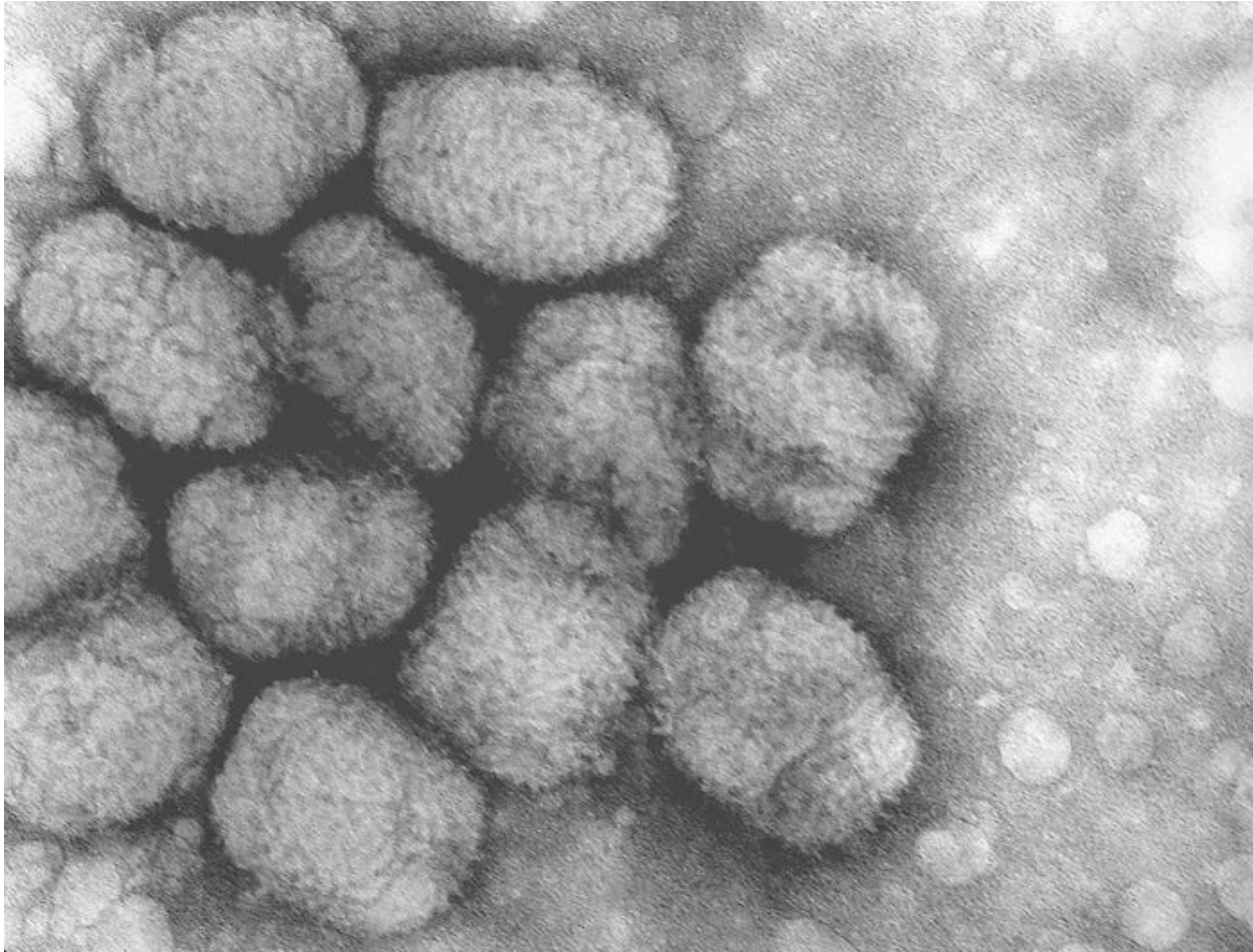


# poxviruses



# Poxviruses

- Infect humans, birds, mammals, and insects.
- DsDNA brick shaped, enveloped multiply in the cytoplasm, 100x200x300 nm.
- lack normal capsid – instead, layers of lipoproteins and fibrils on surface
- Variola (small pox), Vaccinia, Moluscum contagiosum, orf, cowpox, and pseudocowpox.

