advanced-stage disease, cure is expected. Close follow-up without adjuvant therapy of women with stage I tumors is reasonable if there is high confidence that the patient and health care team are committed to compulsive and careful follow-up, as chemotherapy at the time of tumor recurrence is likely to be curative.

Dysgerminoma is the ovarian counterpart of testicular seminoma. The 5-year disease-free survival is 100% in early-stage patients and 61% in stage III disease. Although the tumor is highly radiation-sensitive, radiation produces infertility in many patients. BEP chemotherapy is as effective or more so without causing infertility. The use of BEP following incomplete resection is associated with a 2-year disease-free survival rate of 95%. This chemotherapy is now the treatment of choice for dysgerminoma.

FALLOPIAN TUBE CANCER

Transport of the egg to the uterus occurs via transit through the fallopian tube, with the distal ends of these tubes composed of fimbriae that drape about the ovarian surface and capture the egg as it erupts from the ovarian cortex. Fallopian tube malignancies are typically serous tumors. Previous teaching was that these malignancies were rare, but more careful histologic examination suggests that many "ovarian malignancies" might actually arise in the distal fimbria of the fallopian tube (see above). These women often present with adnexal masses, and like ovarian cancer, these tumors spread relatively early throughout the peritoneal cavity and respond to platinum and taxane therapy and have a natural history that is essentially identical to ovarian cancer (Table 117-1).

CERVICAL CANCER

GLOBAL CONSIDERATIONS

Cervical cancer is the second most common and most lethal malignancy in women worldwide likely due to the widespread infection with high-risk strains of human papillomavirus (HPV) and limited utilization of or access to Pap smear screening in many nations throughout the world. Nearly 500,000 cases of cervical cancer are expected worldwide, with approximately 240,000 deaths annually. Cancer incidence is particularly high in women residing in Central and South America, the Caribbean, and southern and eastern Africa. Mortality rate is disproportionately high in Africa. In the United States, 12,360 women were diagnosed with cervical cancer and 4020 women died in 2014. Developed countries have looked at high-technology screening techniques for HPV involving automated polymerase chain reaction in thin preps that identify dysplastic cytology as well as high-risk HPV genetic material. Visual inspection of the cervix coated with acetic acid has demonstrated the ability to reduce mortality from cervical cancer with potential broad applicability in low-resource environments. The development of effective vaccines for high-risk HPV types makes it imperative to determine economical, socially acceptable, and logistically feasible strategies to deliver and distribute this vaccine to girls and boys before their engagement in sexual activity.

HPV INFECTION AND PREVENTIVE VACCINATION

HPV is the primary neoplastic-initiating event in the vast majority of women with invasive cervical cancer. This double-strand DNA virus infects epithelium near the transformation zone of the cervix. More than 60 types of HPV are known, with approximately 20 types having the ability to generate high-grade dysplasia and malignancy. HPV-16 and -18 are the types most frequently associated with high-grade dysplasia and targeted by both U.S. Food and Drug Administration–approved vaccines. The large majority of sexually active adults are exposed to HPV, and most women clear the infection without specific intervention. The 8-kilobase HPV genome encodes seven early genes, most notably *E6* and *E7*, which can bind to *RB* and *p53*, respectively. High-risk types of HPV encode *E6* and *E7* molecules that are particularly effective at inhibiting the normal cell cycle checkpoint functions of these regulatory proteins, leading to immortalization but not full transformation of cervical epithelium. A minority of woman will fail to clear the infection with subsequent HPV integration into the host genome. Over the course of as short as months but more typically years, some of these women develop high-grade dysplasia. The time from dysplasia to carcinoma is likely years to more than a decade and almost certainly requires the acquisition of other poorly defined genetic mutations within the infected and immortalized epithelium.

Risk factors for HPV infection and, in particular, dysplasia include a high number of sexual partners, early age of first intercourse, and history of venereal disease. Smoking is a cofactor; heavy smokers have a higher risk of dysplasia with HPV infection. HIV infection, especially when associated with low CD4+ T cell counts, is associated with a higher rate of high-grade dysplasia and likely a shorter latency period between infection and invasive disease. The administration of highly active antiretroviral therapy reduces the risk of high-grade dysplasia associated with HPV infection.

Currently approved vaccines include the recombinant proteins to the late proteins, L1 and L2, of HPV-16 and -18. Vaccination of women before the initiation of sexual activity dramatically reduces the rate of HPV-16 and -18 infection and subsequent dysplasia. There is also partial protection against other HPV types, although vaccinated women are still at risk for HPV infection and still require standard Pap smear screening. Although no randomized trial data demonstrate the utility of Pap smears, the dramatic drop in cervical cancer incidence and death in developed countries employing wide-scale screening provides strong evidence for its effectiveness. In addition, even visual inspection of the cervix with preapplication of acetic acid using a "see and treat" strategy has demonstrated a 30% reduction in cervical cancer death. The incorporation of HPV testing by polymerase chain reaction or other molecular techniques increases the sensitivity of detecting cervical pathology but at the cost of identifying many women with transient infections who require no specific medical intervention.

CLINICAL PRESENTATIONS

The majority of cervical malignancies are squamous cell carcinomas associated with HPV. Adenocarcinomas are also HPV-related and arise deep in the endocervical canal; they are typically not seen by visual inspection of the cervix and thus are often missed by Pap smear screening. A variety of rarer malignancies including atypical epithelial tumors, carcinoids, small cell carcinomas, sarcomas, and lymphomas have also been reported.

The principal role of Pap smear testing is the detection of asymptomatic preinvasive cervical dysplasia of squamous epithelial lining. Invasive carcinomas often have symptoms or signs including postcoital spotting or intermenstrual cycle bleeding or menometrorrhagia. Foul-smelling or persistent yellow discharge may also be seen. Presentations that include pelvic or sacral pain suggest lateral extension of the tumor into pelvic nerve plexus by either the primary tumor or a pelvic node and are signs of advanced-stage disease. Likewise, flank pain from hydronephrosis from ureteral compression or deep venous thrombosis from iliac vessel compression suggests either extensive nodal disease or direct extension of the primary tumor to the pelvic sidewall. The most common finding of physical exam is a visible tumor on the cervix.

TREATMENT CERVICAL CANCER

Scans are not part of the formal clinical staging of cervical cancer yet are very useful in planning appropriate therapy. CT can detect hydronephrosis indicative of pelvic sidewall disease but is not accurate at evaluating other pelvic structures. Magnetic resonance imaging (MRI) is more accurate at estimating uterine extension and paracervical extension of disease into soft tissues typically bordered by broad and cardinal ligaments that support the uterus in the central pelvis. Positron emission tomography (PET) scan is the most accurate technique for evaluating the pelvis and more importantly nodal (pelvic, para-aortic, and scalene) sites for disease.