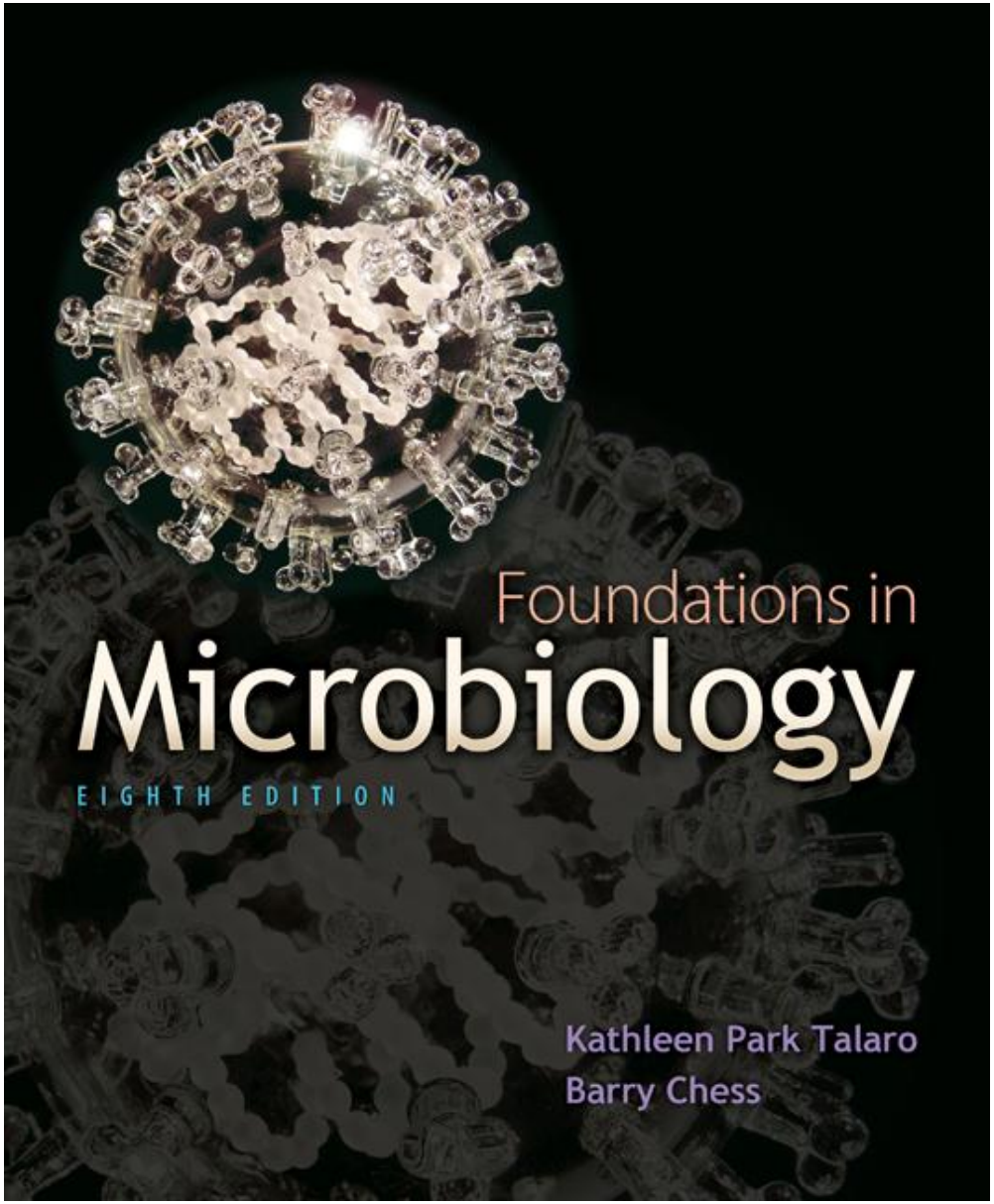
Chapter 24

Introduction to Viruses That Infect Humans: The DNA Viruses



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24.1 Viruses in Human Infections and Diseases

- DNA or RNA molecules are surrounded by a protein coat; obligate parasites that enter a cell, instruct its genetic and molecular machinery to produce and release new viruses
- All DNA viruses are double-stranded except for parvoviruses, which have ssDNA
- All RNA viruses are single-stranded except for dsRNA reoviruses

