

HPV VACCINES CONTROVERSY. A WAY TO PREVENT CERVICAL CANCER?



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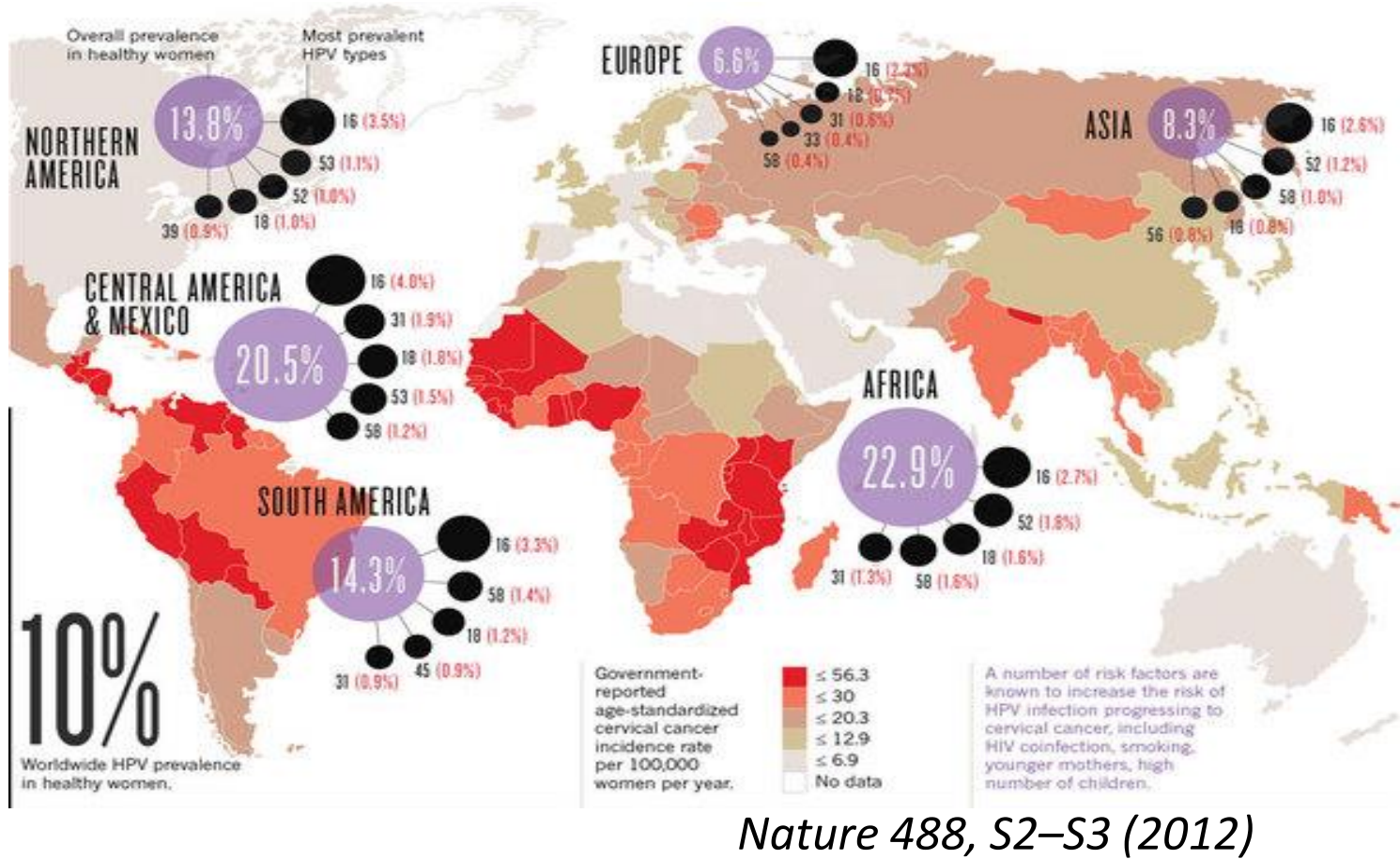
Introduction and goals

The Human Papillomavirus (HPV) is a group of DNA viruses that can cause warts and other subclinical infections which lead to cervical, vulva, vagina and anus cancer in women, or anus and penis cancer in men. In most cases HPV goes away by itself before it causes any health problems. Recently, new possibilities in cervical cancer prevention and immunotherapy have been created. We are going to review these different types of vaccines and consider all the possible arguments to accept or reject them.

