# **Epidemiology of HPV Infection**

Focus on older women

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# Outline

- Natural history of HPV infection
- Challenges in defining the epidemiology of HPV
- Prevalence
  - HPV DNA/seroprevalence
- Incidence
  - Cohorts
- Sexual behavior
- Prevalence of CIN 2/3 and genital warts



#### **Background: natural history**



### Cumulative incidence of any HPV infection Months after sexual initiation, Women





Winer R, et al., Am J Epidemiol, 2003

### **HPV** natural history

- Infection with HPV occurs soon after sexual debut
- Over 90% of infections clear within 2 years, most in the first 6 months
- Cumulative incidence of any HPV is >80% by 50 years; lower for HPV 6, 11, 16, 18
- Persistent infection with oncogenic HPV types is the most important predictor of cervical precancers and cancers

Ho et al., NEJM 1998; Moscicki et al., J Pediatr 1998; Franco et al., JID 1999; Molano et al., Am J Epidemiol 2003



# Challenges in describing epidemiology of HPV infection

- Prevalent infection
  - Reflects acquisition and duration of infection
  - Often high in young women, most infections clear
  - Decreases with age
  - Among women >30 yrs, infection is more likely to be persistent rather than newly acquired infection
  - Infection with multiple types occurs



# Challenges in describing epidemiology of HPV infection (2)

#### Incident infection

- Less feasible to conduct studies
- When "incident" infection is detected in older women, it is difficult to differentiate:
  - Reinfection
  - New (first time) infection
  - Reactivation of previously acquired infection



#### **Prevalence of HPV in women**

- HPV prevalence peaks in the 20s, and declines with age
- Smaller secondary peaks in prevalence among older women have been observed in some geographic regions
- A variety of sexual behaviors are risk factors for prevalent and incident infections



#### Any HPV Prevalence among females, by age NHANES, 2003-2004 (N=1921)



Dunne et al., JAMA 2007

# Prevalence of low risk and high risk HPV types among females, by age NHANES 2003-2004





Dunne et al., JAMA 2007

#### Prevalence of HPV-16, by age Guanacaste, Costa Rica



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#### HPV 16 and 11 seroprevalence National Health and Nutrition Examination Survey (NHANES), U.S., women





Stone KM, JID 2002, Dunne EF, JID 2004, Hariri S, JID 2008

# Incidence of HPV 6,11,16 or 18 per 100 person years, by age Protocol 019: Placebo Arm

Age Group (years)	Incident Infection Rate (95% CI)		
24-29	7.4 (5.90, 9.21)		
30-34	3.6 (2.42, 5.05)		
35-39	2.4 (1.50, 3.60)		
40-45	1.9 (1.15, 2.95)		



Haupt R, Merck presentation to ACIP, Feb 2008

## Incidence of HPV 16, 18, 6 or 11 by age, Columbia Evaluation over 5 years



Munoz N, et al., JID 2004

### **Incident infection**

- Evidence for some proportion of incident infections due to acquisition:
  - Epidemiologic data
    - new sex partners are associated with incident HPV infection
    - women who were single, separated or divorced more likely to have HPV infection
  - Sexual behavior data



# Sexual behavior women 25-44 years, U.S. NSFG, 2002

- Mean no. lifetime sex partners was 3.8
- Most women had 1 partner in last 12 months, but 7-10% had >1 partner
  - Divorced/separated women had higher % of sex partners in the last 12 months



# Sex partners in past 12 months NSFG, 2002



Percent

Mosher et al. NCHS report. 2006.

# Sex partners in past 12 months by marital status NSFG, 2002

Marital Status	No. sex partners past 12 months		
	0	1	>1
Divorced/separated	22.3	56.6	21.1
Married	3.4	95.2	1.4
Never married	30.4	55.8	13.8



Leichliter. Unpublished data analyses, 2008.

# **Natural history of incident HPV**

- Incidence declines with age
- In studies of incident infection in older women:
  - Unclear if these are reinfections, reactivations
    from a previous infection acquired earlier, or new infections
  - Questions remain on the natural history of incident infection in older women

Munoz et al., JID 2004; Castle PE et al., JID 2005 Grainge et al., EID 2005, Rodriquez AC JNCI 2008 in press



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#### Genital wart diagnoses by age group, Medstat, 2000 Men and Women



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Insigna R, CID 2003

# Incident cervical intraepithelial neoplasia (CIN) 2/3 Kaiser NW, 1998





Insigna RP, Am J Ob Gyn 2004

#### Summary

- Among women in their mid 20s, with increasing age
  - HPV prevalence decreases
  - HPV incidence decreases
  - Likelihood of having acquired HPV infection increases
- Seroprevalence to HPV 16 in U.S. is ~25% among women in their 20s; this underestimates cumulative infection
- Disease outcomes (genital warts, CIN 2/3) peak among women in their mid to late 20s
- Questions remain on natural history of incident infections in older women



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