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Pathology Newsletter
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Cervical Cancer in Women's month

by Dr. Adele Visser

Cervical cancer causes an estimated 342 000 deaths annually worldwide, making it the fourth most common cancer amongst women globally. Of these, approximately 90% occur in low-and middle-income countries, with women living with HIV having a 6-times higher risk as compared to their HIV negative counterparts.

Comprehensive cervical cancer control is required to effect real change in these numbers. This requires primary prevention through vaccination, secondary prevention through screening programmes, tertiary prevention through the early diagnosis and effective treatment of established cancer as well as adequate palliative care.

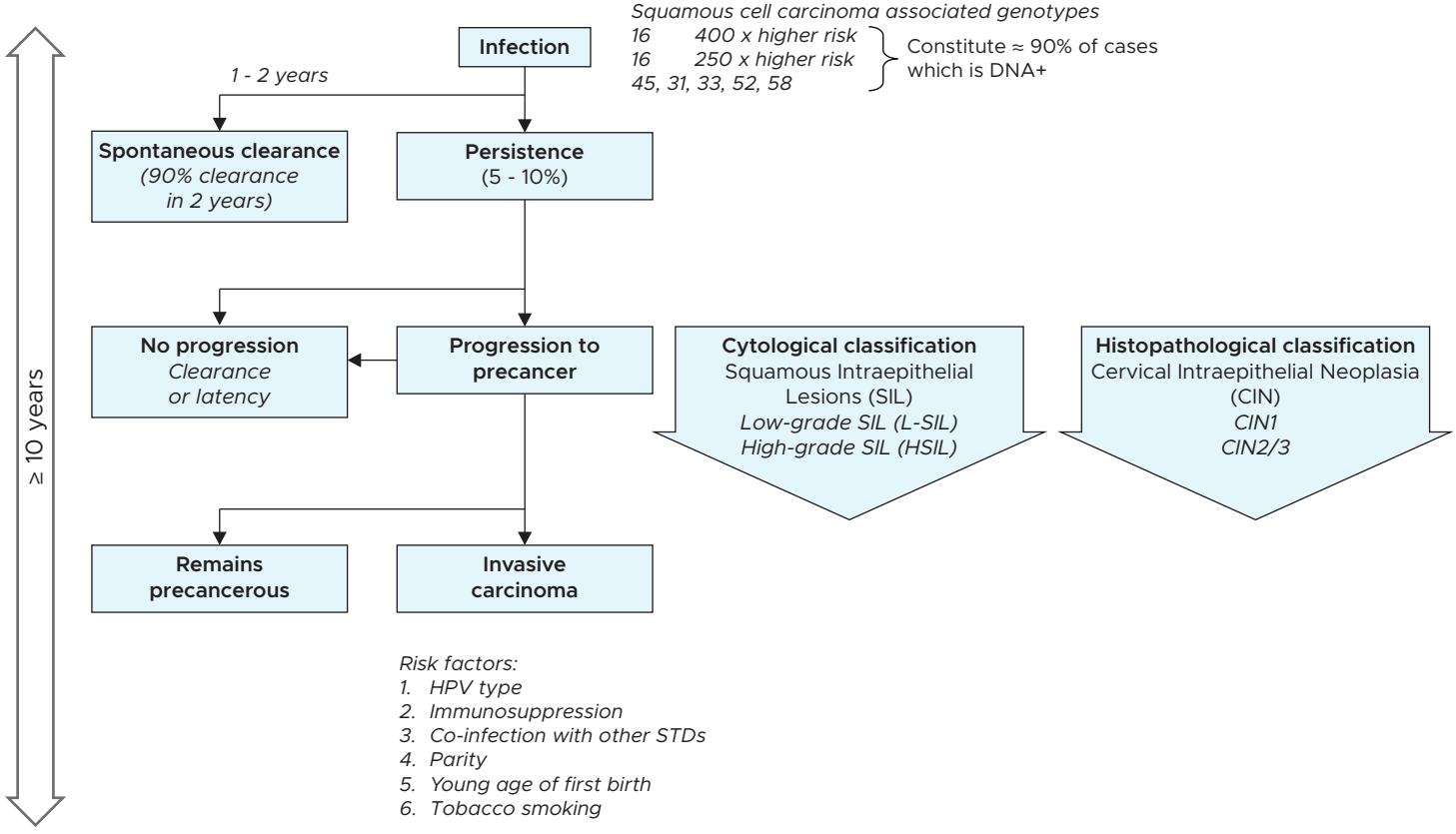

Figure 1. Natural progression of infection with HPV

Disease pathogenesis

More than 95% of cervical cancers are caused by HPV. HPV is a non-enveloped double stranded DNA virus from the Papilllomaviridae family.

The capsid consists of a major (L1) and minor (L2) viral coat protein. HPV is highly tissue-specific and infects only cutaneous and mucosal epithelium.

Of the more than 190 genotypes of HPV, twelve are known to be associated with cancers in humans. These are types 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58 and 59.

Nearly 70% of all high-grade cervical pre-cancerous lesions are caused by type 16 or 18 HPV.

Primary Prevention

The WHO advocates in the introduction HPV vaccines into the Expanded Programmes on Immunization (EPI) globally.

By March 2017, 71 countries globally had already incorporated this as part of their national schedules. The aim of vaccination is to establish immunity prior to exposure, and therefore preceding sexual debut.

The WHO therefore advocates inclusion of the HPV vaccine from age 9 to 14 years, specifically for females.

Although males may also have benefit in terms of reduction of various genito-urinary malignancies, the cost-benefit analysis cannot be used to justify implementation within a cost-restricted setting.

