

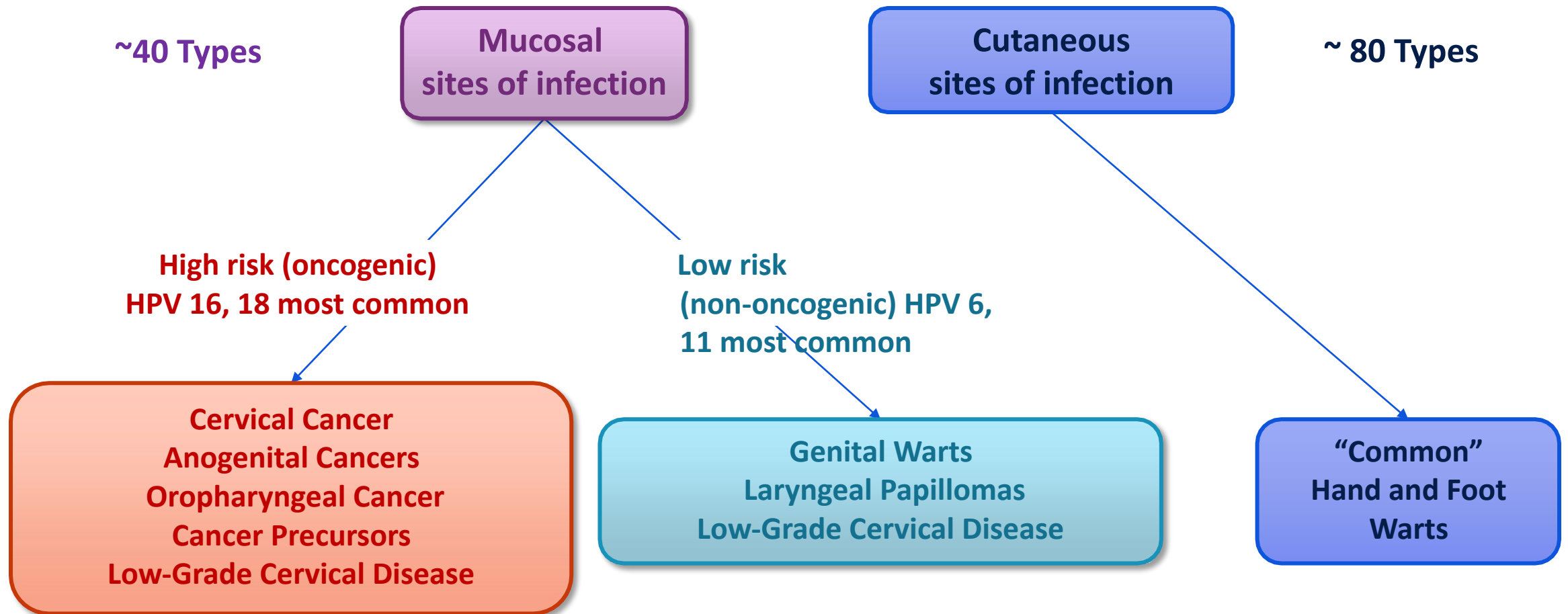
Practices in HPV Disease

Learning Objectives

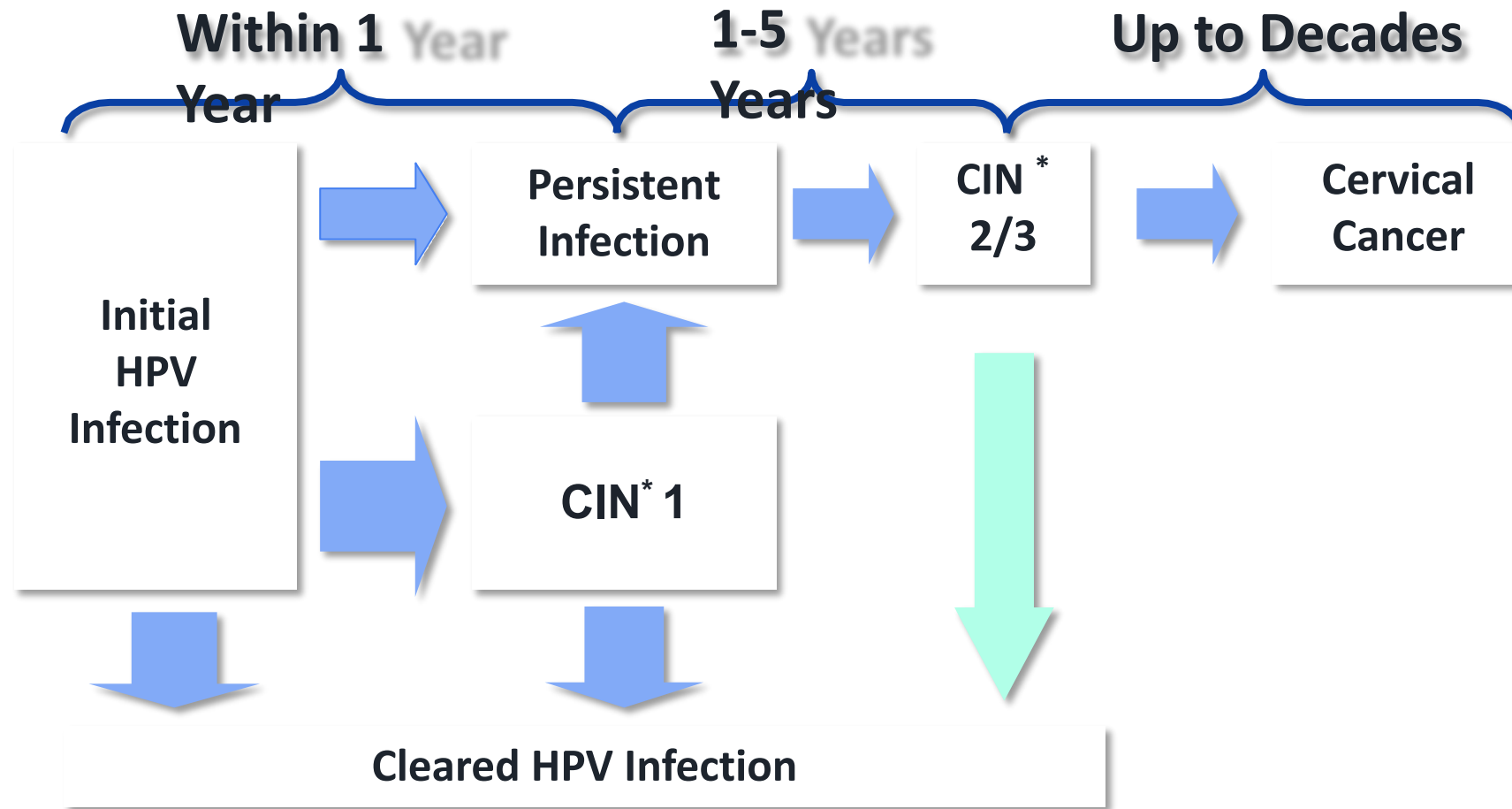
- Understand HPV-related diseases.
- Describe the Advisory Committee on Immunization Practices General Best Practice Guidelines on HPV Immunization.
- Describe strategies for improving HPV vaccination.

HPV = human
papillomavirus.

