Anal-rectal cytology and applications of the Bethesda System

The use of anal-rectal cytology is a relatively new method of screening for human papillomavirus (HPV) associated anal dysplasia. Its effectiveness as a diagnostic and screening tool is still being investigated, especially in high-risk populations, such as those infected with the human immunodeficiency virus (HIV) and men who practice receptive anal intercourse. It is important to note, though, that anal intraepithelial neoplasia (AIN) and peri-anal intraepithelial neoplasia (PAIN) are also common in women, especially those with cervical dysplasia. In the 2001 Bethesda System for Reporting Cervical Cytology, the editors acknowledged that Bethesda System terminology has been used for reporting anal-rectal cytology, since there are many parallels between cervical-vaginal and anal-rectal screening.

Cytologic sampling is generally done under direct visualization, although some have reported using methods similar to colposcopy or using a small anoscope to introduce the collection device. It is important, as with the cervix, to sample the transformation zone, which in the anus is the zone between the keratinized and non-keratinized epithelia. There is no specific evidence to support one collection device over another, although both Dacron fiber swabs and cytobrushes have been used. While both conventional smears and liquid-based cytologic preparations have been used, liquid samples have been shown to increase diagnostic yield.

Although the literature regarding what constitutes an adequate sample is sparse, the editors of the Bethesda System endorse a minimum adequacy cellularity of approximately 2,000-3,000 nucleated, unobscured squamous cells for conventional smears. For liquid-based specimens, this would be equivalent to 1-2 nucleated squamous cells per high-power field (hpf) for ThinPrep™ and 3-6 nucleated squamous cells per hpf for SurePath™. Anucleate squamous cells are not considered to be adequate for diagnosis. The presence of squamous metaplastic cells and/or rectal columnar cells indicates that the transformation zone has been sampled. Although many consider the presence of the anal-rectal transformation zone necessary for adequacy, it is not clearly stated as a requirement for an adequate sample per the Bethesda System 2001.

The cytomorphologic criteria used for the evaluation of anal-rectal smears are analogous to those for cervical-vaginal cytology. The major differences include (1) koilocytic or HPV-related changes may not be as pronounced even in low-grade dysplasia of the anal canal, although binucleation and multinucleation may be prominent, and (2) anal-rectal dysplasia often displays more cytoplasmic keratinization compared with cervical lesions (e.g. widespread parakeratosis and dyskeratosis).
Detection of HPV DNA in anal-rectal cytology specimens has been shown to be significantly associated with AIN. The majority of AIN lesions are positive for HPV types 6 and 11, and HPV type 16 has been shown to be associated with a higher risk of progression to carcinoma. Most studies have used a polymerase chain reaction (PCR) based method for HPV detection, so it is unclear if hybrid capture will be as useful in these specimens as in cervical cytology.

Although anal cytology seems to be a sensitive technique for identifying patients with HPV-related anal disease, on its own it is often unable to differentiate between those patients who simply have anal condylomata and those who also have AIN. A biopsy is usually necessary to make the latter diagnosis. This has important implications for use of anal cytology as a screening test. The pathogenesis of anal carcinoma and the natural history of AIN are unknown. While it is likely that anal tumors develop from AIN in a manner resembling the development of cervical carcinoma from cervical intraepithelial neoplasia, the regression rate of anal condylomata and AIN is not well established. Thus, anal cytology may be insufficient for triaging patients for anoscopy and biopsy.

At present, anal cytology seems to be a more useful technique for screening, diagnosis and follow-up of high-risk individuals, and detecting occult AIN may represent an effective cancer prevention strategy. However, using cytologic screening for AIN and guidelines for interpreting anal cytology have not been well established.