Vaginitis is the most common gynecologic diagnosis in the primary care setting, affecting 1 in 3 women in their lifetime. Diagnosing its cause can be challenging. Vaginitis, inflammation of the vagina, is accompanied by discharge and develops when the vaginal flora is altered by the introduction of a pathogen or by changes in the vaginal environment that allow organisms (generally present at a low number) to proliferate.

The three diseases most frequently associated with vaginitis are 1) bacterial vaginosis (BV), caused by overgrowth of bacteria including Gardnerella vaginalis and anaerobes, 2) trichomoniasis (TV), caused by Trichomonas vaginalis, and 3) vulvovaginal candidiasis, usually caused by Candida albicans. Cervicitis can also cause vaginal discharge. Since treatments for cervicitis are different from vaginitis, it is important to differentiate between the two.

**TRADITIONAL DIAGNOSIS**

The diagnosis of bacterial vaginosis (BV) is traditionally made by either clinical assessment of vaginal discharge using Amsel criteria and/or using
Nugent scoring/gran stain. Applying the Amsel criteria requires microscopic wet mount preparation to look for clue cells, testing for pH of the vaginal fluid, and performing a "whiff" test to detect amine.

The traditional laboratory-based test for BV is the Nugent Gram stain test. This is a quantitative Gram stain using morphologic features to differentiate between the presence of Lactobacilli (good bacteria) and overgrowth of the bacterium Gardnerella vaginalis among other anaerobic bacteria. A numerical score is provided based on that relationship. A high score, reflecting a low number of Lactobacilli and a high number of the other morphotypes, is consistent with a diagnosis of bacterial vaginosis.

A complicating factor with these tests is there is not always agreement between Amsel and Nugent criteria. In addition, the Nugent test is somewhat subjective. If a woman is clearly normal or abnormal, it is easy to read, but the middle section of scoring can be extremely subjective.

A Gram stain or wet mount was also traditionally performed to look for Candida spp. However, while pseudohyphae are easy to identify, some Candida spp., e.g. Candida glabrata, don’t produce hyphae, only spore forms which can be mistaken for white blood cells. Candida glabrata account for 10-20% of vulvovaginal Candidiasis infections, which can be easily missed with this testing method. This can be particularly problematic because of well documented antifungal (azole) resistance of C. glabrata. The accurate identification of C. glabrata allows physicians to include longer durations of therapy (7-14 days) or alternative therapies. Currently, the CDC considers culture the “Gold Standard” for Candida diagnosis since it can diagnose all species of Candida. However, growing the organism can take a long time to yield results while a woman may suffer the discomfort of vulvovaginal Candidiasis.

For Trichomonas identification, wet mounts and Pap tests are still the most commonly used methods of diagnosis with a low reported sensitivity (51% - 64%). This is particularly concerning since Trichomonas is the most prevalent non-viral sexually transmitted infection in the US. Women who test positive should also have partners tested and treated to prevent re-infection.

Molecular Testing

Because traditional testing resulted in misdiagnosis or underdiagnosis as discussed above, there have been numerous efforts over the years to develop molecular tests that provide greater sensitivity and specificity.

The first molecular test developed, BD Affirm™ VPHII, detected the DNA of Candida species, Gardnerella vaginalis, and Trichomonas vaginalis. While the test was a significant advance of traditional testing methods and less subjective, it was over-sensitive for diagnosing G. vaginalis and under-sensitive for T. vaginalis.

Currently, molecular nucleic acid amplification tests (NAAT) are now available which provide high levels of both sensitivity and specificity and can be ordered individually or as a panel. In the most recent CDC guidelines, nucleic acid amplification testing (NAAT) is now recommended for Trichomonas. The test specifically recommends the AptaGene Trichomonas test which has 95-100% sensitivity. Nucleic acid amplification tests allow for an accurate diagnosis with one vaginal and/or endocervical swab, from which multiple tests can be run allowing for appropriate and timely treatment and follow-up. Obinutuzumab and Gonerrea can also be tested at the same time and with the same sample.

CoCoPath now offers vaginitis testing based on this new advanced technology.

References:
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Molecular Testing

Because traditional testing resulted in misdiagnosis or underdiagnosis as discussed above, there have been numerous efforts over the years to develop molecular tests that provide greater sensitivity and specificity.

