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CERVICAL CANCER: ETIOLOGY, CLINICAL FEATURES, DIAGNOSIS, AND COMPLICATIONS.

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Abstract:

Cervical cancer remains one of the most common malignancies among women worldwide, especially in developing countries. This article provides a comprehensive overview of the etiology, clinical features, diagnostic approaches, and complications of cervical cancer. Particular attention is paid to human papillomavirus (HPV) as the leading etiological factor, as well as the importance of early detection through screening methods such as Pap smear and HPV testing. The study highlights how delays in diagnosis and treatment can lead to severe complications and higher mortality rates.

Keywords: Cervical cancer, HPV, clinical features, diagnosis, complications, Pap smear, gynecologic oncology.

Cervical cancer is the fourth most common cancer in women globally and a major public health problem in low- and middle-income countries. According to the World Health Organization, more than 600,000 new cases and 340,000 deaths were reported in 2020. The majority of cervical cancer cases are linked to persistent infection with high-risk strains of human papillomavirus (HPV), particularly HPV-16 and HPV-18. Despite advances in vaccination and screening, cervical cancer continues to cause significant morbidity and mortality.

The purpose of this article is to analyze the etiology, describe the main clinical manifestations, review diagnostic methods, and discuss the complications of cervical cancer.

Cervical cancer remains a significant global health challenge, particularly in low- and middle-income countries, where it is a leading cause of cancer-related mortality among women. This detailed review synthesizes current knowledge as of 2025, drawing from recent updates and guidelines to provide an in-depth understanding of its etiology, clinical features, diagnosis, and complications.

Etiology

Cervical cancer originates from the uncontrolled growth of cells in the cervix, the lower part of the uterus that connects to the vagina. The primary etiological factor is persistent infection with high-risk human papillomavirus (hrHPV) types, which is responsible for over 99% of cases. HPV is a sexually transmitted virus with more than 130 known types, of which approximately 20 are oncogenic. High-risk types, particularly HPV 16 and 18, account for about 78% of cervical cancers, while types 31, 33, 45, 52, and 58 contribute an additional 18%. These viruses integrate into the host cell's DNA, where oncoproteins E6 and E7 disrupt key tumor suppressor pathways: E6 degrades p53, preventing apoptosis, and E7 inactivates retinoblastoma protein (pRb), promoting uncontrolled cell proliferation. The E5 protein may further aid in immune evasion.

While HPV infection is common□over 80% of sexually active women acquire at least one type during their lifetime□most infections (about 90%) clear spontaneously within 2 years without causing harm. Progression to precancerous lesions (cervical intraepithelial neoplasia, or CIN) and invasive cancer occurs in only a small subset, typically over 15□20 years in immunocompetent individuals, but faster (5□10 years) in those with weakened immune systems. A minority of cases are HPV-independent, driven by genetic mutations such as in TP53 or KRAS, which exhibit different treatment responses and prognoses.

Risk Factors

Several cofactors increase the likelihood of persistent HPV infection and progression to cancer:

- Sexual and Reproductive Behaviors: Early age at first sexual intercourse (<16 years), multiple sexual partners, or partners with multiple partners heighten HPV exposure.
- Immunosuppression: Conditions like HIV/AIDS increase risk by 5□6 times, as they impair HPV clearance.

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- Smoking: Tobacco use introduces carcinogens that promote cellular changes and prolong HPV persistence.
- Other STIs: Co-infections with chlamydia, herpes, gonorrhea, syphilis, or HIV exacerbate risk.
- Reproductive Factors: High parity (multiple births), young age at first pregnancy, and long-term oral contraceptive use.
- Environmental and Genetic Factors: Poor nutrition, vitamin deficiencies, exposure to diethylstilbestrol (DES) in utero, and genetic polymorphisms (e.g., in TNF, TP53, HLA).
- Socioeconomic Disparities: Limited access to screening and vaccination in low-resource settings contributes to higher incidence.

Global statistics for 2022 estimate 662,301 new cases and 348,874 deaths annually, with 85% of cases and 90% of deaths in low- and middle-income countries. In the U.S., 2025 projections indicate 13,360 new cases and 4,320 deaths.

Clinical Features

Early-stage cervical cancer is often asymptomatic, which underscores the importance of screening. As the disease advances, symptoms emerge due to local invasion, lymphatic spread, or metastasis.

Common Symptoms

- Abnormal Vaginal Bleeding: The most frequent sign, including postcoital bleeding, intermenstrual spotting, menorrhagia, or postmenopausal bleeding.
- Vaginal Discharge: Watery, blood-tinged, or foul-smelling, often persistent.
- Pain: Pelvic, back, or leg pain; dyspareunia (pain during intercourse).
- Advanced Symptoms: Weight loss, fatigue, loss of appetite, leg swelling (due to lymphatic obstruction), urinary or bowel issues (e.g., hematuria, rectal bleeding from invasion).