Important Medical Considerations in Viral Diseases

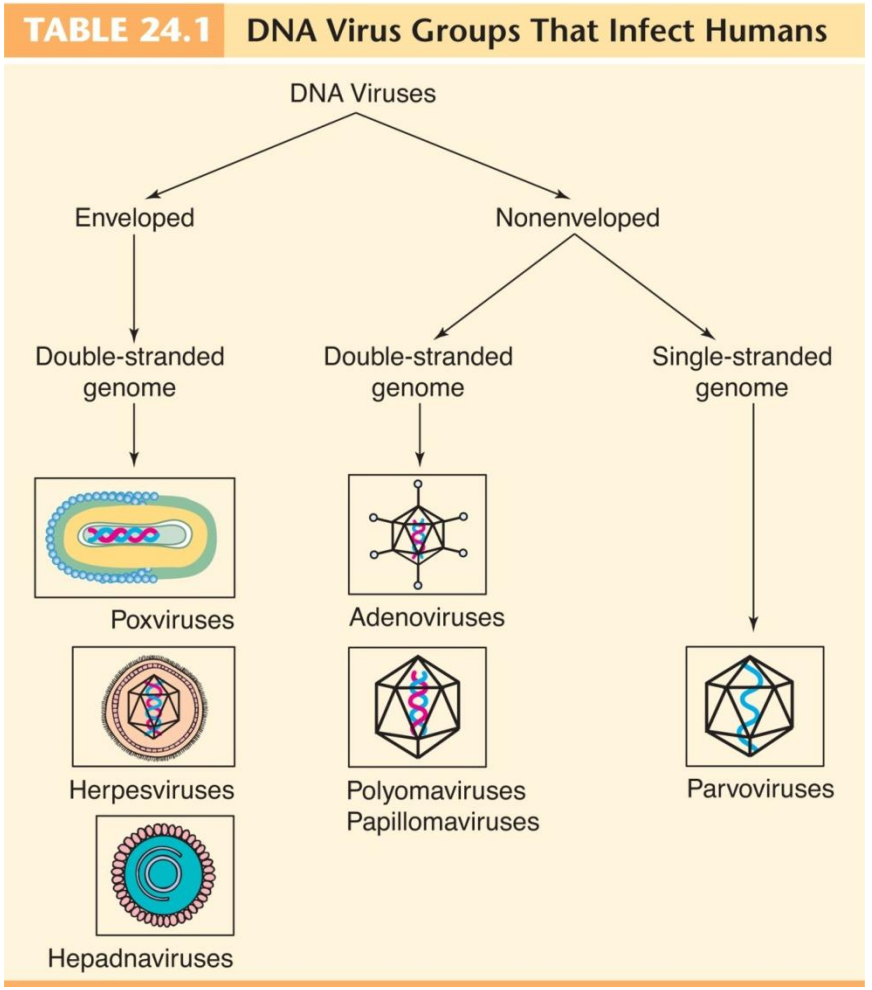
- Viruses are limited to a particular host or cell type
- Most DNA viruses are budded off the nucleus
- Most RNA viruses multiply in and are released from the cytoplasm
- Viral infections range from asymptomatic to mild to life-threatening
- Many viruses are strictly human in origin, others are zoonoses transmitted by vectors

Scope of Infections

- Course of viral disease: invasion at portal of entry and primary infection; some viruses replicate locally, others enter the circulation and infect other tissues
- Common manifestations: rashes, fever, muscle aches, respiratory involvement, swollen lymph nodes
- Body defenses: combined action of interferon, antibodies, and cytotoxic T cells; frequently results in lifelong immunity

Overview of DNA Viruses

- Animal viruses are categorized according to nucleic acid, capsid, and presence or absence of envelope
- 7 DNA families, 14 RNA families
- DNA viruses causing human disease:
  - Enveloped DNA viruses
  - Nonenveloped DNA viruses
  - Nonenveloped ssDNA viruses