HPV Types Differ in Their Disease Associations



Natural History of HPV Infection



*CIN = cervical intraepithelial neoplasia

HPV Clinical

Features

- Most HPV infections are asymptomatic and result in no clinical manifestations

- **Clinical manifestations of HPV infection include:**
 - Anogenital warts
 - Recurrent respiratory papillomatosis
 - Cervical cancer precursors (cervical intraepithelial neoplasia)
 - Cancer (cervical, anal, vaginal, vulvar, penile, and some oropharyngeal cancers)

Number of HPV-Associated and HPV-Attributable Cancer Cases Per Year, U.S., 2014–2018

Cancer site	Number of HPV-associated cancers	Percentage probably caused by any HPV type	Estimated number probably caused by any HPV type*		
			Female	Male	Both sexes
Cervix	12,200	91%	11,100	0	11,100
Vagina	863	75%	600	0	600
Vulva	4,191	69%	2,900	0	2,900
Penis	1,365	63%	0	900	900
Anus**	7,288	91%	4,500	2,100	6,600
Oropharynx	20,236	70%	2,300	12,100	14,400
TOTAL	46,143	79%	21,400	15,100	36,500

*Estimates were rounded to the nearest 100. Estimated counts might not sum to total because of rounding.

**Includes anal and rectal squamous cell carcinomas

Sources: <https://www.cdc.gov/cancer/hpv/statistics> and <http://www.cdc.gov/cancer/dataviz>

Common Factors Associated With HPV Infection

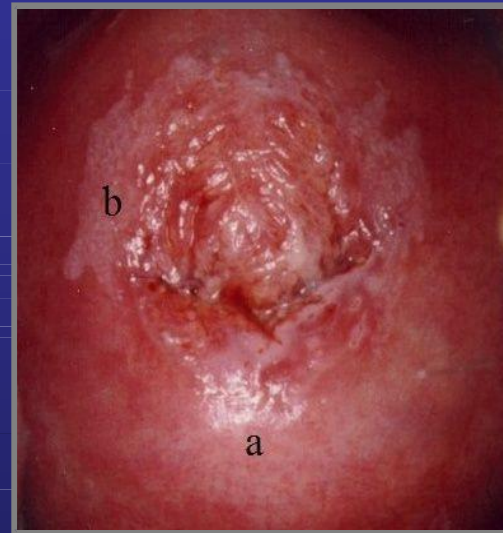
- Young age
 - Peak age group 20 to 24 years of age¹
- Increased number of sexual partners during lifetime²
- Early age of first sexual intercourse³
- History of smoking²
- Oral contraceptive use²
- Uncircumcised male partners⁴
- Male partner sexual behavior³

HPV Epidemiology

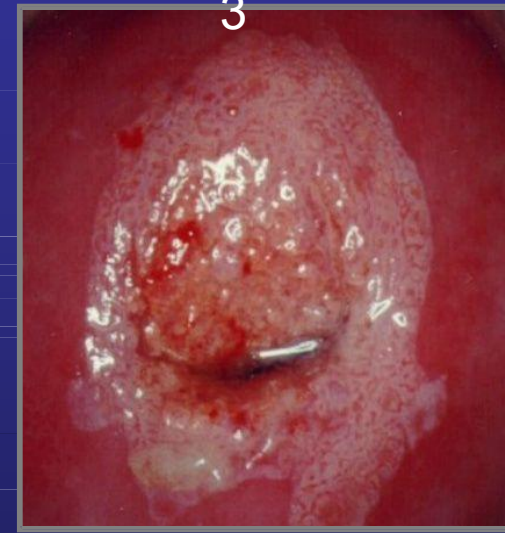
Reservoir	Human
Transmission	Direct contact (skin to skin)
Temporal pattern	None
Communicability	Presumed to be high

Cervical Intraepithelial Neoplasia (CIN)¹

CIN 1 CIN 2



CIN
3



- CIN Stages²
 - CIN 1: Mild dysplasia
 - CIN 2: Moderate dysplasia
 - CIN 3: Severe dysplasia; includes carcinoma in situ (CIS)

1. Reprinted with permission from Dr. JW Sellors & Dr. R Sankaranarayanan. Sellors JW et al, eds. Lyon, France: International Agency for Research on Cancer;2003. *Colposcopy and Treatment of Cervical Intraepithelial Neoplasia. A Beginner's Manual*. Reprinted with permission of the International Agency for Research on Cancer, World Health Organization. 2. Bonne W et al. In: Richman DD et al, eds. *Clinical Virology*. 2nd

