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Human papillomavirus (HPV) and cervical cancer — the facts



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Introduction

Worldwide, after breast cancer, cervical cancer is the second most common cancer that affects women. In 99.7% of all cases, cervical cancer results from a history of persistent infection by a ‘high risk’ subset of a family of viruses called human papillomavirus – or HPV – (Walboomers, 1999). Some cancer-causing HPV types (particularly HPV-16) are also believed to cause a substantial number of other genital cancers, as well as some cancers of the mouth, throat and anus.

To support you in the delivery of informed care to patients and clients, this publication gives you up-to-date and comprehensive information about HPV, its links to cervical cancer and the latest developments related to the identification and treatment of HPV.

Practice points

The following key points are essential to understand and communicate in your practice:

- ◆ HPV infection is almost a normal consequence of sex
- ◆ in most women, HPV will cause no long-term harm and will be eradicated by the immune system
- ◆ genital warts do not cause cervical cancer
- ◆ there are no visible physical signs of high-risk HPV; you can only tell you have it by undergoing specific tests

- ◆ regular smear tests will pick up the changes which could progress to cancer
- ◆ two vaccines to protect against high risk HPV types have been developed; one has already been licensed and the second is likely to be in the next few months. They are expected to be given, in the first instance, to girls before they start having sex.

Types of cervical cancer

There are two main types of cervical cancer; squamous cell carcinoma (SCC) and adenocarcinoma. SCC is the most common and accounts for approximately 90% to 95% of all cervical cancers.

The precursor lesions for SCC are identified as dyskaryosis (cell change) through cervical smear tests, and through colposcopy and biopsy as cervical intraepithelial neoplasia (CIN) – the abnormal growth of precancerous cells in the cervix.

There are three distinct CIN classifications or grades for categorising abnormal (pre-cancerous) cell growth; CIN 1, CIN 2 and CIN 3. These generally correspond to the smear results of mild (CIN 1), moderate (CIN 2) or severe dyskaryosis (CIN 3) respectively.

In most women it takes many years to progress from a normal cervix to CIN 3. However, it should be noted that not all women with CIN 3, even if left untreated, will go on to develop cancer (McIndoe, 1984). The challenge is in identifying those women who have the potential to progress to cancer and those who do not. As a result, we treat all

women with CIN as if they have the potential to develop cervical cancer.

Adenocarcinoma is far more difficult to detect at a pre-cancerous stage. Smear testing is unreliable at picking-up the glandular changes that indicate that an adenocarcinoma could develop.

Human papillomavirus (HPV)

As long ago as 1995 the causative association between HPV and SCC was recognised (International Agency for Research on Cancer, 1995). The HPV family of viruses contains more than 100 types; some HPVs cause benign skin warts, or papillomas, for which the virus family is named.

Approximately 40 HPV types affect the genital area. They can be sub-divided into those that are low risk for cervical cancer (such as HPV-6 and HPV-11, which are responsible for causing genital warts) and those which are high risk for cervical cancer. The high risk types occurring most frequently in cervical cancer include HPV-16 and HPV-18; together these account for over 70% of SCCs (Munoz, 2005). HPV-18 is also thought to account for approximately 50% of all adenocarcinomas.

The identification of HPV

Testing positive for a high risk HPV does not guarantee that a woman will go on to develop cervical cancer. It does, however, indicate that she is at greater risk than a woman who tests negative. In most women, the immune

system successfully deals with any initial HPV infection. This happens before the HPV can completely incorporate itself into the cell DNA and disrupt cell reproduction, leading to CIN.

Confirmation of the presence of high risk HPVs can only be achieved using bio-molecular HPV testing. There is currently only one commercially available HPV test – Digene's Hybrid Capture II. HPV testing is not routinely available on the NHS but may be done privately or as part of a research programme. Outside the UK, however, this test may be performed during a routine gynaecological check-up.

Reporting an HPV identified through a smear test or seen at colposcopy is not always valuable, as there is no way of identifying if the HPV is a high risk or low risk strain – it's like telling someone they have a mole which might become a malignant melanoma, but there's no way of confirming this potential until the changes start to occur.

HPV and cervical cancer

Around 30 HPV types are transmitted through sexual contact, including the high risk HPVs implicated in cervical cancer. An increase in the incidence of genital HPV infection occurs when individuals begin to engage in sexual activity. The great majority of genital HPV infections never cause any overt symptoms and are spontaneously cleared by the immune system in a matter of months. It's not known whether the immune system clears

the HPV virus from the body, or whether the virus remains but causes little harm.

