

# Human Papillomavirus (HPV) & Vaccination

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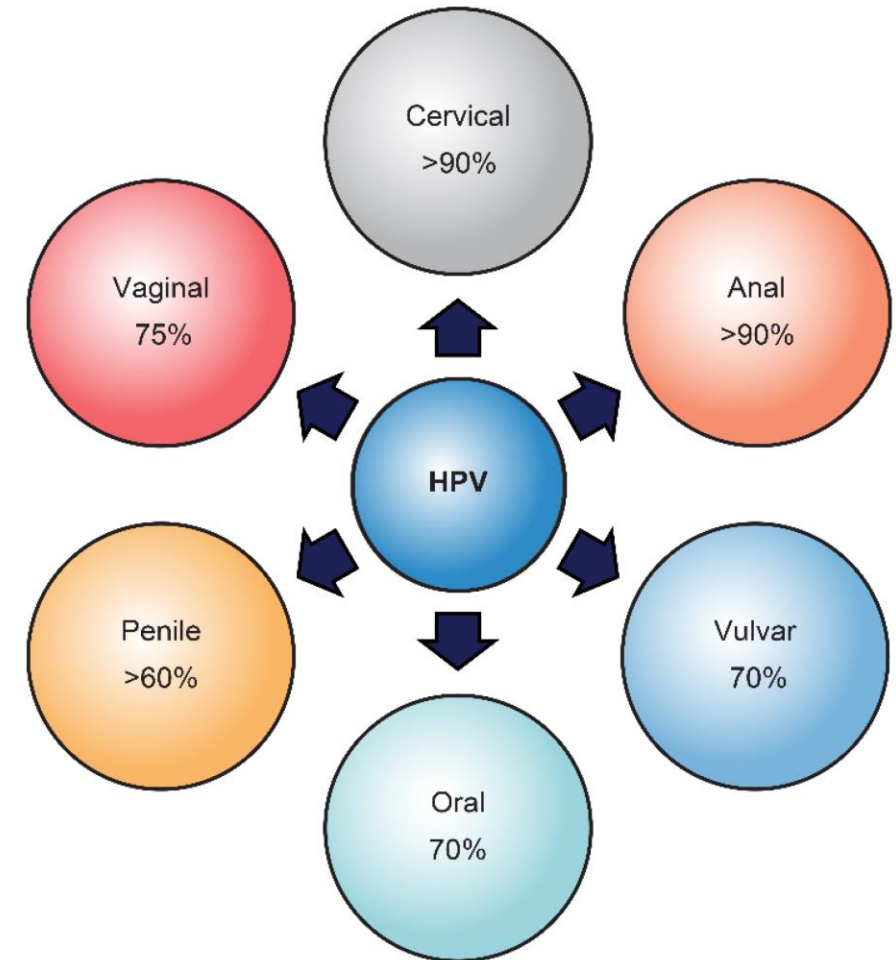
# What is HPV?

Human papillomavirus (HPV) is the most frequently sexually transmitted infection in the United States.

- Modeling suggests that over **80% of sexually active women** will have acquired a form of genital HPV by the age of 50 years old.
- Persistent infection by high-risk variants can lead to cancerous lesions if left untreated.

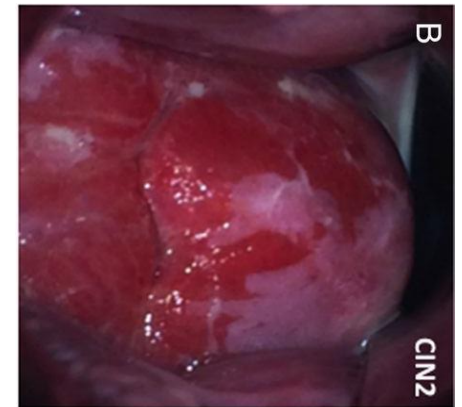
# Clinical Interest in HPV

- Research shows HPV infection leading to:
  - Many sexually transmitted infections (STIs)
  - Invasive cancers to the anus, penis, vulva, vagina, and cervix



# Pathophysiology of HPV

- 100 types of HPV have been identified to date
  - Predilection for mucous membrane is a common characteristic for HPV types infecting urogenital tract – (40 types)
- Low-risk types known to cause genital warts, benign/low-grade cervical epithelial cell changes, recurrent respiratory papillomatosis
- High-risk types known to cause low/high-grade abnormalities in cervical cells that can be precursors to cervical and anogenital cancers
  - Not new infection, but persistent infection that leads to concern.