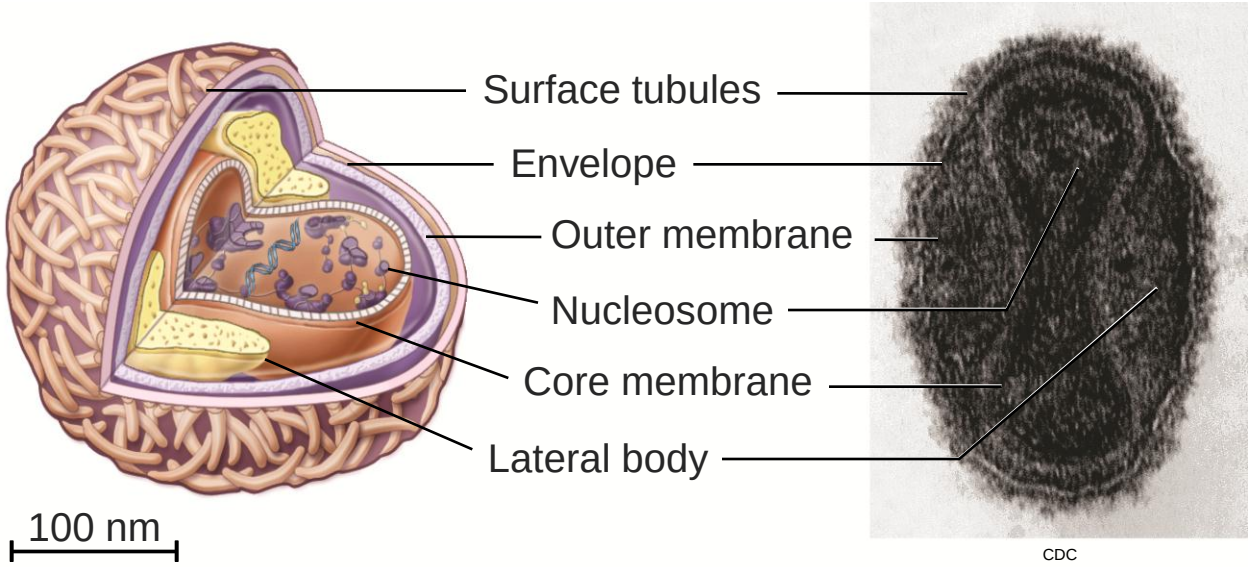


24.2 Enveloped DNA Viruses: Poxviruses

- Poxviruses
- Herpesviruses
- Hepadnaviruses

Poxviruses: Classification and Structure

- Produce eruptive skin pustules called **pocks** or **pox**, that leave scars
- Largest and most complex animal viruses
- Have the largest genome of all viruses
- dsDNA
- Multiply in cytoplasm in factory areas, appear as inclusion bodies in infected cells
- Specificity for cytoplasm of epidermal cells and subcutaneous connective tissues



Smallpox: A Perspective

- *First disease to be eliminated by vaccination*
- Exposure through inhalation or skin contact
- Infection associated with fever, malaise, prostration, and a rash
  - **Variola major**: highly virulent, caused toxemia, shock, and intravascular coagulation
  - **Variola minor**: less virulent