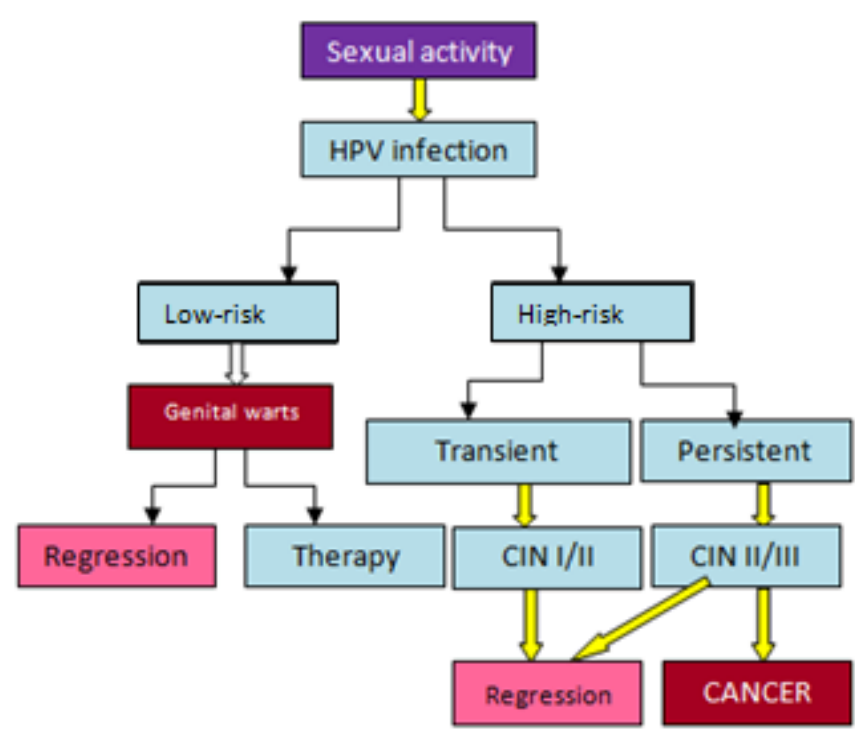
Human Papilloma Virus (HPV)

Virus description:

- Papillomaviridae family.
- Double stranded DNA, no envelope and icosahedral symmetry.
- Early and late genes (E1-E7, L1 and L2).
- More than 40 types of HPV can infect the genital area of males and females.
- Worldwide prevalence: 10%.