Symptoms and Treatment of VIN

- HPV 16 and 18 contribute to 6.8% of VIN 1 and 76% to 86.6% of VIN 2/3 lesions.^{1,2}
- Frequent symptoms are pruritus, vulval pain or discoloration, and vaginal discharge.³
- Symptoms may be present for a long time prior to diagnosis (median of 1 year).³
- Recommended treatment is surgery including wide local excision.^{4,5}
- Laser ablative techniques have had variable outcomes and can be associated with painful healing.^{3,4}

VIN = vulvar intraepithelial neoplasia.

VIN 3



Photo courtesy of Dr. J Monsonego.

VIN 3



Photo courtesy of Dr. EJ Mayeaux.

1. Insigna RP et al. *Cancer Epidemiol Biomarkers Prev.* 2008;17:1611–1622. 2. Hampf M et al. *Obstet Gynecol.* 2006;108:1361–1368. 3. Herod JJ et al. *Br J Obstet Gynaecol.* 1999;106:119–150. 4. Huh HK et al. *J Clin Oncol.* 2000;18:2999–3004. 5. Jansen RW et al. *J Clin Oncol.* 1995;13:1919–1929.

Genital Warts: An Important Health care Issue



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- HPV 6 and 11 are responsible for >90% of anogenital warts.¹
- Anogenital warts are common² and highly contagious³:
 - Based on National Health and Nutrition Examination Survey (NHANES) study, an estimated 4% of sexually active men 18 to 59 years of age have ever been diagnosed with genital warts.²
 - >75% of sexual partners develop warts when exposed.³
- Peak prevalence⁴
 - Women 20 to 24 years of age (6.2/1,000 person-years).
 - Men 25 to 29 years of age (5.0/1,000 person-years).
- Clinically apparent in ~1% of sexually active US adult population.⁵

1. Gissmann L et al. *Proc Natl Acad Sci USA*. 1983;80:560-563. 2. Dinh T-H et al. *Sex Transm Dis*. 2004;35(4):357-360. 3. Soper DE. In: Berek JS, ed. *Novac's Gynecology*. 13th ed. 2002:453-470. 4. Insinga RP et al. *Clin Infect Dis*. 2003;36:1397-1403. 5. Koutsky L. *Am J Med*. 1997;102:3-8.

HPV Disease Burden in the U.S.

- **Estimated 42 million persons are infected**
 - ~13 million persons with a new infection annually
- **Common among adolescents and young adults**
 - 50% of new infections occur in persons 15–24 years of age
- **Approximately \$10.8 billion spent annually on management of sequelae of HPV infections**
- **Most people will never know that they have been infected**

HPV Vaccine

- **HPV vaccine (9vHPV, Gardasil 9) is currently licensed for use in the United States**
 - Only HPV vaccine currently available in the United States
- **Two other HPV vaccines, quadrivalent HPV vaccine (4vHPV, Gardasil 4) and a bivalent HPV vaccine (2vHPV, Cervarix) are licensed in the United States, but are no longer available in this country**

HPV Children and Adult Vaccination Schedule

Vaccine	Birth	1 mo	2 mos	4 mos	6 mos	9 mos	12 mos	15 mos	18 mos	19–23 mos	2–3 yrs	4–6 yrs	7–10 yrs	11–12 yrs	13–15 yrs	16 yrs	17–18 yrs	
Human papillomavirus (HPV)																		See Notes

Vaccine	19–26 years	27–49 years	50–64 years	≥65 years
Human papillomavirus (HPV)	2 or 3 doses depending on age at initial vaccination or condition	27 through 45 years		

- Non-live vaccine
- Administered by intramuscular (IM) injection

HPV Vaccine

HPV Vaccines	9-valent 9vHPV (Gardasil 9)
L1 VLP types	6, 11, 16, 18, 31, 33, 45, 52, 58
Manufacturer	Merck
Contraindications	Hypersensitivity to yeast
FDA indications	Females (9–45 yrs): Anal, cervical, vaginal, vulvar, oropharyngeal and other head and neck cancers, genital warts; precancerous or dysplastic lesions Males (9–45 yrs): Anal, oropharyngeal and other head and neck cancers, genital warts, and precancerous or dysplastic lesions

- Only 9vHPV vaccine is available in the U.S.