Figure 24.3 smallpox infection

CDC

Smallpox Control

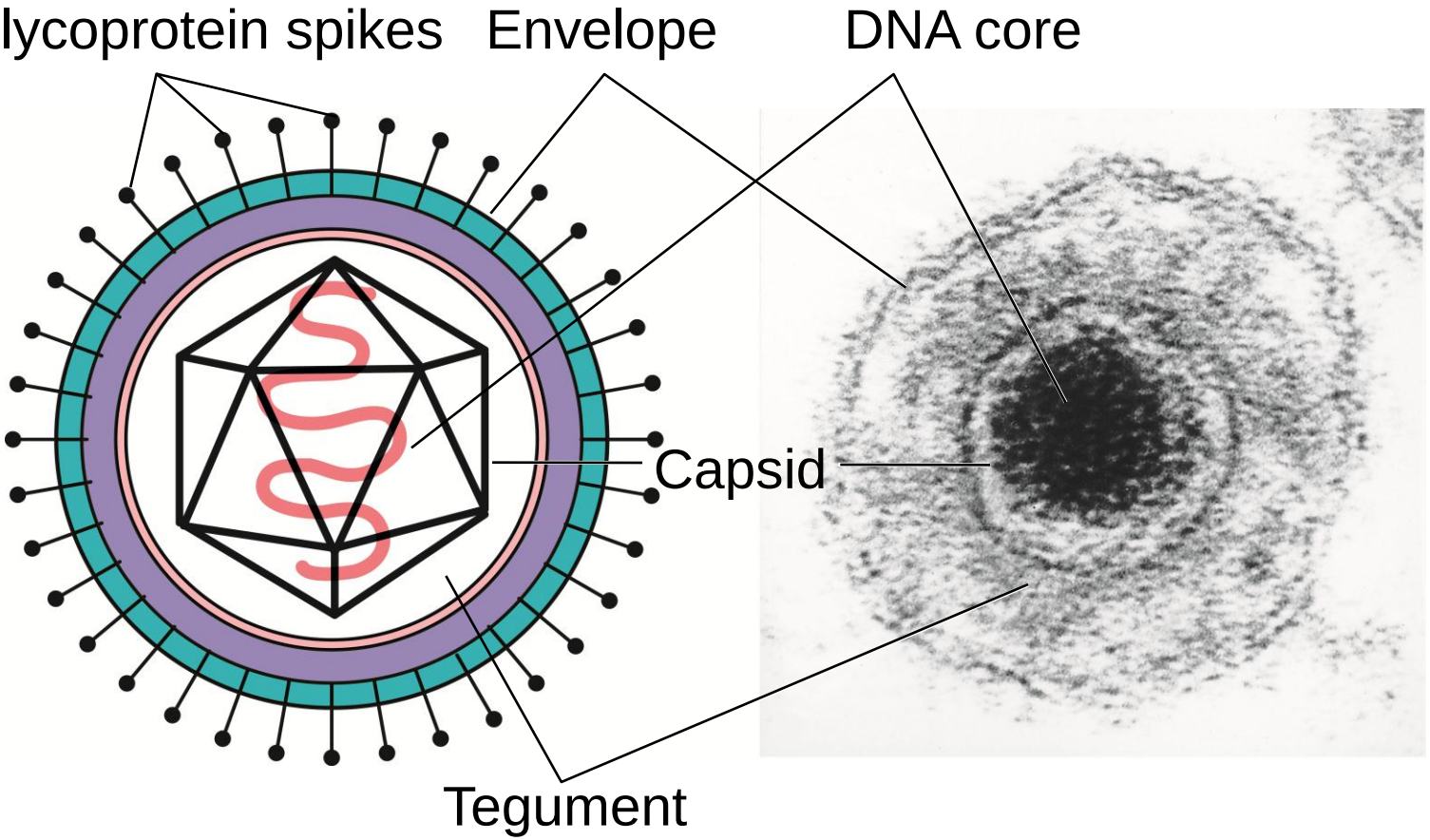
- Routine vaccination ended in U.S. in 1972
- Vaccine reintroduced in 2002 for military and medical personnel

24.3 Enveloped DNA Viruses: The Herpesviruses

- All members show latency and cause recurrent infection; viral DNA forms episome (extrachromosomal)
- Clinical complications of latency and recurrent infections become more severe with advancing age, cancer chemotherapy, or other conditions that compromise the immune defenses
- Common and serious opportunists among AIDS patients

Figure 24.5 The Structure of Herpesviruses

- Large enveloped icosahedral dsDNA
- Replicates within nucleus



Herpesviruses

- Large family; 8 infect humans

HSV-1 – herpes simplex 1: fever blisters

HSV-2 – herpes simplex 2: genital infections

VZV – varicella zoster virus: chicken pox / shingles

CMV – cytomegalovirus: infects salivary glands

EBV – Epstein-Barr virus: infects lymphoid tissue

HHV-6 – herpevirus 6: roseola

HHV-7 – herpevirus 7: roseola

HHV-8 – herpevirus 8: implicated in Karposi sarcoma

General Properties of Herpes Simplex Viruses

- Humans susceptible to 2 varieties
- **HSV-1**: usually lesions on the oropharynx, cold sores, fever blisters
  - Occurs in early childhood
- **HSV-2**: lesions on the genitalia, possibly oral
  - Occurs in ages 14-29
  - Can be spread without visible lesions

