# Human papilloma virus (HPV), Cervical dysplasia and Cervical Cancer

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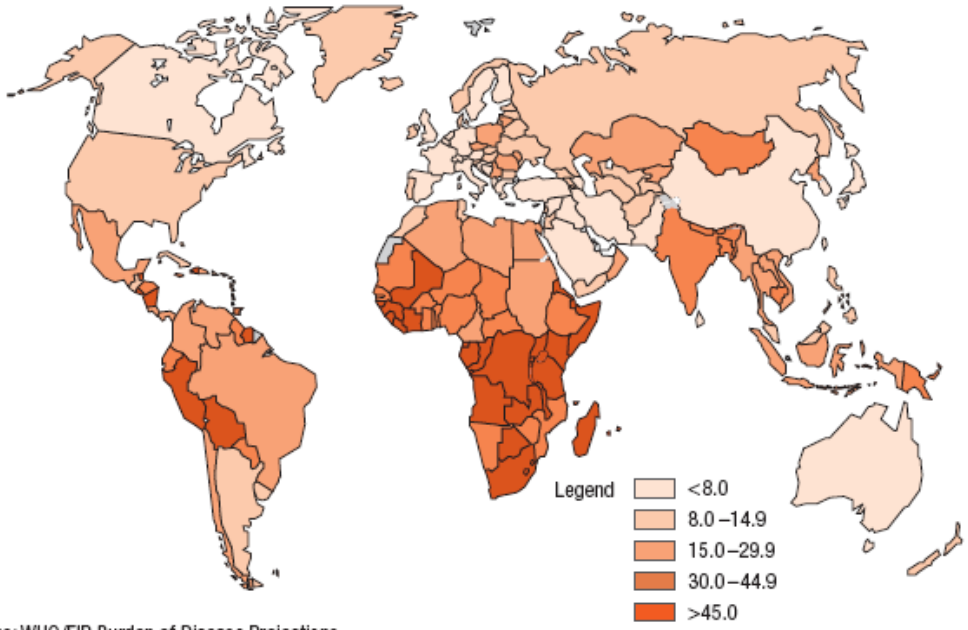
# Screening, Diagnosis and Management of Cervical Cancer

- Statistics
- Diagnosis of cervical dysplasia, cervical cancer
- Screening for cervical cancer
- Relationship between HPV and cervical dysplasia/cancer
- Management of cervical dysplasia
- Management of cervical cancer

# Cervical cancer

- Globally, breast and cervical cancer are the most prevalent cancers in women
- In 2005, 260,000 deaths annually and 2.7 million years of life lost
- Highest areas of incidence in Latin America, Sub-Saharan Africa, the Caribbean, south-east Asia
- In the United States for 2008, there were about 11,000 women diagnosed with cervical cancer and about 3,900 deaths attributable to cervical cancer
- Economic costs attributable to cervical diseases are about $4 billion USD annually (Insinga, Womens Health Issues, 2006)
- Differing economic burdens from cervical cancer

**Figure 1. Worldwide incidence of cervical cancer per 100 000 females (all ages), age-standardized to the WHO standard population, 2005**



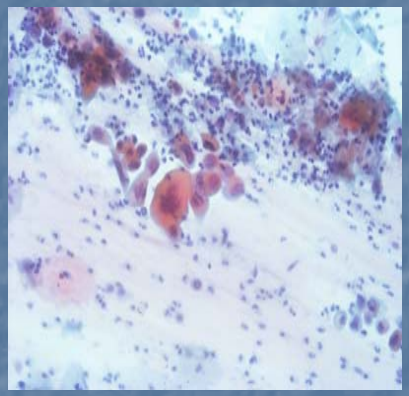

*Source:* WHO/EIP Burden of Disease Projections (http://www.who.int/healthinfo/statistics/bodprojections2030/en/index.html).

