

The Perils of Papilloma:
Building a Vaccine to Prevent
HPV-related Cancer:
Is it Possible?

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Introduction – HPV, Cervical Cancer and Vaccines

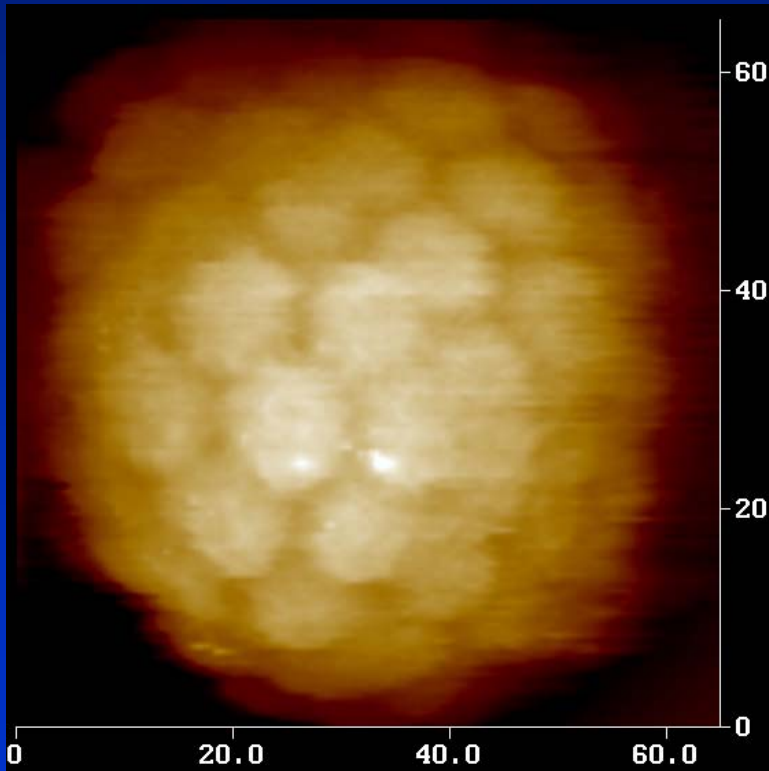


Image courtesy of Dr. Darron Brown,
Indiana University

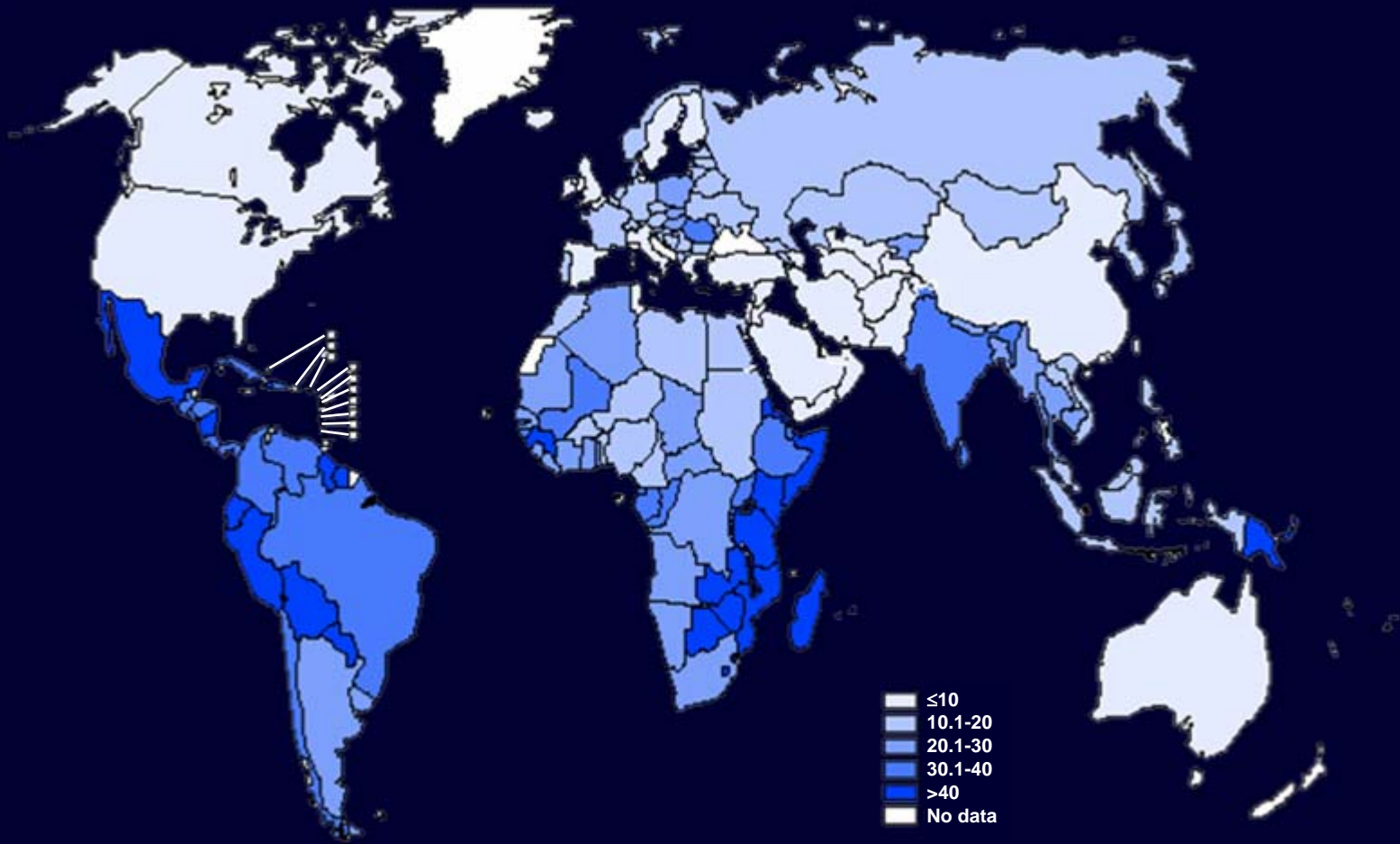
- Cervical cancer is usually caused by human papilloma virus (HPV)
- Worldwide cervical cancer is a significant cause of death with 250,000 deaths/yr
- Clinical trials of subunit vaccines show promise for preventing HPV infection and sequelae

Infections and Cancers: Global Burden

Infection	Cancer	# cases worldwide	% worldwide
<i>H. pylori</i>	stomach	490,000	5.4
HPV	Cervix etc	550,000	6.1
Viral hepatitis	Liver	390,000	4.3
Totals		1.6 million	17.7

Source: WHO, 2003

Estimated Age-Standardized Incidence of Cervical Cancer Per 100,000 Women, Year 2000