# Variola (small pox)

- Variola major (smallpox) (3-35%), V. minor (alastrim) (<1%).
- Uniform papulovesicular rash, pustules with significant mortality.
- Survives well in the extracellular environment.
- Highly contagious, saliva, skin and fomites.
- Eradicated in 1977. Only humans, no asymptomatic carriers.

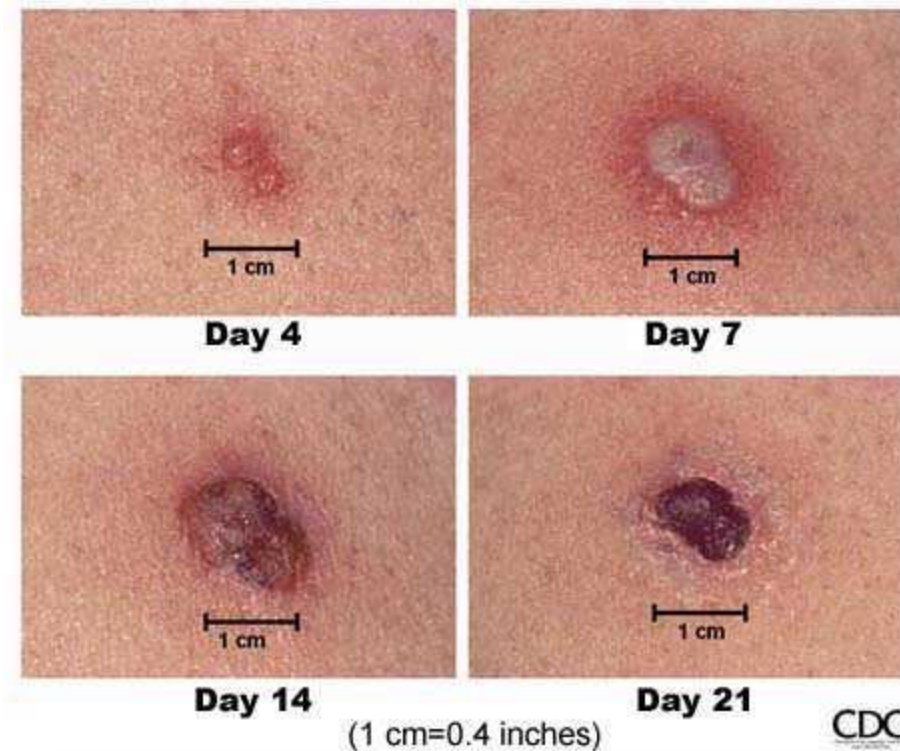
- Concern for recurrence
  - Stable virus especially in freeze dried form
  - High infectivity in humans
  - Vaccine supplies are limited
  - No specific antiviral drug

## **Pathogenesis**

- Switches off cellular protein synthesis to synthesize its own proteins.
- Change in cell permeability and cell lysis
- Eosinophilic inclusions, Guarnieri's bodies in cytoplasm.

# Manifestations

- IP=12-14 days, can be short to 4-5 days.
- Abrupt onset, fever, chills, myalgia, rash 3-4 days later.
- Firm papulovesicles, pustular in 10-12 day, crust and slowly heal
- All in the same stage of evolution
- Hemorrhagic rash (sledge hammer).
- Bacterial superinfection leads to death.





# Diagnosis and prevention

- Diagnosis: take vesicular scraping, culture, electron microscopy, PCR.
- Edward Jenner, milkmaids, cowpox, immune to smallpox
- Vaccinia virus, recombination cowpox and smallpox, used as a vector for vaccine
- Vaccination resembles real infection, localised.
- Immunity wane after 3 yrs

# Molluscum contagiosum

- Spread by direct contact, towels, sex
- IP=2-8 weeks
- painless nodule, pearl-like lesion, cheesy material in the center
- No systemic symptoms
- Dx: clinical picture which can be confirmed by the presence of eosinophilic inclusions in cytoplasm of epithelial cells (molluscum bodies).
- No specific treatment, disappear in 2-12 months, removed by curettage







orf: sheep and goat  
Solitary lesion, begins as  
Vesicle, evolve into a nodule  
That has necrotic center.  
Resolve in 35 days



milkers nodules and cowpox  
Lesion similar to ORF  
Resolve in 6-8 weeks

# Human Papilloma Virus

- Small, naked, double stranded circular DNA virus with icosahedral capsid
- Capsid composed of 2 proteins L1 and L2
- Genome encodes eight early genes (E1-E8) and 2 structural capsid proteins L1 and L2
- The virus does not encode any polymerase and therefore dependent on the host cell transcription and replication machinery.
- There are over 100 different types of the HPV virus - most types are totally harmless
- Difficult to propagate in cell culture
- Cause papilloma and warts in a wide range of vertebrates.