# HPV is a contact virus

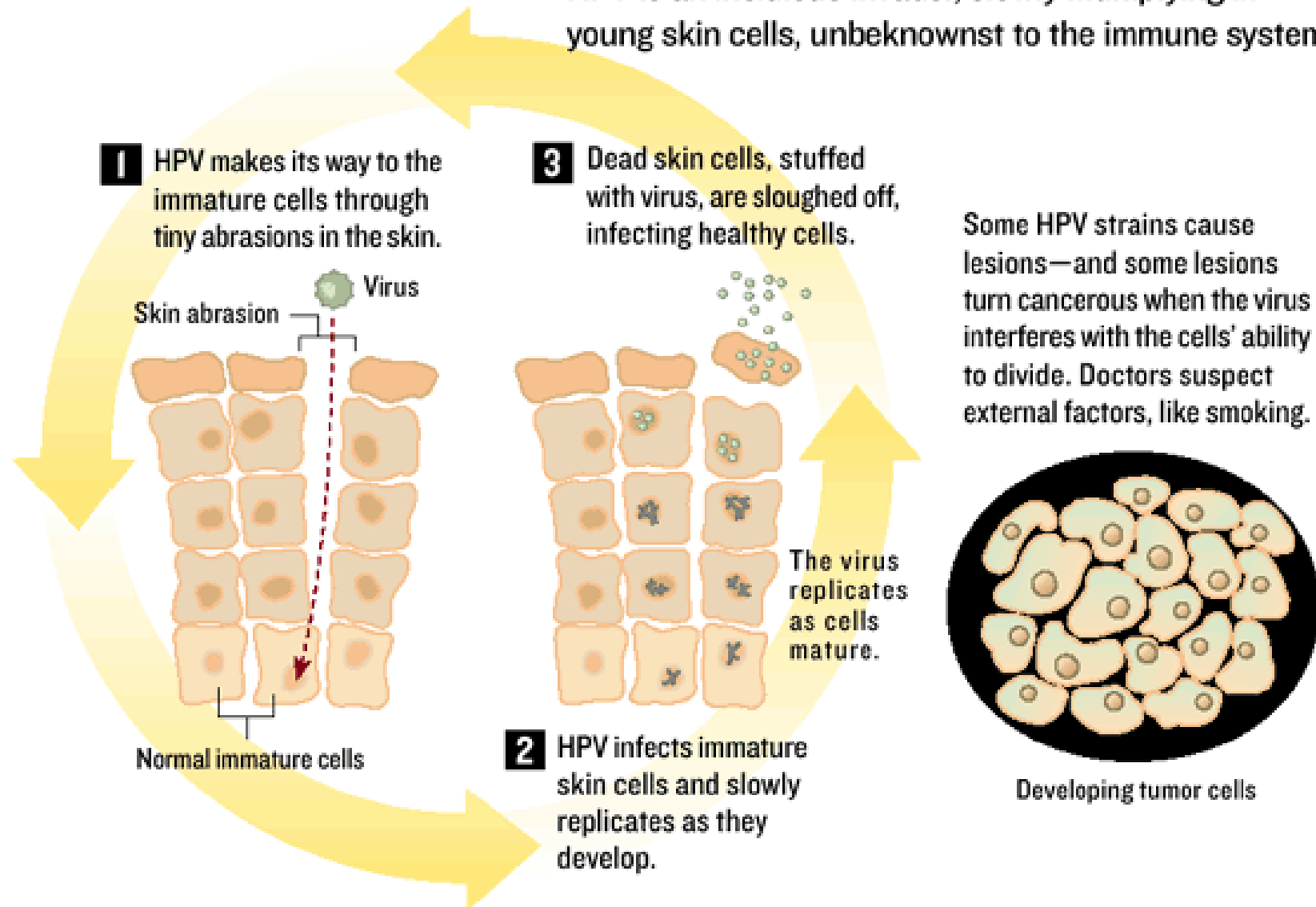
- Virus stays in cells near point of infection rather than spreading through body.
  - Infection points – usually the vagina, vulva, penis, anus, mouth, or throat.
- Testing for HPV in these areas is scientifically possible though not common.
- Pap smears collect cervical cell samples to look for concerning changes, but do not look for HPV specifically.