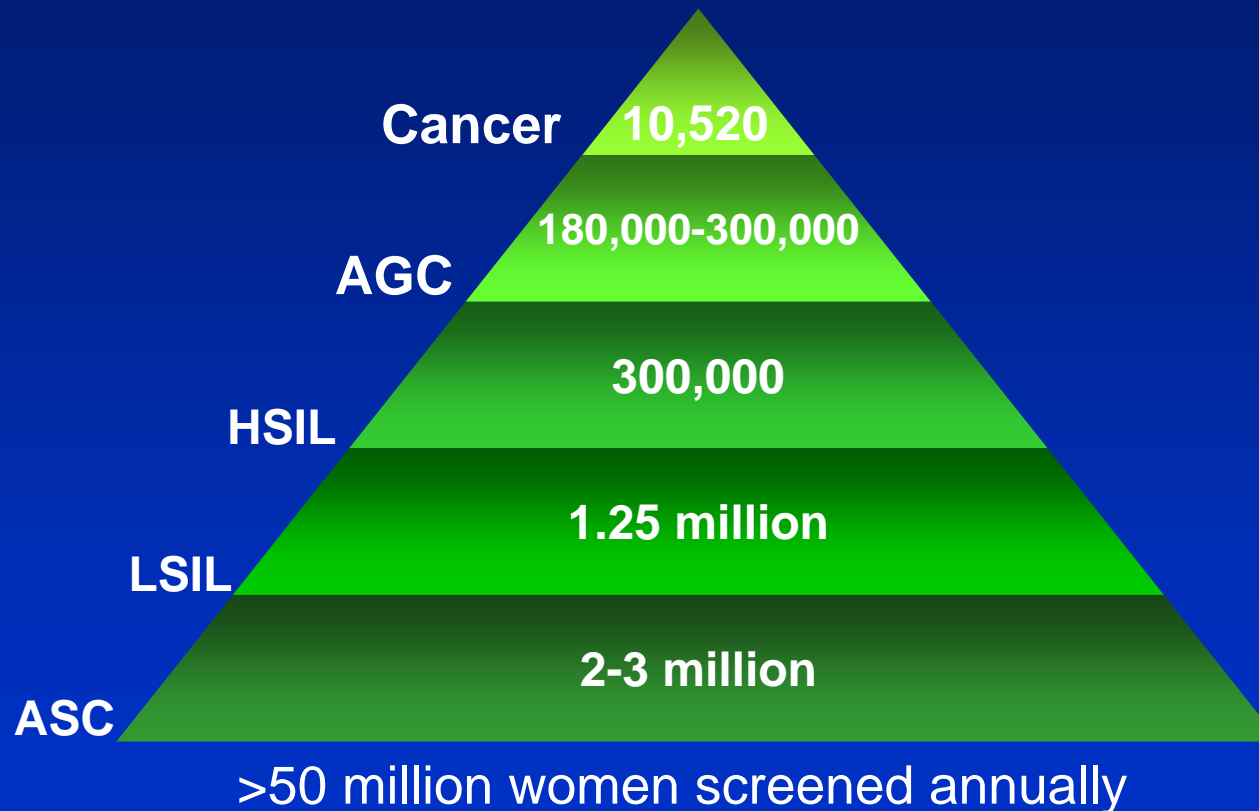
Source: WHO

Burden of Disease due to HPV

- In developed world, most costs associated with detection and treatment of pre-malignant disease
- Cost in USA - \$ 3 Billion
- Cervical cancer in USA in poorly screened populations
- Lifetime risk of cervical cancer without screening – 2 to 4 %

See Leyden *et al* '05

Abnormal Pap Tests in the US



ASC = atypical squamous cells; AGC = atypical glandular cells; SIL = low-grade squamous intraepithelial lesion; HSIL = high-grade squamous intraepithelial lesion

Sirovich *et al* '04

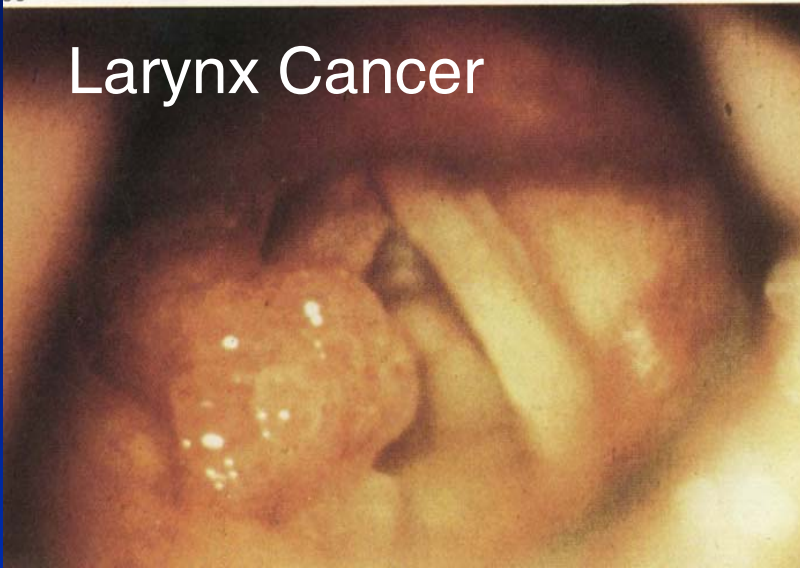
HPV Types and Disease

	Frequent Association (HPV Type)	Less-Frequent Association (HPV Type)
Cutaneous warts	1, 2	3, 4, 7, 10, 26, 27, 28, 29, 38, 41, 49, 57, 63, 65, 75, 76, 77, 80, 83, 84, 86, 87
Epidermodysplasia verruciformis	2, 3, 10, 5, 8, 9, 12, 14, 15, 17	19, 20, 5, 21, 22, 23, 24, 25, 36, 37, 38, 47, 50
Condylomata acuminata (Laryngeal papillomas)	6, 11	30, 42, 43, 44, 45, 51, 54, 55, 70
Cervical Intraepithelial Neoplasia (including other anogenital dx)	6, 11, 16, 18	30, 31, 33, 34, 35, 39, 40, 42, 43, 44, 45, 51, 52, 53, 56, 57, 58, 59, 61, 62, 64, 66, 67, 68, 69, 71, 74, 82
Cervical carcinoma	16, 18	31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66, 68, 70