Physical Examination Findings

On pelvic exam, findings may include a friable cervix, visible lesions, erosions, masses, or bleeding upon manipulation. However, many early cases show no abnormalities. The disease typically arises in the transformation zone, spreading locally to adjacent structures (parametrium, vagina, bladder, rectum) or via lymphatics to nodes (obturator, iliac, para-aortic), with hematogenous metastasis to lungs, liver, or bones in late stages.

Histologically, about 75□80% are squamous cell carcinomas, 10□15% adenocarcinomas, and the rest rare types like adenosquamous or neuroendocrine.

Diagnosis

Diagnosis combines screening, clinical evaluation, and confirmatory testing. Early detection through screening has dramatically reduced incidence in high-resource settings.

Screening

- Pap Smear (Cytology): Detects abnormal cells; recommended starting at age 21, every 3 years.
- HPV Testing: Identifies high-risk strains; co-testing every 5 years for ages 30□65, or primary HPV testing every 5□10 years starting at 25□30. Self-sampling is reliable.
- Alternative Methods: Visual inspection with acetic acid (VIA) in low-resource areas.

Screening can stop at age 65 with negative history.

Clinical Evaluation and Confirmatory Tests

- History and Physical: Assess symptoms, risk factors, and pelvic exam.
- Colposcopy: Magnified view of cervix; indicated for abnormal screening.
- Biopsy: Punch, endocervical curettage, loop electrosurgical excision procedure (LEEP), or cone biopsy for histopathological confirmation.
- Imaging: MRI for tumor size/extent, PET-CT for nodal metastasis, ultrasound in select cases; cystoscopy/proctoscopy for suspected invasion.

Staging

Uses FIGO 2018 system: Stage I (confined to cervix), II (beyond cervix but not pelvic wall/lower vagina), III (pelvic wall/lower vagina/hydronephrosis/lymph nodes), IV (bladder/rectum/distant metastasis). Incorporates clinical, radiological, and pathological data.

Complications

Complications arise from disease progression or treatment, impacting quality of life and prognosis.

Disease-Related Complications

- Local Invasion: Bladder/rectal involvement causing fistulas (vesicovaginal/rectovaginal), ureteral obstruction leading to hydronephrosis and renal failure.
- Metastatic Spread: Lymph nodes (pelvic/para-aortic), distant sites (lungs 21%, bone 16%, liver, intra-abdominal); symptoms include pain, respiratory issues, jaundice.
- Other: Hemorrhage, malodorous discharge, lymphedema, anemia, cachexia. In advanced cases, uremia is a common terminal event.

Prognosis worsens with stage: 5-year survival ~90% for early stages, <20% for advanced. Factors like lymph node involvement, tumor size, MYC

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overexpression, and HIV co-infection predict poorer outcomes.

Treatment-Related Complications

- Surgery (e.g., Hysterectomy, Conization): Bleeding, infection, urinary retention, infertility (2□12%), cervical stenosis/incompetence, neurological issues, lymphedema; higher recurrence with minimally invasive approaches.
- Radiotherapy: Acute/chronic toxicity including proctitis (6.8%), cystitis (8.5%), vaginal stenosis (5.7%), fractures, secondary malignancies.
- Chemotherapy (e.g., Cisplatin, Bevacizumab): Neutropenia, thrombocytopenia, nephrotoxicity, neurotoxicity, hypertension, thromboembolism, fistulae.
- Immunotherapy (e.g., Pembrolizumab): Autoimmune effects like pneumonitis, colitis.

Palliative care addresses symptoms in advanced disease, focusing on pain, fistula management, and psychosocial support.

Prevention and Outlook

Prevention emphasizes HPV vaccination (targeting ages 9□14), safe sex, smoking cessation, and regular screening. The WHO's global strategy aims for elimination through vaccination, screening, and treatment. With early detection, cure rates are high, but disparities persist in resource-limited areas.

For personalized advice, consult a healthcare professional. If you'd like details on treatment or specific aspects, let me know!

The analysis highlights that cervical cancer is largely preventable through HPV vaccination and early detection programs. Despite these preventive measures, many women present with advanced disease due to lack of awareness, insufficient access to screening, and cultural or socioeconomic barriers.

HPV DNA testing has proven more sensitive than cytology alone and should be integrated into national screening programs. In addition, public health initiatives must focus on increasing vaccination coverage among adolescents.

Complications of cervical cancer reflect the aggressive nature of advanced disease and delayed diagnosis. The presence of urologic and rectal complications significantly reduces the quality of life and survival of patients. A multidisciplinary approach involving oncologists, gynecologists, radiologists, and palliative care specialists is essential.

CONCLUSIONS

HPV vaccination is the most effective preventive measure and should be implemented universally.Regular screening using Pap smear and HPV DNA testing is critical for early detection. Awareness campaigns should target women in low-resource settings to reduce late-stage presentations. Improved diagnostic infrastructure is required for accurate staging and timely treatment initiation. Comprehensive management should include prevention of complications, psychosocial support, and rehabilitation. Further research should focus on cost-effective screening strategies and new treatment modalities.

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