Huh et. al. 2017



# A Vicious Viral Cycle

HPV is an insidious invader, slowly multiplying in young skin cells, unbeknownst to the immune system.

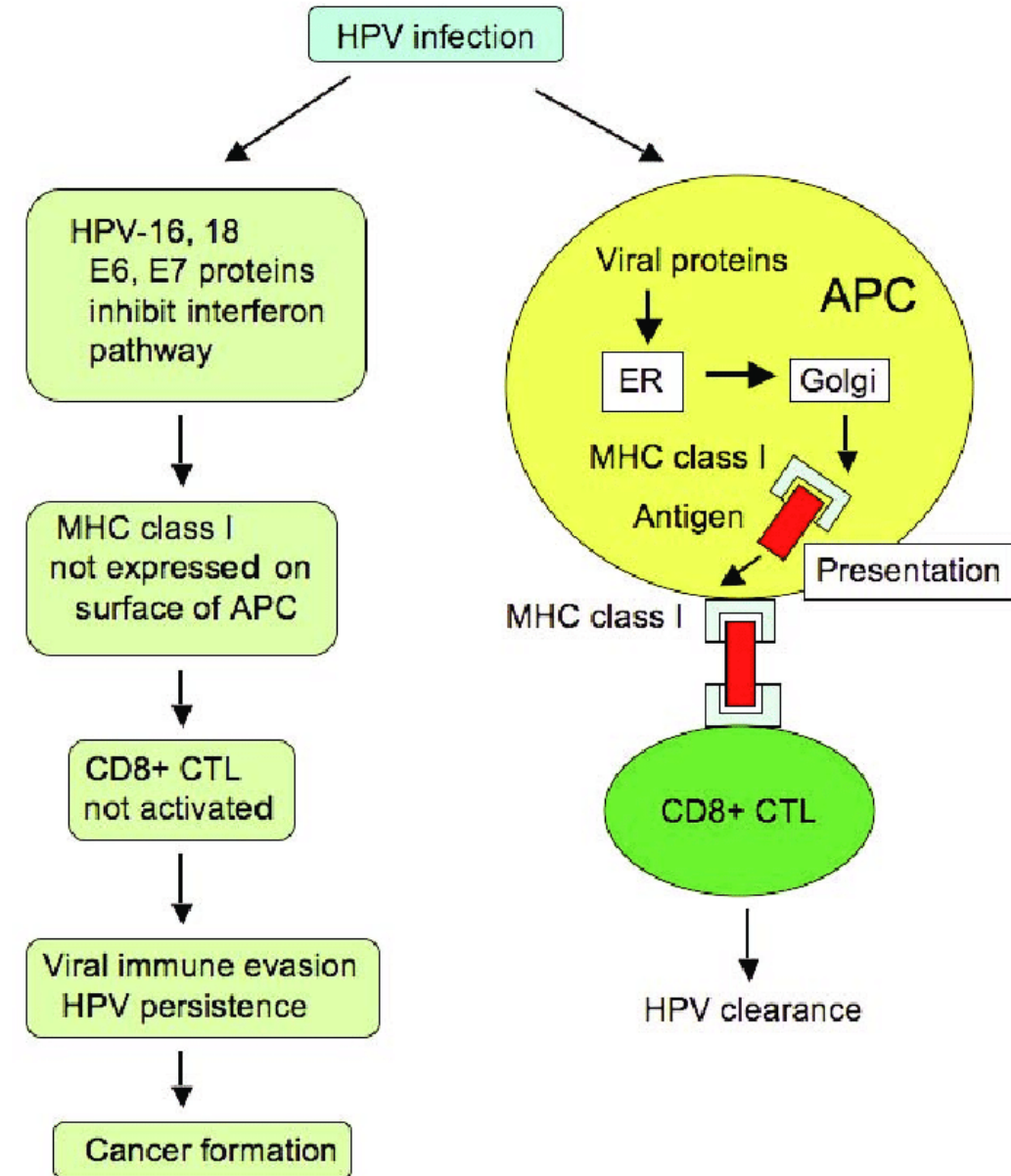




# HPV vs. Immune System

- **Two outcomes:**
  - **HPV persistence** (cancer formation)
    - Induces immune evasion of infected cells.
    - Induction of immunotolerance of host's immune system important mechanism for cervical lesions.
  - **HPV clearance**
    - Can sometimes clear infection naturally within 2 years.
    - Those with HPV type-16, strong T-cell response to E2 protein (critical to virus life cycle) associated with lack of cervical disease progression.

Brown et. al. 2018



If the Immune System can fight off HPV infections, and exposure creates immunological defense....

Why are vaccines necessary?

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# Necessity for Vaccination

- Despite T-cell response, large percentages of women struggle to fight off these infections with natural immunity alone.
- Even though viral exposure creates immunological response... presentation of viral infection through a vaccine is MUCH safer to individual than natural exposure to HPV infection outright.

# HPV Vaccine Development

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- June 8, 2006 - first quadrivalent HPV vaccine developed by Merck and Co., Inc. licensed for distribution by FDA – ***Gardasil***
- Vaccine used the L1 capsid protein of HPV in yeasts; self-assembles to form empty shells with no genetic material, imitating the virus.
  - Vaccine uses VLPs (*virus-like particles*) as antigens, which induce a strong protective immune response
    - Creates recognition for next potential infection.