<https://www.fda.gov/vaccines-blood-biologics/vaccines/Gardasil-9>

HPV Vaccine

Efficacy

High efficacy among females without evidence of infection with vaccine HPV types (more than 95%)

- No evidence of efficacy against disease caused by vaccine types participants were infected with at the time of vaccination
- Prior infection with one HPV type did not diminish the efficacy of the vaccine against other vaccine HPV types

Expanded age indication for 9-valent HPV vaccine

- **Manufacturer filed an application with FDA in April 2018 to expand age indication through 45 years**
 - **FDA approved October 2018**
 - **Evidence based on bridging data from a study of the quadrivalent HPV vaccine in this age group**
 - **ACIP made a recommendation for shared clinical decision-making in this age group in 2019.**
- 

HPV Vaccine Duration of Protection

- **Studies suggest that vaccine protection is long-lasting**
- **No evidence of waning protection**
 - Available evidence indicates protection for *at least* 12 years
 - Multiple studies are in progress to monitor

Knowledge Check

- A provider is evaluating a 52-year-old woman with a history of multiple sex partners and genital warts. She has not previously received any HPV vaccine. Is HPV vaccine recommended for her?
 - A. Yes
 - B. No



Human Papillomavirus Vaccine Routine Recommendations

- **Routinely vaccinate boys and girls at 11–12**
 - Vaccination series can be started at 9 years of age
 - HPV vaccination recommended for all males and females aged 13 through age 26 years: if not adequately vaccinated

HPV Vaccine Dosing Schedule, United States


Population	Number of vaccine doses	Interval between doses
Persons initiating vaccination at 9 through 14 years, except persons with immunocompromising conditions	2	0, 6–12 months*
Persons initiating vaccination at 15 through 26 years and persons with immunocompromising conditions initiating vaccination at 9 through 26 years	3	0, 1–2, 6 months ⁺

* In a 2-dose schedule of HPV vaccine, the minimum interval between first and second doses is 5 months.

⁺ In a 3-dose schedule of HPV vaccine, the minimum intervals are 4 weeks between the first and second doses, 12 weeks between the second and third doses, and 5 months between the first and third doses

- **Persons are considered adequately vaccinated if they completed a recommended schedule with 9vHPV, 4vHPV, or 2vHPV vaccine.**

HPV Vaccination Schedules

- **Data from clinical trials showed 2 doses of HPV vaccine given in younger adolescents (9–14 years) produced an immune response similar to or higher than the response in young adults (16–26 years) who received 3 doses**
 - **Data available to date show that a 3-dose schedule in older adolescents and young adults provides long-lasting protection**
 - **Data suggest that a 2-dose schedule given to younger adolescents will also provide long-lasting protection**
- 

ACIP HPV Immunization Recommendations

Previously Unvaccinated Adolescents: Age 9–14

years

- Administer 2 doses of HPV vaccine to adolescents starting the series at 9–14 years of age.
- **Follow the routine 2-dose schedule:**
 - Administer the second dose 6-12 months after the first dose.
- **If a second dose is inadvertently administered prior to 5 months, default to a 3-dose series.**

ACIP HPV Immunization Recommendations

Previously Unvaccinated Adolescents: Age 15 years or older

- **Administer 3 doses to adolescents starting the series on or after the 15th birthday**
 - Even those who initiate vaccination at age
- **Routine 3-dose schedule: 0, 1–2, 6 months**
 - Dose #2 should be administered at least 1 month after dose 1
 - Dose #3: Administer at least:
 - 12 weeks after dose 2 AND
 - 5 months after dose 1
- **An accelerated schedule using minimum intervals is not recommended**