Frazer '04 and Munoz *et al* '03

HPV Related Cancers

Larynx Cancer



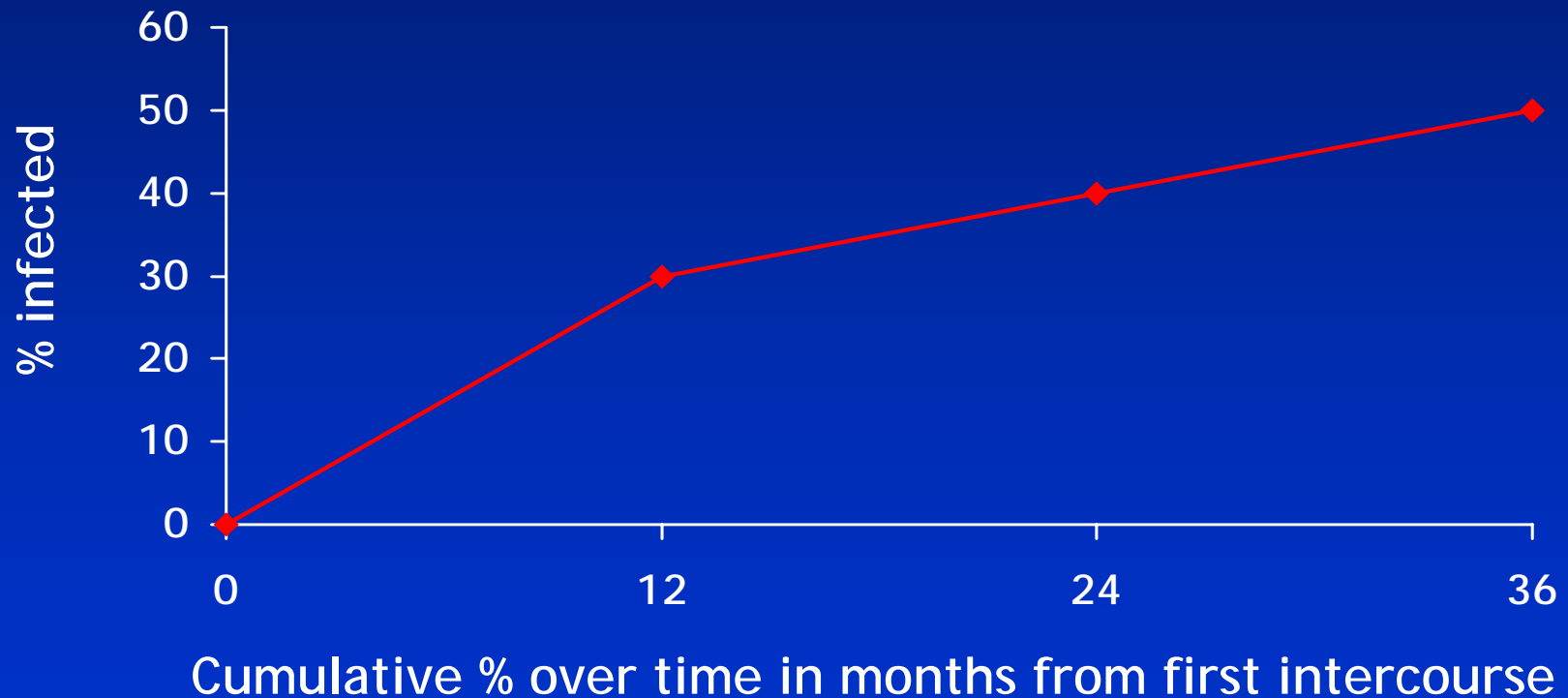
Cervical Cancer



“AISL”