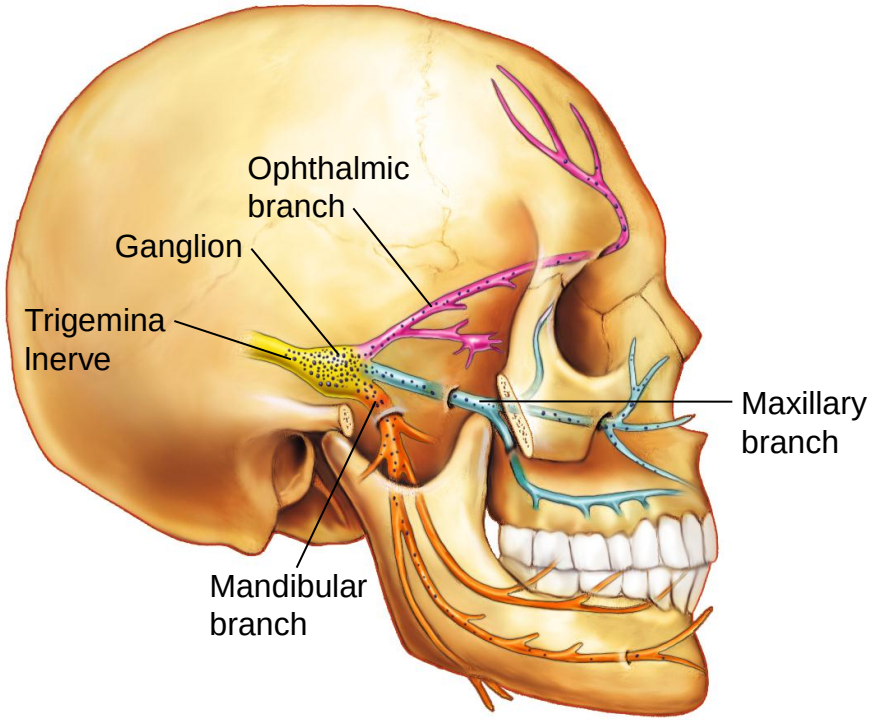
TABLE 24.2 Comparative Epidemiology and Pathology of Herpes Simplex, Types 1 and 2

	HSV-1	HSV-2
Usual Etiologic Agent of*	Herpes labialis Ocular herpes Gingivostomatitis Pharyngitis	Herpes genitalis
Transmission	Close contact, usually of face	Sexual or intimate contact
Latency	Occurs in trigeminal ganglion	Occurs primarily in sacral ganglia
Skin Lesions	On face, mouth	On internal, external genitalia, thighs, buttocks
Complications		
Whitlows	Among personnel working on oral cavity	Among obstetric, gynecological personnel
Neonatal encephalitis	Causes up to 30% of cases**	Causes most cases through contact with birth canal

Epidemiology of Herpes Simplex

- Transmission by direct exposure to secretions containing the virus; active lesions most significant source; genital herpes can be transmitted in the absence of lesions

- HSV multiplies in sensory neurons, moves to ganglia
  - HSV-1 enters 5th cranial nerve
  - HSV-2 enters lumbosacral spinal nerve trunk ganglia



Epidemiology of Herpes Simplex

- Recurrent infection is triggered by various stimuli – fever, UV radiation, stress, mechanical injury

- Newly formed viruses migrate to body surface, producing a local skin or membrane lesion

Type 1 Herpes Simplex in Children and Adults

- **Herpes labialis – fever blisters, cold sores**; most common recurrent HSV-1 infection; vesicles occur on mucocutaneous junction of lips or adjacent skin; itching and tingling prior to vesicle formation; lesion crusts over in 2-3 days and heals (a)
- **Herpetic gingivostomatitis** – infection of oropharynx in young children; fever, sore throat, swollen lymph nodes (b)
- **Herpetic keratitis** – ocular herpes – inflammation of eye; gritty feeling in the eye, conjunctivitis, sharp pain, and sensitivity to light

CDC

(a)

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(b)

Type 2 Herpes Infections

- **Genital herpes – herpes genitalia** – starts with malaise, anorexia, fever, and bilateral swelling and tenderness in the groin; clusters of sensitive vesicles on the genitalia, perineum, and buttocks; urethritis, painful urination, cervicitis, itching; vesicles ulcerate
- Recurrent bouts usually less severe, triggered by menstruation, stress, and concurrent bacterial infection

CDC

Herpes of the Newborn

- HSV-1 and HSV-2
- Potentially fatal in the neonate and fetus
- Infant contaminated by mother before or during birth; hand transmission by mother to infant
- Infection of mouth, skin, eyes, CNS
- Preventative screening of pregnant women; delivery by C-section if outbreak at the time of birth