ACIP HPV Immunization Recommendations

Previously Unvaccinated Adolescents: Immunocompromised

- **Administer 3 doses for persons who have immunocompromising conditions**
 - Even for those who initiated vaccination at age 9–14 years
- **Routine 3-dose schedule: 0, 1–2, 6 months**

HPV Vaccination of Adults 27–45 Years of Age

- Shared clinical decision-making is recommended for adults 27–45 years of age
- Shared clinical decision-making includes adults who may have received doses prior to the 27th birthday

Considerations for Shared Clinical Decision-Making Regarding HPV Vaccination of Adults Aged 27–45 Years

- HPV is a very common sexually transmitted infection. Most HPV infections are transient and asymptomatic and cause no clinical problems.
- Although new HPV infections are most commonly acquired in adolescence and young adulthood, some adults are at risk for acquiring new HPV infections. At any age, having a new sex partner is a risk factor for acquiring a new HPV infection.
- Persons who are in a long-term, mutually monogamous sexual partnership are not likely to acquire a new HPV infection.
- Most sexually active adults have been exposed to some HPV types, although not necessarily all of the HPV types targeted by vaccination.

Considerations for Shared Clinical Decision-Making Regarding Human Papillomavirus (HPV) Vaccination of Adults Aged 27 through 45

- **No clinical antibody test can determine whether a person is already immune or still susceptible to any given HPV type.**
- **HPV vaccine efficacy is high among persons who have not been exposed to vaccine-type HPV before vaccination.**
- **Vaccine effectiveness might be low among persons with risk factors for HPV infection or disease (e.g., adults with multiple lifetime sex partners and likely previous infection with vaccine-type HPV), as well as among persons with certain immunocompromising conditions.**
- **HPV vaccines are prophylactic (i.e., they prevent new HPV infections). They do not prevent progression of HPV infection to disease, decrease time to clearance of HPV infection, or treat HPV-related disease.**

Knowledge Check

- A 30-year-old woman received a first dose of HPV vaccine at 25 years of age. Is shared clinical decision-making recommended to continue the series?
 - A. Yes
 - B. No



Human Papillomavirus Vaccine and Pregnancy

- HPV vaccination should be delayed until after pregnancy.
- If a person is found to be pregnant after starting the HPV vaccine series, second and/or third doses should be delayed until they are no longer pregnant.
- If a person receives HPV vaccine and later learns that they are pregnant, there is no reason to be alarmed.
- Anyone who learns they are pregnant when they received an HPV vaccine can contact the manufacturer at 1-877-888-4231
- Any suspected adverse events following HPV vaccination during pregnancy should be reported to

<https://www.cdc.gov/vaccines/imz/hpv/hcp/recommendations.html>

VAERS.

HPV Vaccine Administration

- **Administer HPV vaccine via IM injection:**
 - Needle size: 1- through 1½-inch, 22- to 25-gauge
 - Site: Deltoid muscle in the upper arm
- **Follow proper injection practices:**
 - Use aseptic technique
 - Use a new needle and syringe for each injection
- **Administer HPV vaccine at the same medical visit as other vaccines.**

Contraindications

HPV

Severe allergic reaction (e.g., anaphylaxis) after a previous dose or to a vaccine component, including yeast

Precautions

HPV

Moderate or severe acute illness with or without fever

HPV Vaccine Safety Summary: Selected Sources of data and Key Findings

- **Over 135 million doses distributed in the United States through 2020**
 - More than 14 years of monitoring
- **Vaccine Adverse Event Reporting System (VAERS)**
 - No unusual outcomes identified; syncope are one of the common reports
 - 4vHPV, 2vHPV and 9vHPV
- **Vaccine Safety Data Link (VDS)***
 - Other studies to investigate associations**
 - No safety concerns for pre-specified autoimmune, neurologic or other diseases
- **World Health Organization Global Advisory Committee on Vaccine Safety**
 - Multiple reviews – most recently 2020⁺