# Administration

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- Each 0.5-mL dose of the vaccine contains L1 proteins for HPV-6, HPV-11, HPV-16, and HPV-18
- Vaccine available as a sterile suspension for injection or in single-dose vial or prefilled syringe.
- Females are rarely infected with all four targeted strains of HPV covered by the vaccine, thus vaccination before becoming sexually active is crucial.

# Administration

## HPV Vaccines: Bivalent and Tetravalent

	<u>Bivalent vaccine</u>	<u>Tetravalent vaccine</u>
Types of HPV	HPV-16, HPV-18	HPV-16, HPV-18, HPV-6, HPV-11
Adjuvant	Aluminum hydroxide	Amorphous aluminum hydrosulfate
Extent of Protection	70% of cervical cancers	70% of cervical cancers 90% of genital warts

# HPV Vaccine Protocols

## Target Populations:

- **Females:**
  - Recommendation – starting vaccine series at 11-12 y/o
  - Women can be vaccinated up until 26 y/o
- **Males:**
  - Can undergo vaccination series between 13-21 y/o age bracket

## Dosing Frequency:

- Three separate doses are administered – 0, 2, 6 months
  - Minimum of 4 wks between 1<sup>st</sup> and 2<sup>nd</sup> dose, and minimum of 12 wks between 2<sup>nd</sup> and 3<sup>rd</sup> dose.

Huh et. al. 2017

Parham et. al. 2021



# Historical Changes to Delivery

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- Changes made in Delivery protocols in 2010:
- CDC now recommends that patients undergo a two-dose regimen if the vaccination series is started before the 15<sup>th</sup> birthday
- Due to the immunological response decreasing in rigor after this milestone, patients receiving the vaccination series after their 15<sup>th</sup> birthday are recommended the three-dose HPV vaccine series
  - Additionally, those suffering with autoimmune disorders or immunocompromised, including HIV/AIDS patients, are recommended the three-dose series.