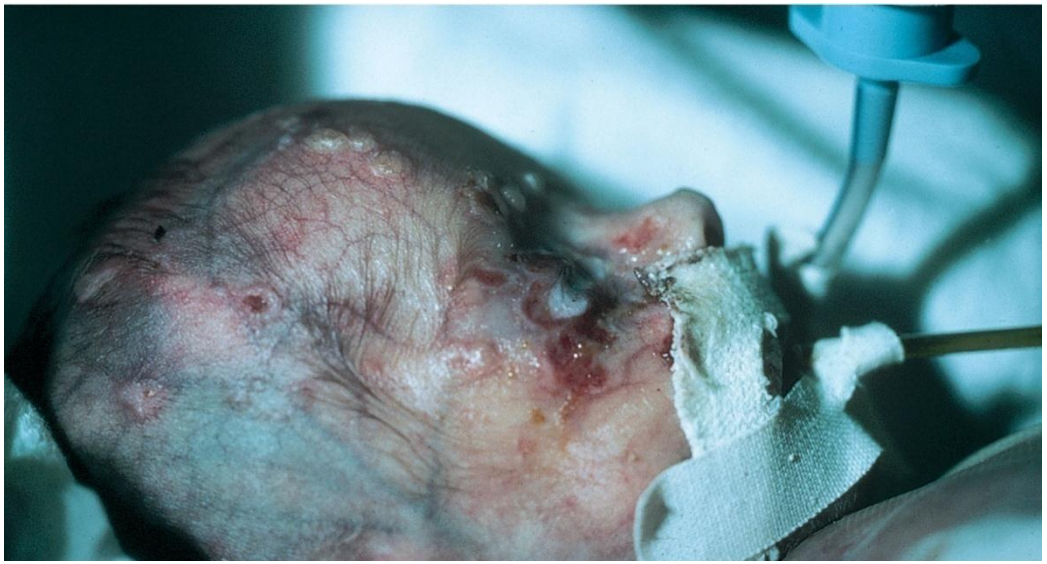

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Figure 24.9 Premature infant, classic “cigarette burn” of HSV infection.

Miscellaneous Herpes Infections

- **Herpetic whitlow** : HSV-1 or HSV-2 can penetrate a break in the skin and cause a localized infection; usually on one finger; extremely painful and itchy (below)

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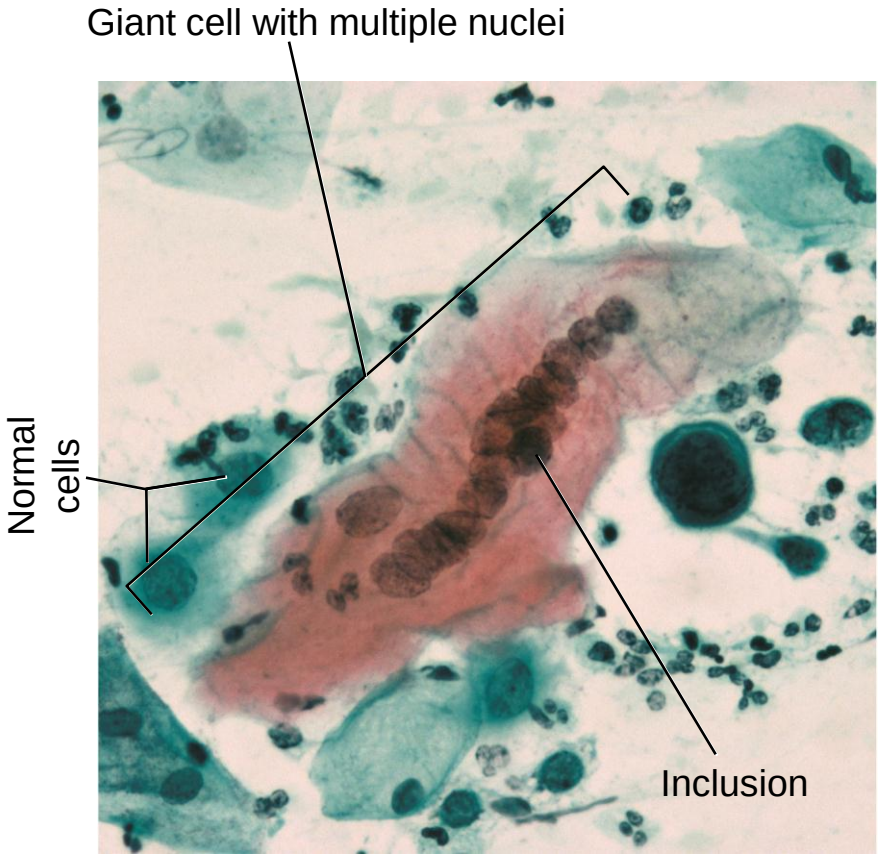
- **HSV-1 encephalitis** – rare complication but most common sporadic form of viral encephalitis in the U.S.
- Those with underlying immunodeficiency are prone to severe, disseminated herpes

Diagnosis, Treatment, and Control of Herpes Simplex

- Vesicles and exudate are typical diagnostic symptoms, scrapings from base of lesions showing giant cells, culture and specific tests for diagnosing severe or disseminated HSV; direct fluorescent antibody tests
- Treatment: acyclovir, famciclovir, valacyclovir; topical medications

