Acta Microbiologica et Immunologica Hungarica, 48 (3–4), pp. 511–517 (2001)

SEXUAL AND NON-SEXUAL TRANSMISSION OF HUMAN PAPILLOMAVIRUS

(A SHORT REVIEW)*

JUDIT CZEGLÉDY

Department of Microbiology, University of Debrecen, Medical Faculty, Debrecen, Hungary

(Received: March 22, 2001; accepted: March 30, 2001)

Benign tumors and lesions of the anogenital tract are caused by human papillomaviruses (HPVs). They are also major risk factors for cervical cancer. Introduction of the polymerase chain reaction (PCR) revealed that HPV infections are much more common among young asymptomatic women than it had been previously suspected.

The side-specificity of genital HPVs led to the assumption that HPVs were primarily transmitted by sexual contact. However, since HPVs have been detected in virgins, infants/children and juvenile laryngeal papillomatosis was shown to be caused by these viruses, it became acknowledged that HPVs may be transmitted by other – non-sexual – routes as well.

The evidence for sexual and different non-sexual routes of transmission of HPVs will be reviewed here.

Keyword: human papillomavirus transmission

Sexual transmission of human papillomavirus

A lot of epidemiological studies analyse genital HPV infections in a large number of cytologically normal cervical smears from women aged 15–70 years, using different techniques [1–7].

PCR detects latent, subclinical and clinical HPV manifestations, so the most reliable screening method is the combination of general-primer-mediated and type-specific PCR (GP-PCR/TS-PCR). With these tests an age-dependency was shown in

* This paper was written to commemorate to the fiftieth anniversary of the foundation of the Hungarian Society for Microbiology.

1217-8950/2001/$ 5.00

HPV prevalence with a maximum between 20 and 24 years: statistically significant difference in HPV prevalence was found between women aged 15–34 years and women aged 35–55 [8]. Transient genital HPV infection (fluctuation, clearance) was also documented [9]. Few cases of childhood condylomata acuminata have evidence of sexual abuse [10].

Non-sexual transmission of human papillomaviruses

Vertical transmission of human papillomaviruses

Periconceptual transmission

Transmission of certain viruses to the fetus occurs most frequently during their viraemic phase by spread of infected leukocytes and macrophages. Chorionic and placental tissues may be infected by direct spread of the virus to amnionic cells that are subsequently ingested by the fetus.

The existence of a viraemic phase has not been confirmed in case of HPV infection: haematogenous transmission of the virus to the embryo/fetus and their compartments is unknown. No viral DNA was found in any chorionic villi samples collected by transabdominal sampling at the 22nd week of gestation, however, 25% of patients carried HPV in the cervix [11]. In some early first-trimester pregnancies our results confirm the HPV infection of embryonic and trophoblastic tissues even in HPV negative women (unpublished observation). The presence of HPV DNA was also demonstrated in syncytiotrophoblastic cells of first-trimester spontaneous abortion materials [12]. Earlier studies showed that Percoll-purified human sperm cells could carry HPV DNA and RNA [13, 14].

These observations indicate that the earliest HPV infection of human being might occur prior to implantation, possible by fertilization of the oocyte by an HPV carrying spermatozoon. According to our study more embryonic than trophoblastic tissues carried HPV, thus the subsequent virus-spreading might originate from the embryo.

Prenatal transmission

Several studies have reported an increase of the prevalence of genital HPV infections during pregnancy [15, 16, 17]. Hormonal changes may encourage increased transcription mediated by the glucocorticoid response elements in the non-coding

region of HPVs. Also a higher prevalence of the virus may be due to the natural transient immunosuppression, which accompanies pregnancy.

Transmission from mother to the fetus may occur in clinically apparent, subclinical and latent maternal infection. Anatomic changes in the lower uterine segment of a genital HPV infected women far gone with child and rupture or premature rupture of the membranes might lead occasionally to prenatal infections.

In third-trimester pregnancies detection of HPV DNA in amnionic fluid, cord blood and in the mucosa of neonates born by Cesarean section present evidence for a possible ascending infection [18]. A case report describes the prenatal transmission of the cutaneous HPV types 5 and 8 [19]. The delivery was by Cesarean section and amnionic fluid was taken prior to the rupture of membranes. The same variants of the virus detected in the skin of newborn were disclosed in the amnionic fluid and in the placenta.

All these variants were found in cervical scrapes – not in peripheral blood mononuclear cells – taken from the mother and in the mouth and hair of the child, examined 6 months after birth.

Perinatal transmission

It is probable that passage of the neonate through an infected birth canal or birth canal with HPV lesions explains both the source and route of HPV detection in infants [20]. However, the risk of perinatal transmission seems to be relatively low, as indicated by a prospective cohort study [21].

Women who transmit infection to their infants have significantly greater quantities of viral DNA in cervico-vaginal samples than those who do not so [22]. Several studies have revealed that HPV DNA positive specimens of infants may merely reflect passive contamination with infected maternal cells, rather than an established – transcriptionally active – infection in the infant. However, several studies have proved that HPV DNA positivity of samples on the external genitalia and/or in the buccal cavity of 24-hour-old infants, persisted in high percentage until they were 6 weeks, six month and 2 years of age, respectively. These observations suggested that replicative infections had been established usually with the same HPV genotype [23, 24, 25, 26].

Horizontal transmission of human papillomaviruses

Some viruses (e.g. HIV) may be transmitted via breast milk, but it seems unlikely that "non-bloodborn" HPVs are present in breast milk. Also there is no evidence that these viruses are associated with breast lesions.

However, a child bathing with her mother having HPV condylomata may be infected and later presents the same lesions [27]. The virus may also be transmitted via

HPV-contaminated fomites and clothing of relatives/friends [28, 29]. Numerous results also suggest that horizontal buccal infection may occur in infants and children of HPV negative mothers [30, 31].

Genital HPV infection of children

PCR studies have indicated that the prevalence of HPV type 16 DNA in the buccal cavity of children may range from 0.25–52% and ~ 17% in vulval swabs [32, 33, 34, 35, 36]. HPV16 DNA was detected in buccal swabs of 3–11 years old children in 52% using nested PCR. In some cases a transcriptionally active infection was also demonstrated [37]. Serological studies support childhood infection using HPV16 virus-like particles, as antigen. Enzyme immunoassay (EIAs) – with different HPV16 peptides, fusion proteins – have shown seroprevalence of between 4–44% among children between 0–13 years [36, 38, 39, 40–42].

In the future HPV infections – transmitted mostly by vertical routes – might be prevented by prophylactic HPV vaccines given at birth.

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