There are currently three prophylactic HPV vaccines. These are the quadrivalent (genotypes 6, 11, 16 and 18), approved 2006, bivalent (genotypes 16 and 18) in 2007 and nonavalent (genotypes 6, 11, 16, 18, 31, 33, 45, 52 and 58) in 2014.

In addition, primary prevention also includes sex education, provision of condoms, male circumcision as well as counseling around the use of tobacco products.

Secondary Prevention

Regular screening through PAP-smears, for pre-cancerous lesions of the cervix is indicated from age 30 years in HIV negative and age 25 years in HIV positive women. The additional screening using molecular HPV testing should be considered every 5 to 10 years, should funding allow for it.

This period is shortened for patients living with HIV, whereby screening should ideally be undertaken every 3 to 5 years.

Options include HPV DNA testing specific for high-risk types, as well as the detection of HPV mRNA in the process of cellular transformation.

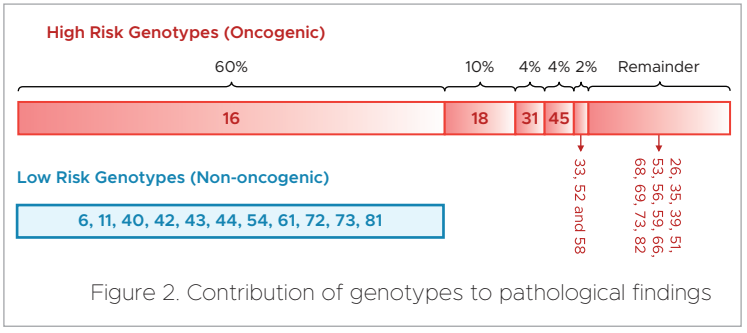

Figure 2. Contribution of genotypes to pathological findings

Tertiary Prevention

The tertiary tier of prevention of death is undertaken within any female needing treatment at any age, by means of surgery, radiotherapy, chemotherapy or palliative care.

Endpoints

Finally, the three tiers of prevention are required in order to reduce the global disease burden of HPV and cervical cancer.

Implementation of one tier does not negate the importance of another, and it should be considered as a comprehensive programme of prevention. In view of this, the WHO holds the following targets aimed to be attained by 2030:

1. To have 90% of all girls fully vaccinated by age 15.
2. To provide high-performance molecular screening to 70% of women at age 35 years, and there-after age 45 years.
3. To identify and provide treatment to 90% of women.

References

1. https://www.who.int/teams/immunization-vaccines-and-biologicals/diseases/ human-papillomavirus-vaccines-(HPV)

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