Figure 24.11 stained specimen showing a herpes infection – a Pap smear of a cervical scraping



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The Biology of Varicella-Zoster Virus (VZV)

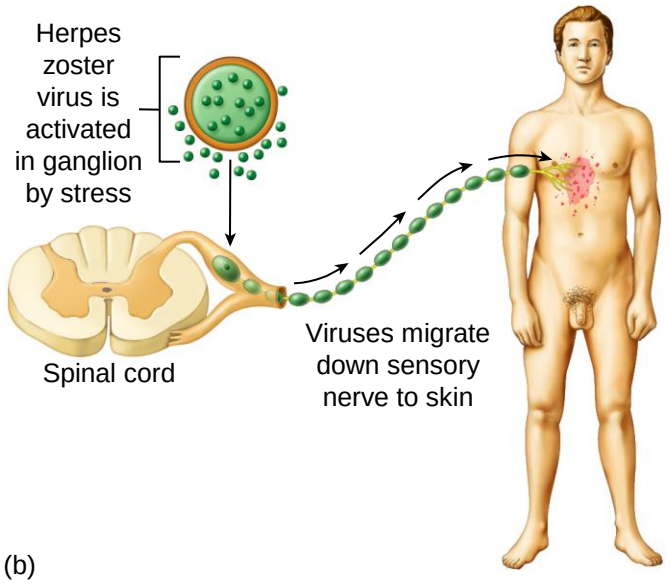
- Causes **chickenpox** and **shingles**
- Humans only natural host
- Transmitted by respiratory droplets and contact
- **Primary infection – chickenpox – characteristic vesicles**
- Virus enters neurons and remains latent

Figure 24.14 rash

(a) CDC

Varicella-Zoster Virus (VZV)

- Later, reactivation of the virus results in **shingles** with vesicles localized to distinctive areas, dermatomes
- More common in older patients
- Treatment: treat symptoms in uncomplicated infections; acyclovir, famciclovir, interferon for systemic disease
- Live attenuated vaccine for chickenpox and shingles



(b)

(c) Clinical appearance of shingles

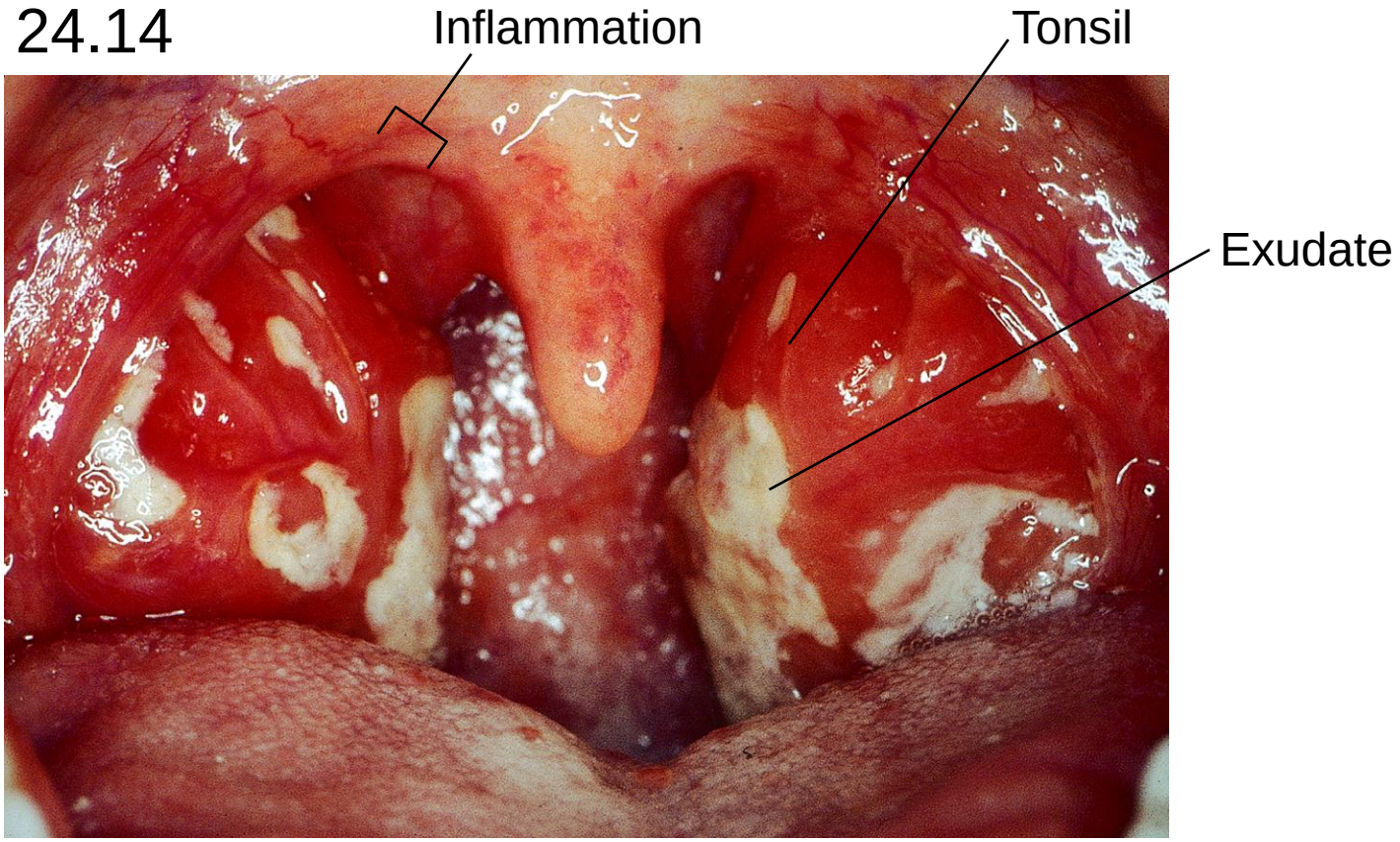
Epstein-Barr Virus (EBV)