*Gee et al. Vaccine 2011; Gee et al. Vaccine 2017; Donahue et al. Pediatrics 2019; **Chao et al. J Intern Med 2012; Arnheim-Dahlstrom et al. BMJ 2013. Grimaldi-Bensouda et al. J Intern Med 2013; Scheller et al. JAMA 2015; Gee et al. Hum Vaccin Immunother. 2016; ⁺ WHO WER. July 2017 and [https://www.who.int/publications/m/item/WER-2020-95-28-\(full-issue\)](https://www.who.int/publications/m/item/WER-2020-95-28-(full-issue)) http://www.who.int/vaccine_safety/committee/topics/hpv/June_2017/en/
<https://www.cdc.gov/vaccinesafety/vaccines/hpv/hpv-safety-faqs.html#A10>

HPV Vaccine Adverse Reactions

- Reactions after vaccination can include:
 - Injection site reactions: pain, redness, and/or swelling in the arm where the shot was given
 - Systemic: fever, headaches, nausea, muscle or joint pain
- Life threatening allergic reaction can occur after any vaccine, including HPV vaccines
- Brief fainting spells (syncope) and related symptoms (such as jerking movements) can happen soon after any injection, including HPV vaccine
 - Patients should be seated (or lying down) during vaccination and remain in that position for 15 minutes

Knowledge Check

- **All of the following strategies can be used to help to prevent syncope when vaccinating adolescents EXCEPT?**
 - a. vaccinating while in a sitting position?
 - b. vaccinating while in a standing position?
 - c. vaccinating while in a lying down position?
 - d. observing patients for 15 minutes following vaccination?



HPV Vaccine Communications during the Health Care Encounter

- HPV vaccine is often presented as optional, whereas other adolescent vaccines are recommended.
- Some providers expressed mixed or negative opinions about relatively new vaccines and concerns over safety and efficacy.
- When parents' express reluctance, providers are hesitant to engage in discussion.
- Some providers share parents' views that a teen is not at risk for HPV and vaccination can be delayed until the teen is older.

Goff S, et al. *Vaccine* 2011;10:7343–9

Hughes C, et al. *BMC Pediatrics* 2011;11:74

Perceived Challenges to Adult Vaccination: Survey^{1,a}

Patient Reasons

- *“Doctor hasn’t told me I need it.”*
- Not knowing when to get it.
- The belief that a healthy person doesn’t need it.
- Financial concerns were not a deterrent for most.

Health Care Provider Perceptions

- Side effects.
- Dislike of needles.
- Lack of insurance coverage.
- Lack of knowledge about disease prevention.

Most patients indicated that they were likely to receive a vaccination if their health care provider recommended it.

^aA recent survey was conducted to identify the reasons adult patients may decide to **NOT** receive vaccinations and health care providers’ perceptions regarding patients’ **NOT** being vaccinated.

Consumers (N = 2,002) and health care providers (N = 200) completed structured telephone interviews, e-mails, or faxes emphasizing tetanus, influenza, and pneumococcal vaccines.

1. Johnson DR et al. *Am J Med.* 2008;121(7 suppl 2):S28–S35.

Strategies for Increasing HPV Vaccination Coverage in Clinical Practices

- **Recommend HPV vaccine**
 - Include HPV vaccine when discussing other recommended vaccines.
- **Integrate standard procedures supporting vaccination:**
 - Assess for needed vaccines at every clinical encounter
 - Vaccinate at every opportunity
 - Use standing orders
- **Reminder and recall**
- **Tools for improving uptake of HPV vaccine at**

www.cdc.gov/vaccines/teens

HPV Vaccination Resources for HCP

The screenshot shows the CDC website for HPV Vaccination Resources for Healthcare Professionals. The page is titled "Human Papillomavirus (HPV)" and "For Healthcare Professionals". It features a navigation menu on the left with categories like "For Parents", "For Healthcare Professionals", and "For Partners & Programs". The main content area includes sections for "HPV Cancers are Preventable", "Schedules and Dosing", "Vaccination Information", "Boosting Vaccination Rates", "Vaccine Safety and Effectiveness", and "Answering Parents' Questions". There are also "Educational Materials" and "Continuing Education" sections. The footer contains contact information, CDC information, and social media links.

