33 | PAPILLOMAVIRUSES

33.1 | Disease agent

- Human papillomavirus (HPV)

33.2 | Disease agent characteristics

- Family: Papillomaviridae; Subfamily: *Firstpapillomavirinae*; Genus: *Alphapapillomavirus*
- Virion morphology and size: Nonenveloped, icosahedral nucleocapsid symmetry, spherical particles, 52–55 nm in diameter
- Nucleic acid: Circular, double-stranded DNA, 7.9 kb in length with unidirectional transcription
- Physicochemical properties: Sparse information; presumably susceptible to 0.3% povidone-iodine, to polysulfated and polysulfanated compounds, and to dilute solutions of sodium dodecyl sulfate; ether-resistant, acid-stable, and heat-stable

33.3 | Disease name

- Nongenital skin warts.
- Epidermodysplasia verruciformis.
- Anogenital warts (condylomas).
- Nonmelanoma skin cancer.
- Cervical dysplasia and cancer.
- Anogenital dysplasia and cancer especially in HIV-infected MSM.
- Papillomas of respiratory tract, larynx, mouth, or conjunctiva that includes oral and laryngeal cancers.

33.4 | Priority level

- Scientific/Epidemiologic evidence regarding blood safety: Theoretical
- Public perception and/or regulatory concern regarding blood safety: Absent
- Public concern regarding disease agent: Low/Moderate

33.5 | Background

- Stable in population.
  - HPVs in the United States are so common that nearly all sexually active men and women will acquire infection during their lives. Subclinical infections are most common.
  - Most infections resolve spontaneously.
- HPVs are strictly species-specific and restricted to sites with stratified squamous epithelia that are cornified (skin) or noncornified (genital and nongenital mucosa).
  - The various HPV types (of at least 210) have somewhat specific tissue tropisms and disease associations.
- High-risk types found most frequently in association with cervical cancer.
- New disease associations have been recognized over time.

33.6 | Common human exposure routes

- Infection of basal keratinocytes primarily through wounds or skin abrasions
- Contact with infected tissue or contaminated objects
- Autoinoculation from site to site
- Sexual intercourse
- Delivery through infected birth canal

33.7 | Likelihood of secondary transmission

- High by direct contact, especially in older children and young adults
- High by sexual contact

33.8 | At-risk populations

- Older children and young adults (nongenital skin warts)
- Persons who are sexually active with multiple partners
- Adult patients with Fanconi anemia
- HPV-infected persons exposed to sun or UV light
- Increased susceptibility in immune-suppressed patients

33.9 | Vector and reservoir involved

- None

33.10 | Blood phase

- One study found HPV DNA in PBMCs, serum, and plasma of patients with cervical and neck cancers and in PBMCs from 3 of 19 (15%) healthy blood donors.

33.11 | Survival/persistence in blood products

- Unknown

33.12 | Transmission by blood transfusion

- In a study of 57 HIV-infected children, seven of eight who were HPV DNA positive, had a history of blood and/or plasma derivative transfusion as the cause of their HIV infection.
- Bovine papillomavirus type 2 has been transmitted through blood via intramuscular inoculations.
- In rabbit and mouse models, blood from parenterally infected animals was able to transmit infection to uninfected animals.

33.13 | Cases/frequency in population

- Of over 200 HPV types that have been identified, 13 have been strongly or moderately associated with cervical cancer.
- 2%–3% of women undergoing routine Pap smear have abnormal cytology, the majority of which is associated with HPV.
- The peak prevalence is seen in women 15–25 years of age, which may be 5%–40%, and then declines with increasing age.

33.14 | Incubation period

- In experimental inoculation of human subjects with extracts of cutaneous warts, incubation periods were most commonly 3–4 months, but with a range of 6 weeks to 2 years.

33.15 | Likelihood of clinical disease

- Varies with the particular type

33.16 | Primary disease symptoms

- The typical skin lesion, the wart, is easily recognized, particularly when in its most common location, the hands or feet (plantar warts). Most spontaneously regress.
- Anogenital warts are also easy to recognize but may be internal and only observed following an appropriate examination. These can be recurrent, sometimes painful, and difficult to treat but may spontaneously remit.
- Cervical intraepithelial neoplasia and cervical cancer are often asymptomatic and only detected on routine examination, primarily after cervical cytology has been assessed. Symptoms, such as bleeding and pain, appear as the cancer expands and disseminates.
- Other symptoms depend on location of the papilloma and can include vocal disturbances from laryngeal papillomatosis, pulmonary dysfunction from respiratory tract involvement, and local discomfort from oral lesions.

33.17 | Severity of clinical disease

- Generally benign, except that it can lead to cervical and anal cancers (most common cause of these malignancies), and benign papillomatosis can be debilitating because of location (e.g., laryngeal disease).

33.18 | Mortality

- Highly dependent on genotype and whether cancer ensues. Mortality is low, even in cancer patients if methods for early detection are employed (e.g., Pap smears)

33.19 | Chronic carriage

- Chronic infection is typical although there is late spontaneous clearance. However, chronic viremia is unlikely. HPV may be carried in WBCs that intermittently seed the bloodstream.

33.20 | Treatment available/efficacious

- There are a variety of treatments for disease caused by HPV, ranging from simple intralesional or parenteral interferon or destructive therapy for genital warts, to surgery, laser excision repair, cryotherapy, or chemotherapy for high-grade dysplasia for cervical infection or cervical cancer. Successful therapy is associated with the disappearance of HPV DNA.
- Therapeutic vaccines have had only limited success.

33.21 | Agent-specific screening question(s)

- No specific question is in use; some donors with HPV-associated cancer may be temporarily excluded by current donor history questions.
- Not indicated because transfusion transmission has not been demonstrated.
- No sensitive or specific question is feasible.

33.22 | Laboratory test(s) available

- No FDA-licensed blood donor screening test exists.
- Tissue diagnosis is usually by nucleic acid hybridization or extraction of DNA followed by NAT. Southern blots of extracted DNA are the gold standard and allow for subtyping.
- Electron microscopy for viral particles or immunologic detection of viral capsid antigens has low sensitivity. Detection in PBMCs is generally performed by PCR or nested PCR.

33.23 | Currently recommended donor deferral period

- No FDA Guidance or AABB Standard exists.
- There is no indication for deferral of individuals with known HPV infection unless presenting with a deferrable malignancy.

33.24 | Impact on blood availability

- Agent-specific screening question(s): Not applicable
- Laboratory test(s) available: Not applicable

33.25 | Impact on blood safety

- Agent-specific screening question(s): Not applicable
- Laboratory test(s) available: Not applicable

33.26 | Leukoreduction efficacy

- Unknown, but if virus is carried in peripheral blood, it is probably within PBMCs, and thus leukoreduction would be expected to have some impact.

33.27 | Pathogen reduction efficacy for plasma derivatives

- This is a nonenveloped virus and thus would not be affected by solvent-detergent treatment.
- No data from model viruses.

33.28 | Other preventive measures

- Pathogen reduction strategies based on inactivation of DNA should be effective.
- Highly immunogenic vaccines targeting up to 9 high-risk HPV types causing the large majority of cervical cancer have resulted in nearly complete prevention of HPV-associated genital warts, dysplasia and cancer in vaccinated cohorts.

SUGGESTED READING

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