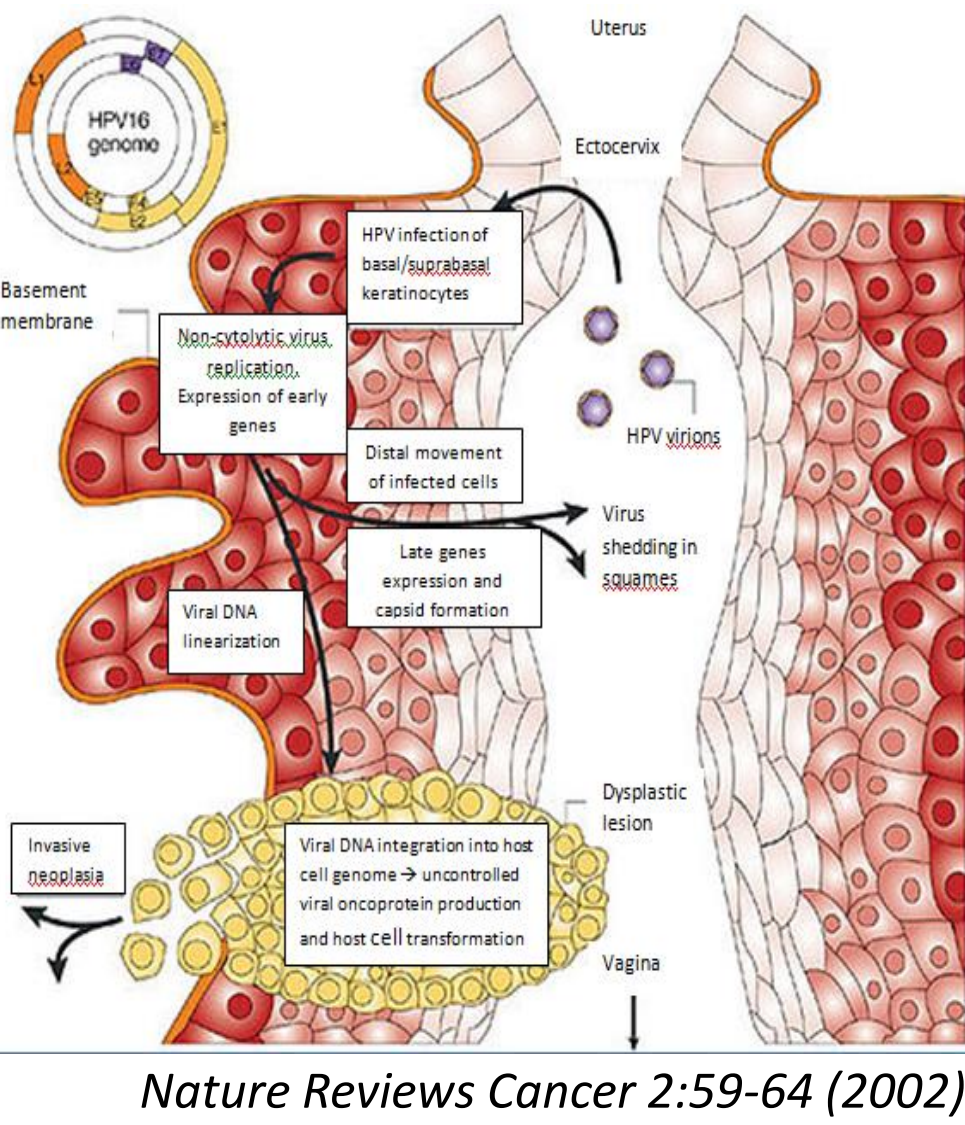


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Infection and transmission:

- Genital HPV penetrate in lesions of the epithelium and infect squamous epithelial cells.
- In most cases, HPV infection is self-limited and asymptomatic. In other cases it can lead to cervical cancer or genital warts.
- Most sexually active population will be in contact with the virus at some point of their lives.
- AIDS increases the chances of becoming infected with HPV. No association between mother's HPV status at pregnancy and child's HPV status.

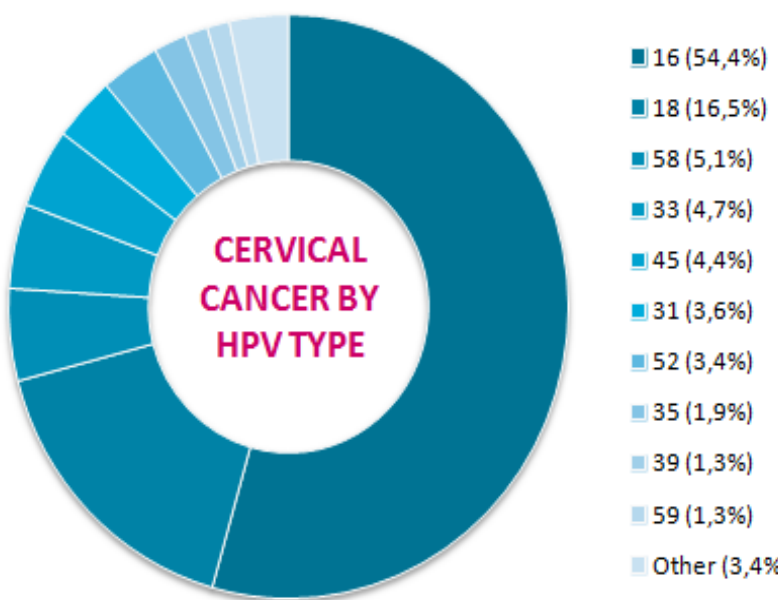


Nature Reviews Cancer 2:59-64 (2002)

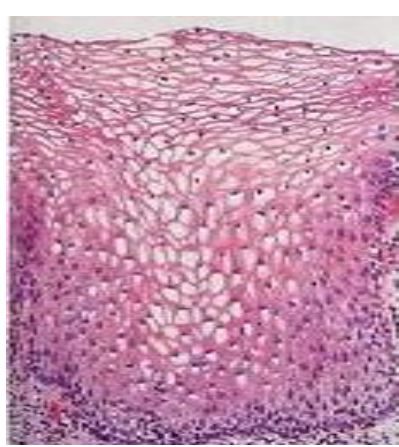
Prevention: use of condoms and vaccination.