Talking to Parents about HPV Vaccine
HPV VACCINE IS CANCER PREVENTION

Recommend HPV vaccination in the same way and on the same day as all adolescent vaccines. You can say, "Now that your son is 11, he is due for vaccinations today to help protect him from meningitis, HPV cancers, and whooping cough. Do you have any questions?" Taking the time to listen and understand parents' concerns can help you respond to their concerns more effectively.

Why does my child need HPV vaccine?
 HPV vaccine is important because it prevents infections that can cause cancer. That's why we need to start the shot series today.

Some HPV infections can cause cancer—like cancer of the cervix or in the back of the throat—but we can protect your child from these cancers in the future by getting the first HPV shot today.

What diseases are caused by HPV?

How do you know the vaccine works?
 Studies continue to prove HPV vaccination works extremely well, decreasing the number of infections and HPV precancers in young people since it has been available.

HPV is a very common infection in women and men that can cause cancer. Starting the vaccine series today will help protect your child from the cancers and diseases caused by HPV.

Is my child really at risk for HPV?

Why do they need HPV vaccine at such a young age?
 Vaccines protect your child before they are exposed to a disease. That's why we give the HPV vaccine earlier rather than later, to protect them long before they are ever exposed. Also, if your child gets the shot now, they will only need two doses. If you wait until your child is older, they may end up needing three shots.

Studies tell us that getting HPV vaccine doesn't make kids more likely to start having sex. I made sure my child (or grandchild, etc.) got HPV vaccine, and I recommend we give your child her first HPV shot today.

I'm worried my child will think that getting this vaccine makes it OK to have sex.

Why do boys need the HPV vaccine?
 HPV vaccination can help prevent future infections that can lead to cancers of the penis, anus, and back of the throat in men.

Yes, HPV vaccination is very safe. Like any medication, vaccines can cause side effects, including pain, swelling, or redness where the shot was given. That's normal for HPV vaccine too and should go away in a day or two. Sometimes kids faint after they get shots and they could be injured if they fall from fainting. We'll have your child stay seated after the shot to help protect him/her.

I'm worried about the safety of HPV vaccine. Do you think it's safe?

Are all of these vaccines actually required?
 I strongly recommend each of these vaccines and so do experts at the CDC and major medical organizations. School entry requirements are developed for public health and safety, but don't always reflect the most current medical recommendations for your child's health.

There is no evidence available to suggest that getting HPV vaccine will have an effect on future fertility. However, women who develop an HPV precancer or cancer could require treatment that would limit their ability to have children.

Can HPV vaccine cause infertility in my child?

For more information, visit [cdc.gov/vaccines/conversations](https://www.cdc.gov/vaccines/conversations)

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 Last updated JULY 2019

https://www.cdc.gov/hpv/hcp/index.html?CDC_AA_refVal=https%3A%2F%2Fwww.cdc.gov%2Fvaccines%2Fyouarethekey%2Findex.html

HPV Vaccine Resources

- **Human papillomavirus resource pages at**
 - <https://www.cdc.gov/vaccines/ed/webinar-epv/>
 - **Includes information for:**
 - Health care providers on:
 - Disease and treatment
 - Vaccine administration, storage, and handling
 - Parents and patients on:
 - Disease
 - Vaccine safety
 - Partners and programs
 - Print materials, articles, online, video and audio resources
- 