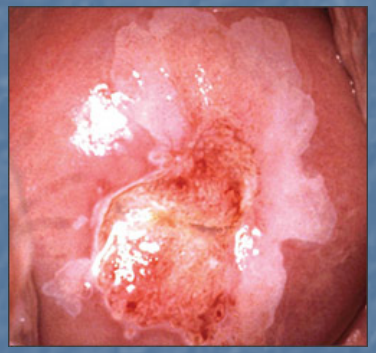
# Diagnosis of cervical cancer

- Risk factors
  - Sexual activity
  - HPV
  - Cervical dysplasia
  - Immunosuppression
  - Racial and ethnic trends
- Symptoms
  - abnormal bleeding/discharge
  - Pain
  - Urinary or bowel symptoms
- Diagnosis of cancer by tissue biopsy

# Screening for cervical cancer

- Very effective as cervical cancer often is preceded by a long pre-invasive phase. Treatment of cancer precursors is simple, effective and preserves function and fertility.
- Large body of data supports a much decreased incidence and mortality risk from cervical cancer in screened populations
- The components of screening include knowledge of risk factors, PAP smears, HPV subtype testing. Follow-up tests include colposcopy and cervical excision.
- The most cost-effective guidelines for screening are still a work-in-progress

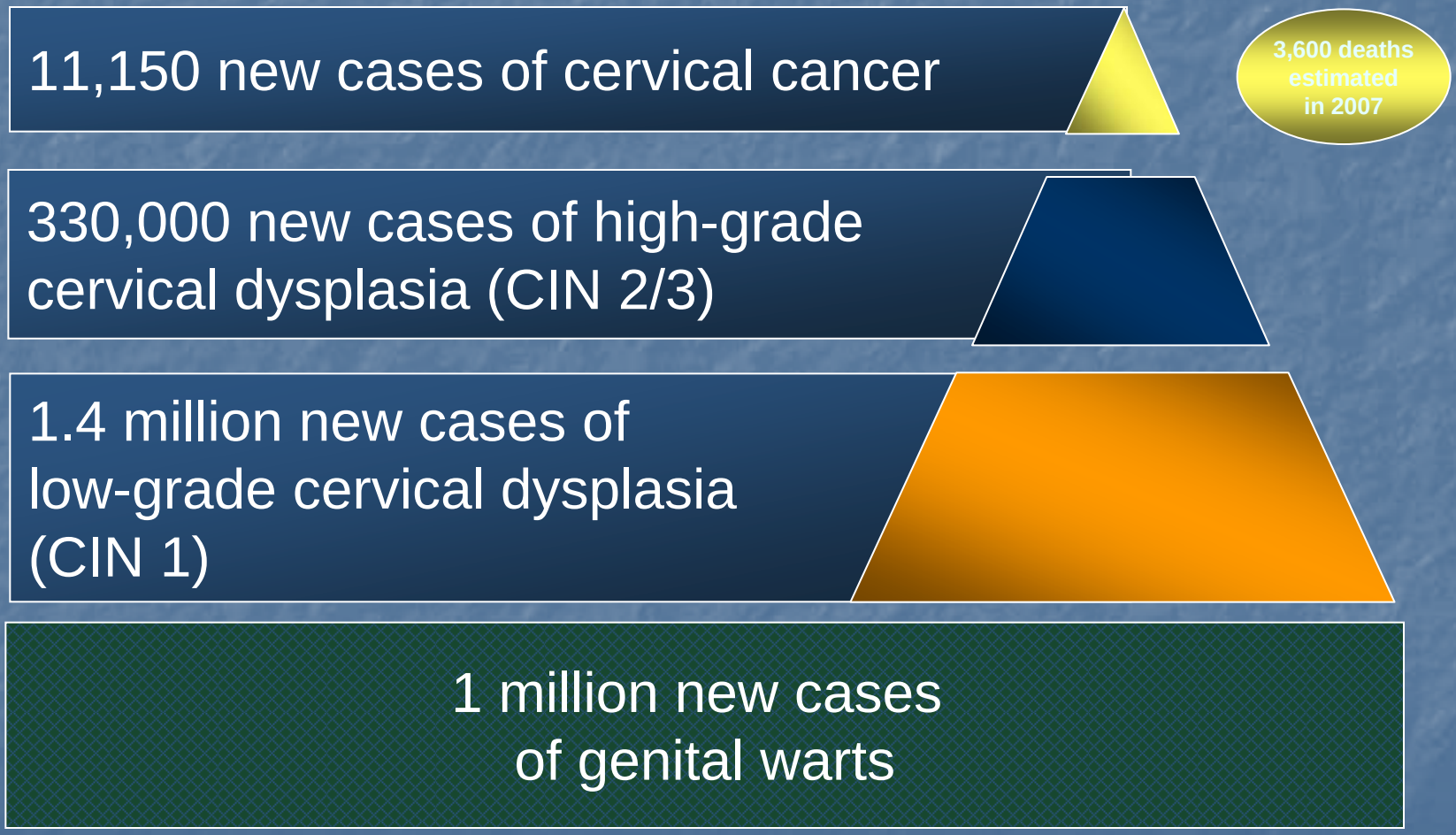




# HPV-basic facts

- DS DNA virus
- 120 subtypes identified, about 40 of which infect the genital tract
- 20 oncogenic types: 16,18,31,33,35,39,45,51,52,58.
- Tissue transforming effect suggested by Zur Hausen in 1974.
- 8 kb circular genome, enclosed by capsid shell, two groups of capsid proteins-L1 and L2. Genes E1 through E7 code for viral replication and host effects
- Most HPV infections resolve spontaneously and are transient

# Estimated Annual Burden of HPV-Related Diagnoses in the United States



# HPV-associated diseases Genital Tract

- Condyloma accuminata
- Intraepithelial neoplasias of the cervix, vagina, vulva and perianal skin
- Invasive cancers of the cervix, vagina, vulva and anus
- Male condyloma, dysplasia and carcinoma

# Oncogenic HPV

- Associated with almost 100% of cases of invasive cervical carcinoma
  - HPV types 16 and 18 account for about 70%
- Associated with 90% of anal cancer
- Associated with 40% of vulvo-vaginal cancers
- Associated with 12% of oropharyngeal cancers
