variation is sufficient when establishing a new range for an unassayed control material or verifying a manufacturer's range for an assayed control material. Acceptability limits for verifying a new lot of control are established by the laboratory director based on the requirements for patient care and assay performance in that specific laboratory and are included in the lab's written procedure. Best practice is to use both an absolute value and a relative percentage when setting acceptability limits. The absolute limit will apply at low analyte concentrations, and the percentage limit will apply at high analyte concentrations.

Your lab is running into trouble at low platelet concentrations because it is using only a relative percentage limit (25 percent) and lacks an absolute limit for platelets. The lab could use an acceptability limit of target ±25 percent or $\pm 10 \times 10^3/\mu L$ ($10 \times 10^9/L$), whichever is greater. In other words, the limit would be ±25 percent for platelet counts of 40 or greater and $\pm 10 \times 10^3/\mu L$ ($10 \times 10^9/L$) for platelet counts of 40 or less.

An alternative is to use a limit of ±25 percent but confine the analysis to samples with a platelet count of $40 \times 10^3/\mu L$ ($40 \times 10^9/L$) or greater. This is the approach taken with CAP proficiency testing, which uses only samples with platelet counts of $50 \times 10^3/\mu L$ ($50 \times 10^9/L$) or greater and an acceptability limit of ±25 percent, as established under CLIA.

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Q. Should an accelerated APTT result be canceled for being clotted, even in the absence of a visible clot?

A.If an activated partial thromboplastin time is accelerated but a clot is not visible in the sample, the sample should be reinspected for the presence of a clot and a redraw for repeat testing should be considered.

In the appropriate clinical context (such as previous thromboembolic events, cancer, or pregnancy) and if the accelerated results can be reproduced, an accelerated APTT can be reported.[1,2] These scenarios are uncommon and should be considered on a case-by-case basis.

An accelerated APTT result from a sample with a visible clot should be canceled.

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