# HPV Replication

- Not well understood
- HPV infect basal layer of squamous epithelium, virus internalized, uncoated and delivered to the nucleus
- Host RNA polymerase transcribes E genes followed by early protein synthesis
- E6 and E7 play a role in cellular transformation leading to excessive cell division
- E6 bind to p53 and E7 to p105RB proteins disrupting cell cycle regulation.
- The dividing cell carry viral genome as extracellular DNA
- Viral DNA synthesis occur at two level directed by cellular DNA polymerase
  - Lower epidermis: viral DNA for latent infection
  - Differentiated epithelial cells: vegetative DNA replication
- Integration of viral DNA may occur occasionally
- epithelial cells differentiate into keratinocytes where capsid proteins are synthesized and DNA replicated
- Virus assembles in the nucleus and virus released by cell lysis

# HPV Prevalence

- Most common STD
  - Yearly incidence of 6.2 million
  - 20 million currently infected
  - 80 million infected at least once between the ages of 15-49
- An estimated 9.2 million sexually active adolescents and young adults 15-24 years of age are infected with genital HPV
- An estimated 5%-30% of people infected with genital HPV are infected with multiple types of the virus
- 316,000 initial visits to physicians' offices -genital wart diagnosis

# Epidemiology

- Cutaneous warts usually occur in children and young adults conferring specific protective immunity
- Most common transmission is by skin-to-skin contact with the penis, scrotum, vagina, vulva, or anus of an infected person. Infectivity 60% though most infections are asymptomatic
- HPV 6 and 11 associated with benign genital warts in males and females and benign cervical cellular dysplasia
- Perinatal transmission is associated with laryngeal papilloma
- HPV 16, 18, 31, 45 and 56 lesions in the vulva, cervix and penis. 16 and 18 may progress to malignancy
- Infection of the anus with HPV is more pronounced in AIDS pts and it is linked with anal neoplasia

-

# Pathogenesis

- HPV has predilection for infection at the junction of squamous and columnar epithelium (anus and cervix).
- Pathogenicity and oncogenicity is not well understood

# **Risk Factors for Acquiring a Genital HPV Infection**

- Young age (less than 25 years)
- Multiple sex partners
- Early age at first intercourse (16 years or younger)
- Male partner has (or has had) multiple sex partners

# HPV

## Transmitted by:

- Direct skin-to-skin contact
  - Usually, but not always sexual contact
- Infected birth canal
  
- Average incubation is 3 weeks to 1 year, Possibly years before appearance of warts or cervical abnormalities



# Common Symptoms of Genital Warts in Males & Females

- Genital warts are unsightly cauliflower-like growths (6, 11)
- Some types are considered “high risk” and can cause pre-cancerous lesions and can lead to cancer of the cervix, anus and other genital areas.(16,18)
- The symptoms may include single or multiple fleshy growths around the penis, scrotum, groin, vulva, vagina, anus, and/or urethra
- They may also include: itching, bleeding, or burning, and pain
- The symptoms may recur from time to time

# HPV Warts



# Diagnosis

- Papanicolaou (Pap) smear
- Test cervical swab by immunoassays to detect viral antigens
- PCR of specific viral DNA

# HPV Treatment

- Chemical agents: podofilox and trichloroacetic acid
- Cryotherapy: freezing with super cold liquid or gas nitrogen
- Electrosurgery: using an electric current to remove warts
- Surgical excision

## **Carcinoma**

- Radiation therapy with radical surgery

# HPV prevention

## **Gardasil**

- First vaccine to prevent cervical cancer
- Recombinant vaccine; inactive L1 proteins
- Approved for use in females aged 9-26
  - Ideally, before becoming sexually active
- Protects against infection with Types 6, 11, 16, 18
- Three injections given over a six-month period
- Initial dose
- Second dose is given 2 months later
- Third and last dose is given 4 months after the second dose or six months after the initial dose
- It is administered in the upper arm or thigh (intramuscularly)

## **Cervarix**

- designed to prevent infection from HPV types 16 and 18