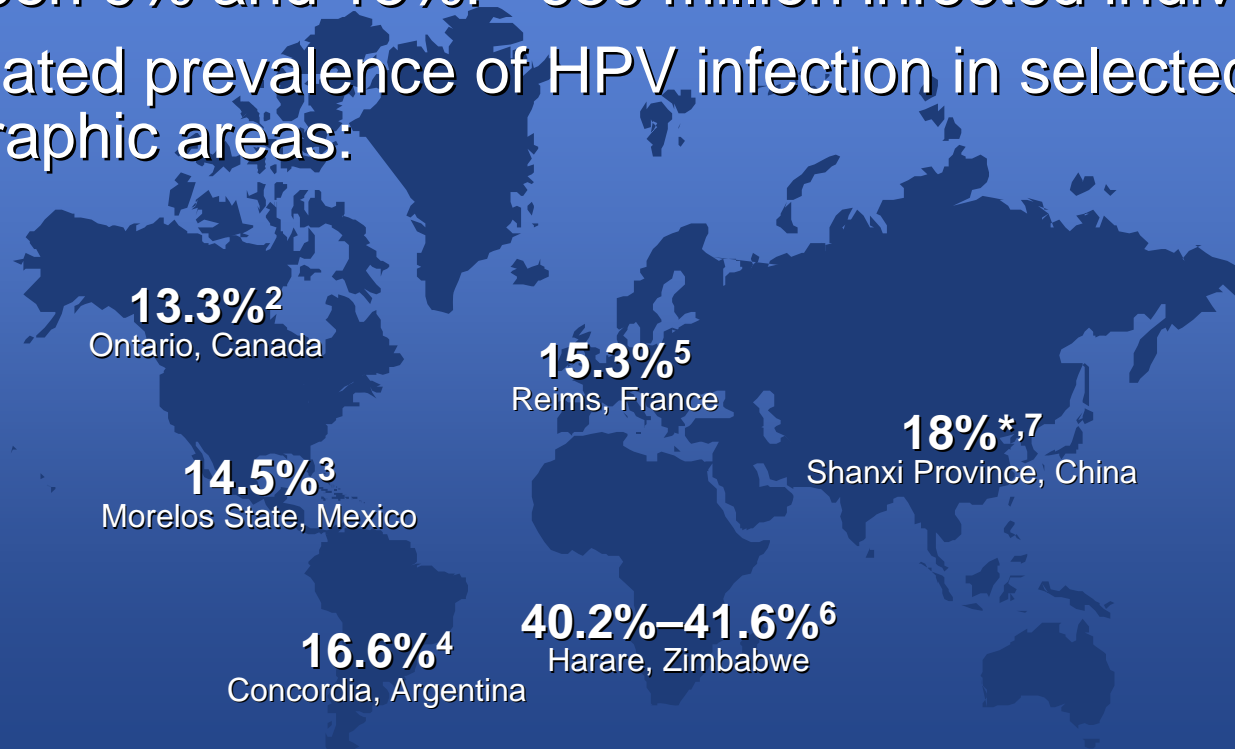
HPV Infection Among College-Age Women



Winer *et al* '03

Global HPV Statistics

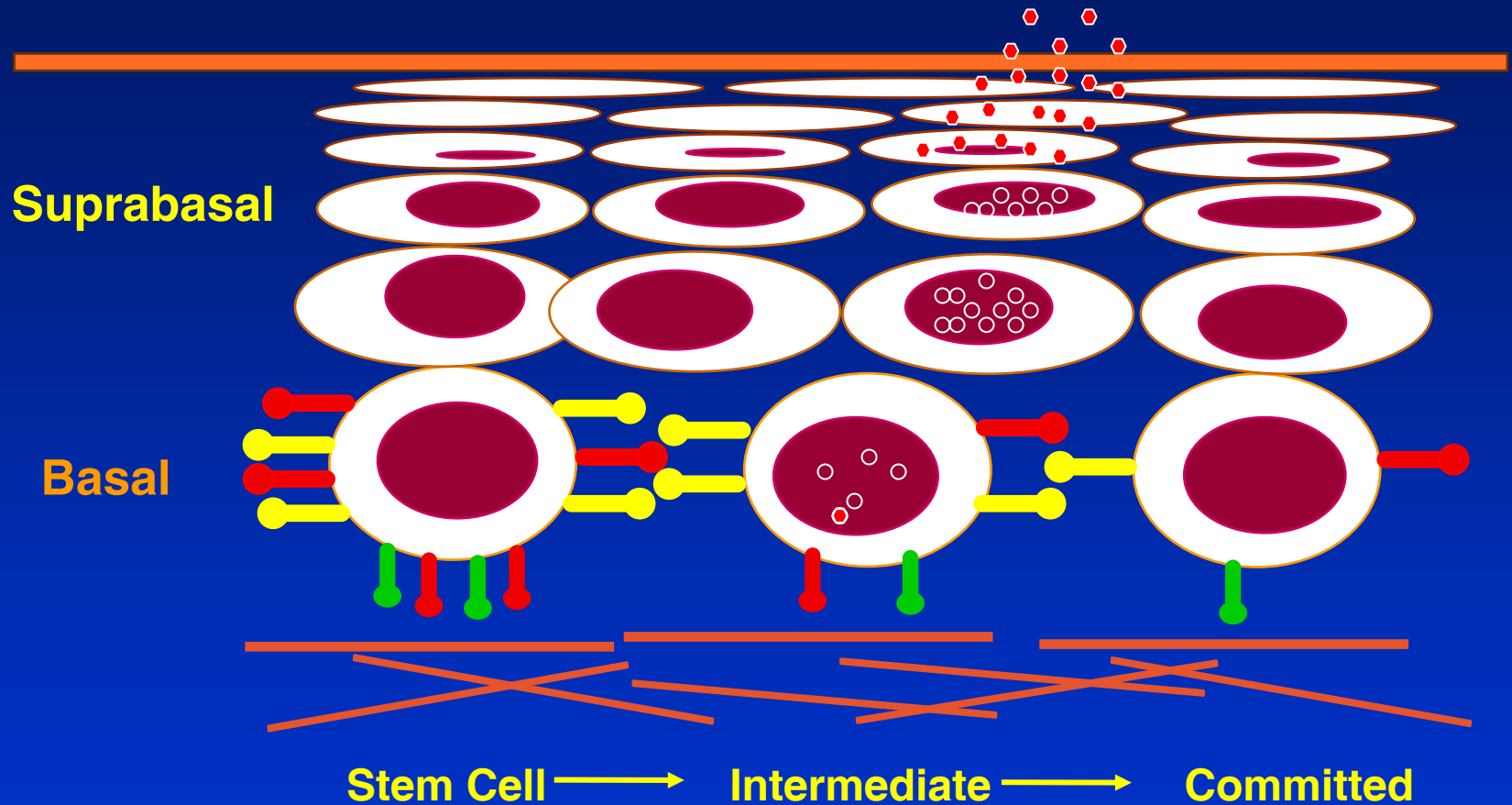
- Worldwide prevalence of HPV infection is estimated to be between 9% and 13%: ~630 million infected individuals.¹
- Estimated prevalence of HPV infection in selected geographic areas:



*Among women 30–45 years of age

1. World Health Organization; 2001. Available at: <http://www.who.int/vaccines/en/hpvrdshtml>. Accessed July 12, 2004.
2. Sellors JW, Mahony JB, Kaczorowski J, et al. *CMAJ*. 2000;163:503–508. 3. Lazcano-Ponce E, Herrero R, Muñoz N, et al. *Int J Cancer*. 2001;91:412–420. 4. Matos E, Loria D, Amestoy GM, et al. *Sex Transm Dis*. 2003;30:593–599. 5. Clavel C, Masure M, Bory JP, et al. *Br J Cancer*. 2001;84:1616–1623. 6. Blumenthal PD, Gaffikin L, Chirenje ZM, McGrath J, Womack S, Shah K. *Int J Gynecol Obstet*. 2001;72:47–53. 7. Belinson J, Qiao YL, Pretorius R, et al. *Gynecol Oncol*. 2001;83:439–444.