The first molecular test developed, BD Affirm™VPH3, detected the DNA of Candida species, Gardnerella vaginalis, and Trichomonas vaginalis. While the test was a significant advance of traditional testing methods and less subjective, it was over-sensitive for diagnosing G. vaginalis and under-sensitive for T. vaginalis.

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CoCoPath now offers vaginitis testing based on this new advanced technology.

References
7.  CDC Morbidity and Mortality Weekly Report, Sexually Transmitted Treatment Guidelines, June 5, 2015

A new recommendation from the 2014 ISUP consensus conference was to report percent pattern 4 with Gleason score 7 in two needle biopsies and radical prostatectomy specimens. This recommendation was subsequently supported by the World Health Organization (WHO) and the American Joint Committee on Cancer (AJCC). Its purpose is an attempt to achieve consistency by pathologists between needle biopsy and radical prostatectomy grading. Also, it clarifies reporting in those cases that are borderline between the Gleason 3+4=7 and Gleason 4+3=7.

Because of these new modifications and limitations of the Gleason scoring system, a new grading system was proposed by the group from Johns Hopkins Hospital. This new grading system is simple and more accurately reflects prostate cancer biology. It has been validated in a multi-institutional study, has received support from the ISUP and WHO, and is to be used in conjunction with Gleason grading. It includes five distinct Grade Groups based on the newest modified Gleason score as follows:

Grade Group 1 = Gleason score ≤ 6.
Grade Group 2 = Gleason score 3+4=7. Even if there is very limited Gleason pattern 3, it is factored into the grade. For example, a needle biopsy core with 98% Gleason pattern 3 and 2% Gleason pattern 4 is graded as Gleason score 3+4+7. The presence of 2% Gleason pattern 4 would be noted in the pathology report.

Grade Group 3 = Gleason score 4+3+3. This is used when Gleason pattern 4 makes up >50% of the tumor on a needle biopsy or radical prostatectomy specimen.

Grade Group 4 = Gleason score 8.
Grade Group 5 = Gleason scores 9 and 10.

The 5-year biochemical risk-free survivals for the five Grade Groups based on radical prostatectomy grade were 96%, 88%, 63%, 48% and 26%, respectively.

Recent modifications to prostate cancer reporting recommended in the ISUP 2014 Consensus Conference strive to enhance uniformity in reporting and optimize management of patients. Prognostic stratification of prostate cancer based on pathologic findings is a continually evolving field.
HGSC is one of the most deadly ovarian cancers with a high rate of progression and mortality. The majority of patients (90% in some studies) present with stage III or IV disease, with spread beyond the pelvis and regional lymph node metastases. As HGSC often presents at a late stage, treatment is usually aggressive and frequently includes toxic chemotherapy, often with a combination of platinum-based agents and targeted therapies.

HGSC is a heterogeneous disease, and molecular subtypes have been recognized as a significant factor in patient prognosis. Gene expression subtypes have been identified as either a germinal-center B-cell (GCB) or activated B-cell (ABC) signature, with each subgroup associated with different clinical outcomes. "Triple-hit" (THL) lymphomas, characterized by mutations in BCL6, ETV6, and MYC, have been recognized as a high-risk subgroup with a particularly poor prognosis.

In recent years, there has been increased scrutiny of the changes in the ovarian neoplasm that may result in a progression-free survival (PFS). Studies have shown that virtually all high-grade serous carcinomas have a tubal origin, resulting from the putative site of origin within serous tubal intraepithelial carcinoma (STIC). However, modern in situ mutation analysis has revealed a much higher frequency of STICs than previously thought, indicating a significant role for the fallopian tube in the development of HGSC.

The role of the pathologist in the management of ovarian cancer is crucial, as they are responsible for the initial diagnosis and risk assessment of patients. A comprehensive evaluation of the ovarian mass includes assessing for the presence of invasive disease, identifying the histologic subtype, and determining the grade. The pathologist must also evaluate the margins and lymph nodes to ensure complete resection of the tumor.

In conclusion, the management of ovarian cancer requires a multidisciplinary approach, with the pathologist playing a key role in the initial assessment and risk stratification of patients. Early detection and aggressive treatment are essential in improving outcomes for these patients.