HPV and cervical cancer

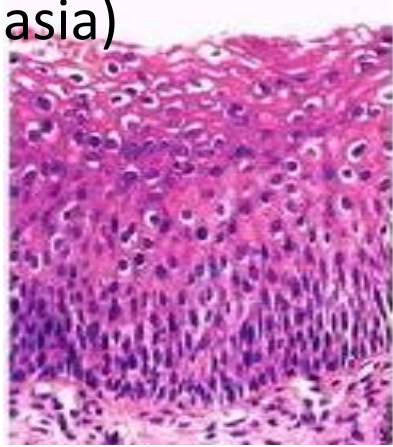
- HPV classification: low risk (ex: types 6 and 11), intermediate and high risk (ex: types 16, 18, 31 and 45).
- HPV infection is necessary to develop cervical cancer.
- Types 16 and 18 cause 70% of the cervical cancer cases.
- Two predominant forms: squamous carcinoma (80% of the cases, mostly associated to type 16) and adenocarcinoma (type 16, 18 and 45).
- Cervical Cancer classification:



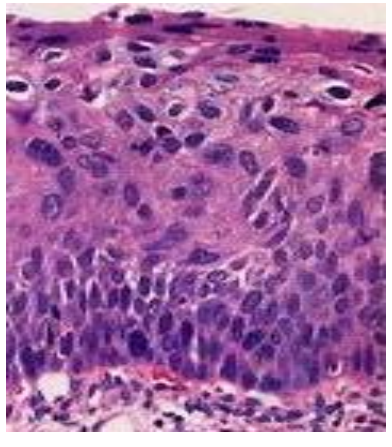
CIN I (low-grade dysplasia)



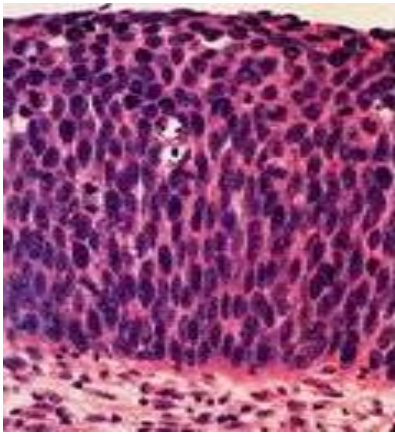
CIN II (moderate dysplasia)



CIN III (severe dysplasia)



Invasive cancer



Immunotherapy

Prophylactic vaccines

Designed to prevent HPV infection and ano-genital cancer in women and men between 9 and 45 years in several countries.

Cervarix™ - bivalent vaccine. It protects against HPV-16 and 18. Produced by GlaxoSmithKline. Based on VLP produced in *Trichoplusia ni* Rix4446, using a baculovirus as expression vector. Adjuvant: ASO4. Intramuscularly administered in three doses (month 0, 1 and 6).



Gardasil™ - quadrivalent vaccine. It protects against HPV types 16, 18, 6 and 11. Produced by Merck. Based on VLP produced in yeast *Saccharomyces cerevisiae*. Adjuvant: aluminum hydroxyphosphate sulfate. Administered intramuscularly in three doses (month 0, 2 and 6).