- Associated with 3% of oral cancers

Parkin and Bray, Vaccine, 2006

# Morbidity and Mortality from HPV-associated diseases

- Condyloma: discomfort, social stigmatization
- Laryngeal papillomas: hoarseness, stridor, dyspnea
- Dysplasia: pruritus, increased relative risk for carcinoma
- Carcinoma: pain, bleeding, treatment related loss of fertility and treatment complications, death

# Measures to reduce cervical cancer and dysplasia

- Safe sex strategies
- Reduction in number of sexual partners
- Condom use
- Male circumcision
- Screening and treatment of precursors lesions
- HPV Vaccination

# HPV vaccination

- Quadrivalent and bivalent vaccines
- Virus-like particles induce an antibody response in the vaccinated individual but contain no viral DNA core
- Large clinical trials have successfully shown high seroconversion rates, reduction in the high-risk HPV subtypes and reduction in high grade cervical dysplasia

# Management of cervical dysplasia

- After confirmation of the diagnosis by biopsy
  - Low grade dysplasia may be managed by observation to allow for spontaneous regression
  - Higher grades of dysplasia are treated by excision (LEEP) or destruction
  - Treatment rarely has impact on fertility and childbearing

# Management of cervical cancer

- Staging to establish extent of disease
- Treatment by radical surgery, radiotherapy often with chemotherapy and chemotherapy
- Treatment most often entails loss of fertility, discomfort, lost time from work and risk of complications

# Conclusions

- Cervical diseases have considerable impact on the health of women
- HPV infection is the critical event in the development of most cervical disease
- Prevention of HPV-related disease by vaccination may be the most effective means of disease control
- Treatment of advanced disease is painful, has significant risk of complications, often is unsuccessful, quality of life is diminished and is costly