Genital HPV infection is very common and all sexually active women are at risk. Indeed, HPV is so common that it can almost be considered a normal consequence of having sex. Estimates suggest that between 50% and 79% of all women who have had sexual intercourse have a lifetime risk of becoming infected with one or more of the sexually transmitted HPV types (Koutsky, 1997). Often the infection is transient and it is only when it becomes persistent, and in a small minority of women, that this may lead to CIN.

It's not certain why in some women, persistent HPV infection causes more serious problems than in others. There are, however, identified co-factors which increase the risk of cervical cancer. These include smoking, having more than four full term pregnancies (Castellsague, 2003), experiencing first intercourse at an early age, having multiple sexual partners, or having intercourse with a male partner who has had multiple sexual partners, and immune suppression.

There is limited evidence to suggest that four or more years of oral contraceptive pill use may have a role (Castellsague, 2003). It's more likely that this is due to an effect on the progression of disease in women with HPV, rather than because of an increased risk of infection (Koutsky, 1997).

The psychological impact of HPV infection

Women who have a positive HPV test frequently express surprise and anxiety about the link to cancer and the stigma of sexually transmitted infection or STIs (McCaffery, 2003 and 2006). These feelings of guilt and shame are closely linked to concerns about transmission, and disclosure to current or future sexual partners.

Women frequently demonstrate confusion between high-risk HPV and genital warts. This bewilderment can be exacerbated by the use of the phrase 'wart virus', a term which women find both baffling and very upsetting. Referring to someone as 'HPV positive' can also lead to misunderstanding and confusion with HIV.

The way information about HPV is delivered, and the quality of this information can impact on a woman's psychological response to a diagnosis of HPV infection (McCaffery, 2005). If health care professionals provide clear accurate information when speaking to women, this can considerably reduce both the anxiety they experience and the possible stigma associated with HPV.

Women should be assured that having sex just once exposes them to many of the HPVs, and that this exposure to HPV should be viewed as a normal occurrence. They will need it explained that most HPV infections clear of their own accord and will not cause cancer.

It will also be important to explain that the 'type' of HPV that causes genital warts is low risk, and therefore unlikely to cause cancer.

HPV transmission

Transmission of HPV infection occurs through skin-to-skin contact; in the case of genital HPVs this transition takes place as a result of sexual activities. Some low risk HPV types, such as genital warts have however been found where an individual has not had a sexual experience.

There is also evidence to suggest that high risk genital HPV has been detected in non-genital areas such as the mouth, oropharynx (back of the throat) and conjunctiva (the thin transparent tissue that covers the outer surface of the eye) (Cason, 1996). It would therefore seem that HPV can be transferred during oral sex and may also be transferred via the hands, but at this moment this remains unproven.

It is usually impossible to identify from whom the virus was initially contracted. It is also not known how long it takes for the virus to cause neoplasia, but it is thought to take many years.

HPV has fewer implications for carcinogenesis in males. Research has shown clusters of cervical and penile cancer in some geographical regions but penile cancer is rare; in 2005, there were only 400 reported new cases in the UK and only 1 in 10 of these was associated with high-risk HPV (Cancer Research UK, 2006).

Treatment and prevention of HPV

Condoms offer a degree of protection against the initial transmission of HPV infections. However, as HPV has a field effect and is present over all the genitalia, this protection is not comprehensive or complete.

There is currently no medical treatment for HPV, but as most HPV infections are cleared rapidly by the immune system, in most cases it's unnecessary to treat a virus which may indeed cause no problems.

Vaccination

Two prophylactic vaccines have been developed; Gardasil (Merck) and Cervarix (GlaxoSmithKline). It is hoped that these will avert 70% or more of SCCs by preventing some HPV infections.

Gardasil is a quadrivalent vaccine, protecting against four types of HPV – 16, 18, 6 and 11. Cervarix is bivalent and protects against HPV types 16 and 18. In September 2006 Gardasil was granted a licence by the European Commission for use in children and adolescents aged 9 to 15 years, and in adult females aged 16 to 26 years. It is anticipated that Cervarix will be granted a licence in the next few months. At the time of going to print there have been no decisions reached regarding NHS national vaccination programmes.

There are, however, some unanswered questions relating to the scope of protection such vaccines will deliver. It is unclear, for

example, how long immunity will last, whether other HPV types will take over as the main carcinogens, and whether cross-protection against other HPV types will occur. Extensive research programmes are currently underway to address some of these issues.

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