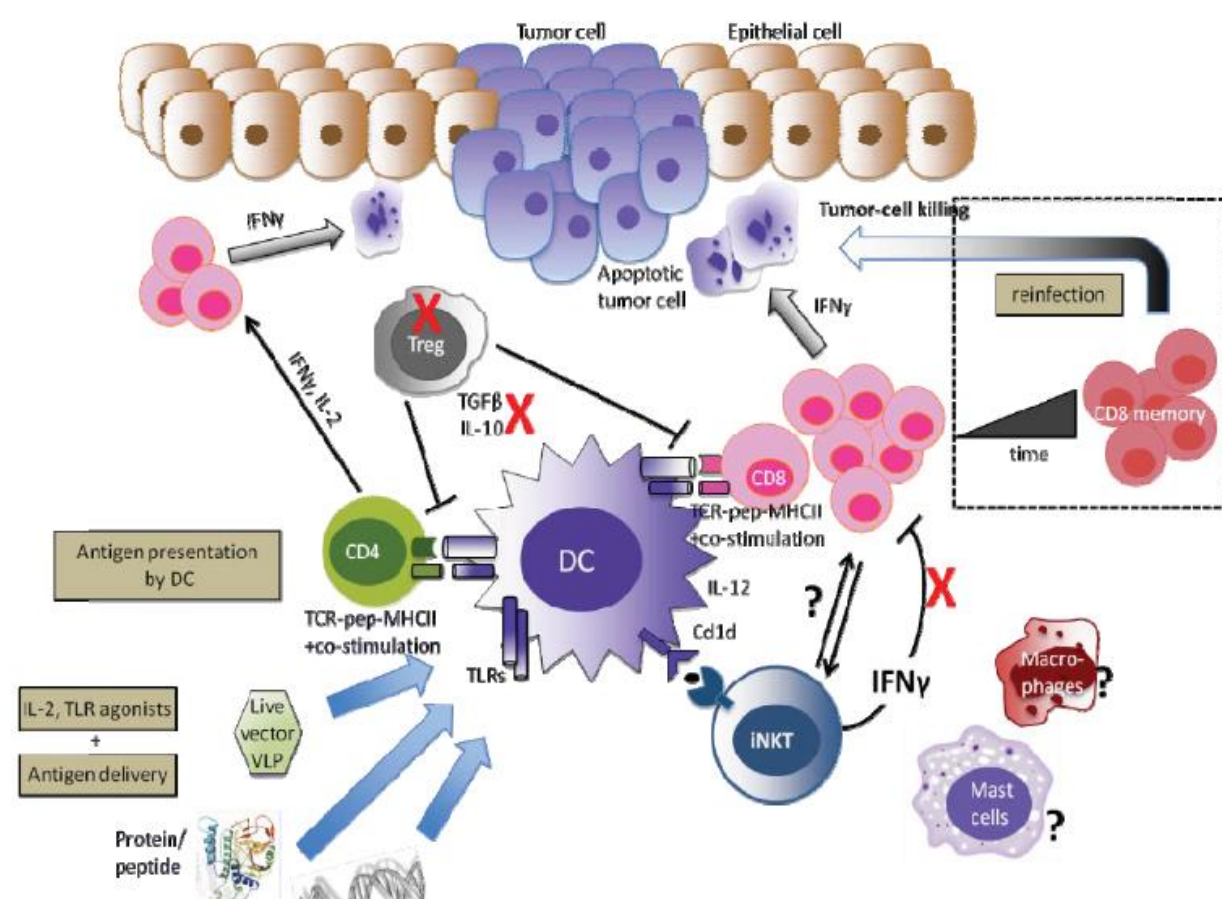
- *Contraindicated for persons with history of allergic reaction to the vaccine or to any of its components and for women during pregnancy. No contraindication for immunosuppressed individuals but immunogenicity is not guaranteed.
- *Few and mild side effects.

Therapeutic vaccines

Designed to treat preexistent cancer by means of improving natural immune response against the tumor.

Many different types of therapeutic vaccines are being developed and studied in phase I and II clinical trials.

Strategies: live vector based, protein or peptide based, nucleic acid (DNA/RNA) based or VLP. Adjuvant: TLR agonists or cytokines.



New Approaches to Immunotherapy for HPV Associated Cancers (2011)

Pros and cons

Pros

- The vaccine guards against four of the HPV strains, two of them have been shown to cause 70% of cervical cancer cases and the other two linked to 90% of the genital warts cases.
- The vaccine has been licensed by the FDA and has been deemed safe and effective by the CDC.
- HPV vaccines are recommended by several important committees.
- Cross-protection against other HPV types.

Cons

- High cost associated precludes its widespread use in the developing countries.
- Benefit or cost-effectiveness of vaccinating males is unknown.
- Twelve years is not the appropriate age to begin sex education.
- Some parents were unwilling to give too many vaccines to their children.
- Continued screening is necessary because the vaccine does not prevent other cancer-causing strains of HPV or other causes of cervical cancer.
- It may be too early to presume long-term efficacy and cost-effectiveness.

Future challenges and conclusions

New research is needed to improve HPV vaccines. Several challenges need to be resolved before HPV vaccination can be implemented in developing countries. It involves one of the most controversial issues in recent times: teenage sexual health, therefore it is needed to increase the efforts to make the population be informed.

However, up to now, Gardasil and Cervarix have been proved to be totally safe and effective after millions of doses administered around the world, no serious event was causally related to vaccination. Maybe at the moment of the introduction of the vaccine there were not evidence enough to take it as a priority but current results are positive.

References

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