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A COMPREHENSIVE LOOK AT COLPOSCOPY AND TARGETED BIOPSY AS CONFIRMATORY METHODS FOR DIAGNOSING CERVICAL PATHOLOGY

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In 2020, WHO approved the Global Strategy to Eliminate Cervical Cancer. One of the three targets of this strategy provides for at least 70% of reproductive age women to have access to highly effective methods of screening (diagnosis) for cervical cancer [1]. At the same time, the already presence of three alternative methods of cervical screening allows us to conclude that at this stage, not a single screening or diagnostic test is ideal. This is why we concider that only the combination of colposcopy with histopathological evaluation of material obtained from equivocal/aceto-white areas during targeted biopsy is currently the best confirmatory method in the diagnsis of the cervical pathology. At the same time, the issue of using an isolated, exclusively visual assessment of the cervix as a confirmatory diagnostic method remains one of the most controversial in cervical diagnostics. And this is mainly due to two problems with colposcopy. Firstly, colposcopy remains an extremely subjective diagnostic method, in which the frequency of false negative results (missed cases of even squamous intraepithelial

pathology/invasive cancer) ranges from 13% to 69% [2, 3] and directly depends on the competence of the specialist. And secondly, in a certain percentage of cases, cervical pathology is difficult to visualize during colposcopy due to its small size or localization in the cervical canal. So, to have a clinical diagnosis, we primarily rely on the histopathological diagnosis obtained after performing a colposcopically guided biopsy. Histopathology remains our fundamental diagnostic method, but, nevertheless, it also tends to overdiagnose precancerous conditions, due to the lack of clear criteria for determining which intraepithelial neoplasias indicate that the lesion will spread, and which indicate the possibility of regression/self-elimination or persistence. The histopathological definition of precancer is particularly prone to false-positive "high-grade lesions" (CIN2 and even CIN3/AIS) [4]. A biopsy, even obtained under colposcopic control, on the contrary, often leads to underdiagnosis and underestimation of the prevalence of precancerous lesions of the cervix [2]. Thus, the majority of histopathological premalignant lesions are found in women with LSIL or equivocal LSIL (ie, ASC-US), rather than with HSIL.В любом случае патоморфологическое заключение не позволяет дифференцировать ткань, изменённую инфекцией ВПЧ от нормальной шейки матки. It is in relation to the tactics of managing women with a positive HPV result that there is a major uncertainty that requires discussion and resolution. For example, according to American Society for Colposcopy and Cervical Pathology recommendations, not all HPV-positive women are subject to colposcopically controlled biopsy [5, 6]. Results from worldwide studies of invasive cancers, including adenocarcinoma, suggest that positive genotyping of HPV16 and HPV18 (and possibly HPV45) types is likely an indication for colposcopy and targeted biopsy to determine further management [7, 8]. At the same time, the importance of identifying other types of HPV, even from the group of carcinogenic ones, requires additional study. Thus, according to current recommendations in the United States, women with the highest risk genotypes identified (HPV16 and HPV18) are immediately sent for colposcopy, and the rest are

retested after a year [5], usually using the partial genotyping technique [9-11]. Of course, in these groups there is a risk of developing cervical precancer/cancer, but it is low and its colposcopic diagnosis can be difficult due to the ability to visualize it. As far as we know, there are no generally accepted recommendations (including those from the FDA) on what to do with women with questionable results from colposcopy, including indications for repeat testing for HPV and the timing of this testing. This is a pressing issue given the evidence that two successive negative HPV test is required to return women to general screening [12]. Thus, there is an urgent need to standardize the conduct of such a confirmatory diagnostic method as colposcopy. First, if only HPV-positive women were referred for colposcopy, pathologists could focus on identifying the histologic features of squamous or columnar atypia without being distracted by the rather subjective histologic features of HPV infection. Secondly, to reduce the number of patients inappropriately referred for colposcopy, it is necessary to improve colposcopic sensitivity. For example, through the standardization of colposcopic terminology, approval of the practice of multiple biopsies of questionable areas under colposcopic control and/or the introduction of Artificial Intelligence models for visual assessment of the coloscopic images [2,13,14].

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