Technical Remarks 2

2.1 Procedures for Obtaining Endometrial Tissue

A *complete curettage* is the ideal method for optimal diagnostic evaluation of the endometrium. A *fractionated curettage* has additional advantages; it helps to localize the site and extent of malignancy and assists in evaluating endocervical changes that develop during hormonal therapy. For functional diagnosis in infertile patients, *endometrial biopsies* will usually suffice if properly taken with a single-stroke biopsy from the uterine fundus, and they offer the advantage that they can be repeated within the same menstrual cycle. Interpreting biopsies taken by brush or aspiration may prove quite difficult and inaccurate, except for advanced carcinomas.

2.2 Selection of the Proper Time for Curettage

In order to obtain optimal diagnostic results, the time for curettage must be carefully selected. In *infertile patients,* differential diagnosis of the various causes of sterility is best made shortly before the onset of menstruation. Only at this late time can the failure in endometrial differentiation be completely surveyed. In *menorrhagia* possibly due to irregular shedding, the best time for curettage is 5–10 days after the onset of menstruation, in order to recognize remnants of nonlysed mucosa. In *metrorrhagia,* curettage is best done without delay when much of the endometrium is still available for examination. With *amenorrhea* in a patient of reproductive age, pregnancy must be excluded before curettage is performed.

Clinical information is equally important to the pathologist, mainly about the patient's age, menstrual history, any hormone therapy, contraceptive device, endocrinologic disorders, and size and cavity of the uterus, including sonographic and/or hysteroscopic reports.

G. Dallenbach-Hellweg et al., *Atlas of Endometrial Histopathology*,
DOI: 10.1007/978-3-642-01541-0_2, © Springer-Verlag Berlin Heidelberg 2010

2.3 Preparation of the Endometrial Specimen

For *fixation*, a 4% neutral solution of formaldehyde is commonly used and is ideal for most of the diagnostic procedures involved in endometrial examination. *Routine staining* of all specimens should include hematoxylin-eosin (H & E) and a connective tissue stain, for instance van Gieson's solution. The latter is particularly important for recognizing endometrial polyps, or portions of them, and hyalinized placental villi. An additional periodic acid-Schiff (PAS) reaction may be helpful in detecting small amounts of glycogen or mucopolysaccharides in glandular epithelial cells. A reticulin impregnation can be useful for verifying tissue lysis or for distinguishing between various types of tumors. These four staining methods suffice for most questions arising in routine examination of the endometrial biopsy.

For subclassification of endometrial carcinomas, sarcomas, carcinosarcomas and other nonepithelial and nonmesenchymal tumors such as neuroectodermal tumors or lymphomas, *immunohistochemical stainings* may be helpful or needed. Among these, monoclonal antibodies against various cytokeratins, vimentin and carcinoembryonic antigen (CEA) are the most important for adenocarcinomas. In addition, immunostainings for the estrogen and progesterone receptor might be desired by the clinicans as a prerequisite for adjuvant hormonal treatment. In case of neuroendocrine differentiation of a carcinoma, chromogranin A, synaptophysin and CD56 are useful. Tumors of neuroectodermal origin (tumors of the PNET-group) typically express vimentin, CD99, NSE, Fli-1, and may partially express CD57, S-100, and neuroendocrine markers. Malignant lymphomas of the endometrium are preferentially B cell lymphomas (see p. 196 ff). Therefore, markers for lymphatic differentiation antigens such us CD3, CD5, CD10, CD11c, CD20, CD23, CD30, CD75 in combination with markers for BCL-2, BCL-6, Cyclin D1, Mum-1, IgM, IgD and immunoglobulin light chains should be applied. To clarify the dignity of a lymphatic proliferation, a molecular pathological clonality analysis with the polymerase chain reaction (PCR method) might be indicated. For all questional reactive processes and neoplastic lesions in the endometrium, the proliferation marker Ki-67 (MIB-1 antibody) and p53 should be applied to clarify the dignity and the clinical behavior. For the distinction between mucinous adenocarcinomas of the endocervix and those of the endometrium p16 may be a helpful additional marker (see p. 163).

2.4 Interpretation of Endometrial Specimens

Since the endometrial biopsy may contain admixtures of small pieces from various endometrial layers, its interpretation is more difficult than that of intact endometrium received with a surgically removed uterus. Only the functional layer is of diagnostic value in the recognition of functional disturbances. On the other hand, early adenomatous or carcinomatous changes may best be detected in the basal layer. The isthmus mucosa is unsuited for functional diagnosis; it may give a false impression of atrophy or functional deficiency (for differential diagnoses, see p. 43). Regions of necrosis in curettings may have various causes; they should always

be reported. Myomatous proliferations may indicate the presence of submucous leiomyomas as the cause of functional bleeding. If the endometrial biopsy contains only endocervical mucosa, the gynecologist may not have reached the endometrial cavity for various reasons, e.g., stenosis of the isthmus or endocervical canal. If fragments of tissue not occurring in the uterine cavity are found in the endometrial biopsy, e.g., fatty tissue, this finding should raise strong suspicions, if not being indicative, of a perforation of the uterine wall and should therefore always be reported (for further details, see Dallenbach-Hellweg 1987).

Artificial changes that should not be misinterpreted may be produced, e.g. when endometrial glands are squeezed by handling the curettage fragments and their lining epithelium intussuscepts to lie within the glandular lumen. Severe freezing artifacts occur when endometrial tissue in formalin solution is allowed to freeze slowly, as may happen when it is sent by mail in winter (Fig. 2.1).

In addition to a histopathologic diagnosis, the pathologist should always try to answer all questions raised by the gynecologist. In postmenopausal patients, there are generally two main reasons for the gynecologist to perform a curettage: either postmenopausal bleeding or a suspicious sonogram. Accordingly, he should explain why the patient was bleeding (e.g., polyps, hyperplasia, spotting from vascular breakage of atrophic vessels, or focal differences in receptor content). If the gynecologist has performed the curettage because of a suspicious sonogram with thickened endometrium and the endometrial specimen obtained is very small, it may not be representative of the lesion. The pathologist should discuss the discrepancy with the gynecologist and encourage him to repeat the curettage if the sonographic lesion is still present.

Fig. 2.1 Freezing artifact of the endometrium. Irregular empty spaces produced by ice crystals separate glands and push stromal cells aside. These spaces have no cellular lining (from Dallenbach-Hellweg 1987)

http://www.springer.com/978-3-642-01540-3

Atlas of Endometrial Histopathology
Dallenbach-Hellweg, G.; Schmidt, D.; Dallenbach, F.
2010, IX, 245 p., Hardcover
ISBN: 978-3-642-01540-3