# Objections to Vaccine

## Religious/moral objections

Some religious groups believe vaccination is “unnecessary due to abstaining from sexual relationships outside of marriage.”

## Political objections

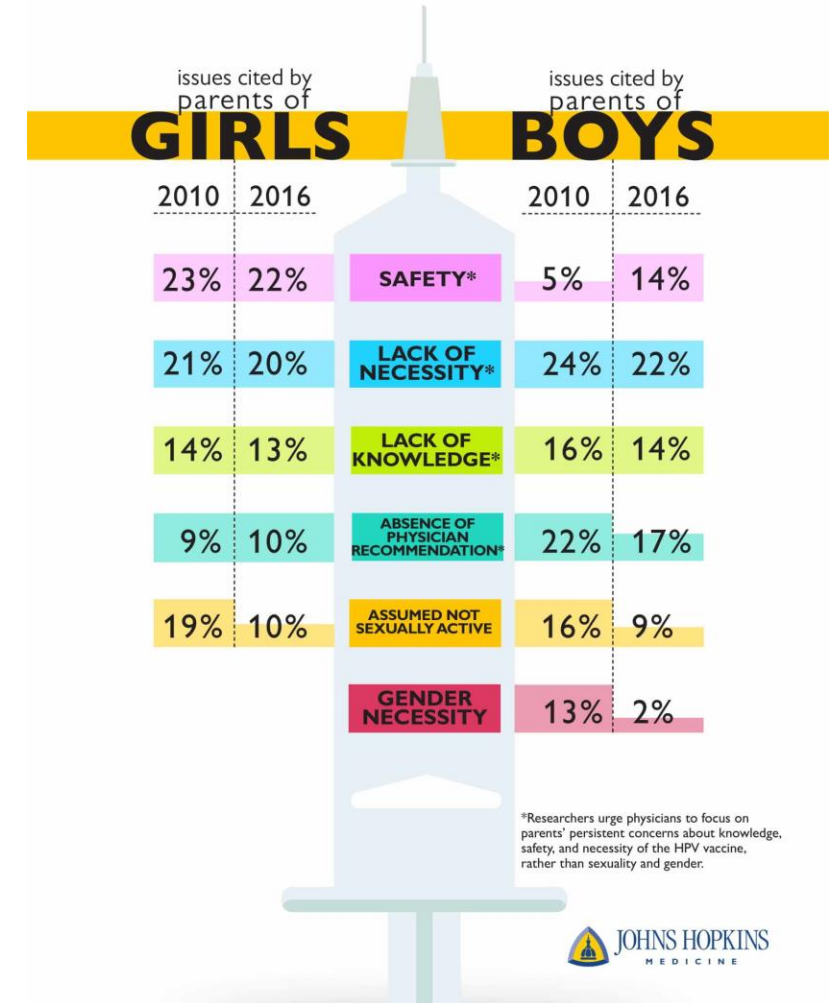
Infringing upon freedoms as an American  
(e.g. – compulsory vaccine mandates)

Balog et. al. 2009

## THE HPV VACCINE:

Why parents really choose to refuse

Study results suggest safety concerns top the list, and that physicians need to step up their patient education and vaccine recommendations.





# Can a vaccine be mandatory?

Yes, technically.... if certain criteria are met.

## Example: Mandatory vaccination against polio (1950s)

- In 1950s, over 58,000 cases of polio reported (21,000 cases of paralytic polio + 3,000 deaths from the disease).
- Compulsory vaccination programs implemented due to precedent from Supreme Court case known as Jacobson vs. Massachusetts in 1905.
  - Vaccine mandates legal **IF certain exemptions** are implemented (e.g. – religious, philosophical).

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