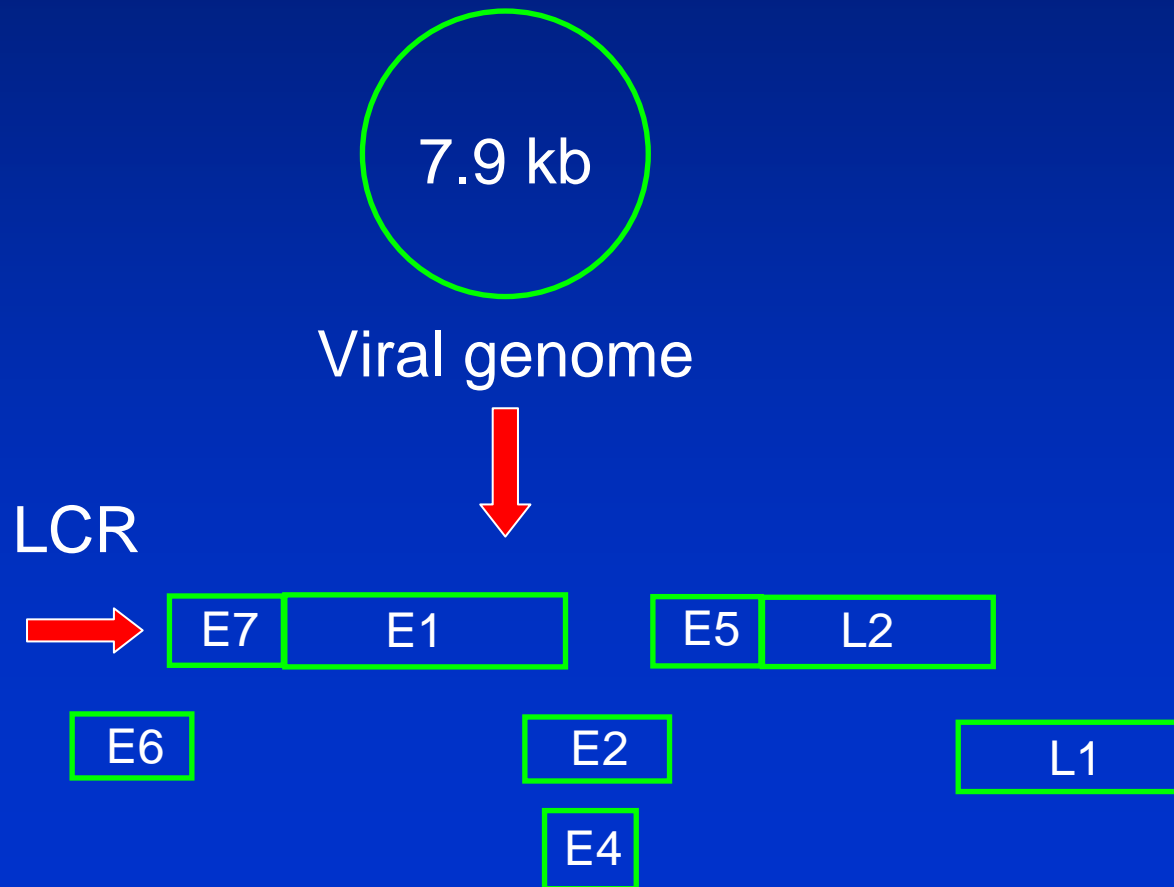
HPV Infection in Squamous Epithelium



Courtesy of Dr. Al Klingelutz, University of Iowa

HPV Genome

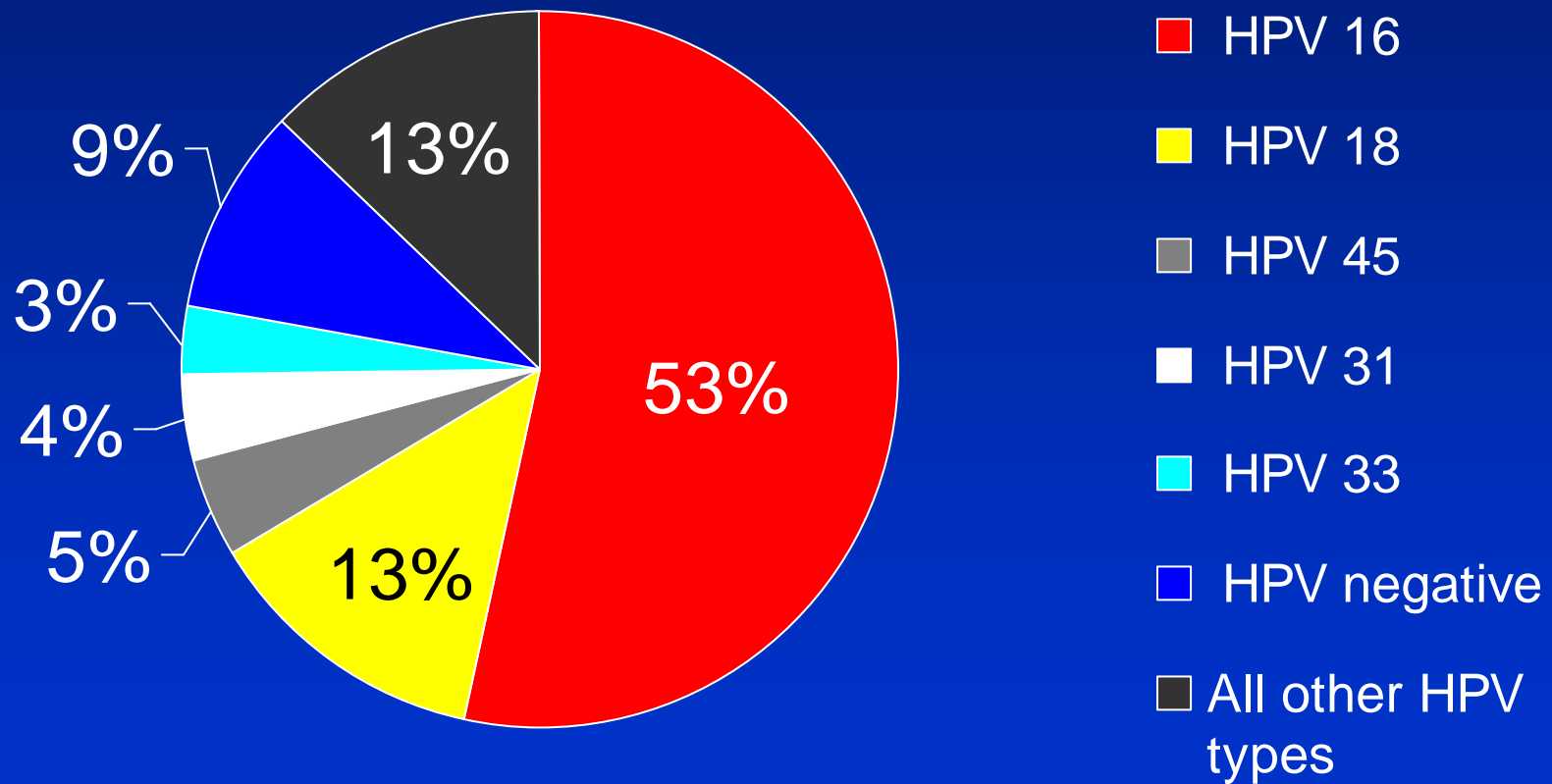
HPV genomic organization



HPV VLP as a Prophylactic Vaccine

- VLP are the product of HPV 16 L1 gene
- Capsid proteins self assemble into “pseudovirions”
- Three injections over a six month period are known to be highly immunogenic and well tolerated
- Similar dosing scheme as hepatitis B
- Works in animal models

HPV Types That Cause Cervical Cancer: A Worldwide Survey



Munoz *et al*, '03 n = 1918

Conclusions: Current State of HPV Vaccines

- Promising efficacy trials with further publications in this year
- Multivalent VLP vaccines are in later-phase clinical trials, quadrivalent vaccine awaiting FDA approval (Dr. Barr)
- Remaining questions include
 - **Duration of protection ?**
 - Cross-protection ? Replacement ?
 - **Protection in HIV positive women?**
 - Herd Immunity?
 - **Acceptance ?**

Cervical Cancer – Past, Present and Future



1930 - cervical cancer # 1
cancer mortality in women
in USA

1941 - Papnicolaou publishes
his paper in the *American
Journal of Obstetrics and
Gynecology*

2004 - 500,000 cases of
Cervical Cancer worldwide

2006 - Cervical Cancer
Vaccine