- Ubiquitous virus; infects lymphoid tissue and salivary glands
- Transmission – direct, oral contact and contamination with saliva
- In industrialized countries, college-age population is vulnerable to infectious mononucleosis (mono or kissing disease)
- By mid-life, 90-95% of all people are infected
- Anyone with an immune deficiency is highly susceptible to EBV

Epstein-Barr Virus (EBV)

- **Infectious mononucleosis** – sore throat, high fever, cervical lymphadenopathy; develop after 30-50 day incubation
- Dormancy in B cells; reactivated; may be asymptomatic

Figure 24.14



Kane, Kay et al, Color Atlas and Synopsis of Pediatric Dermatology, 2/e © 2010. The McGraw-Hill Companies, Inc. Reproduced with permission of the McGraw-Hill Companies

Tumors and Other Complications Associated with EBV

- **Burkitt lymphoma** – B cell malignancy; usually develops in jaw and grossly swells the cheek; central African children 4-8 years old; may be associated with chronic coinfections with malaria, etc.
- **Nasopharyngeal carcinoma** – malignancy of epithelial cells; occurs in older Chinese and African men

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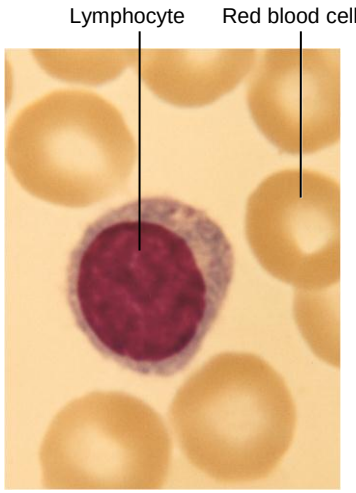
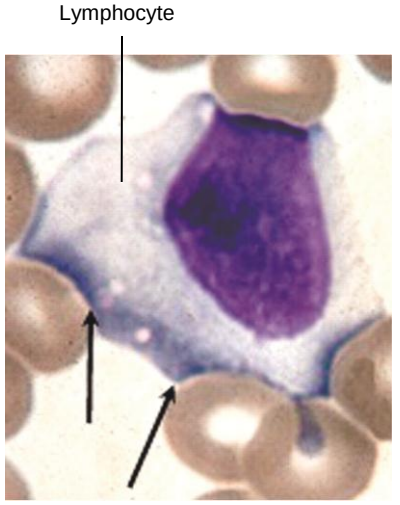
Diagnosis, Treatment, and Prevention

- Differential blood count shows lymphocytosis, neutropenia, and large atypical lymphocytes; serological assays to detect antibodies and antigen
- Treatment directed at relief of symptoms of fever and sore throat
- Disseminated disease may be treated with IV gamma globulin, interferon, acyclovir, and monoclonal antibodies



(a) Normal lymphocyte



(b) Infectious mononucleosis – atypical lymphocyte with irregular nucleus and indented border

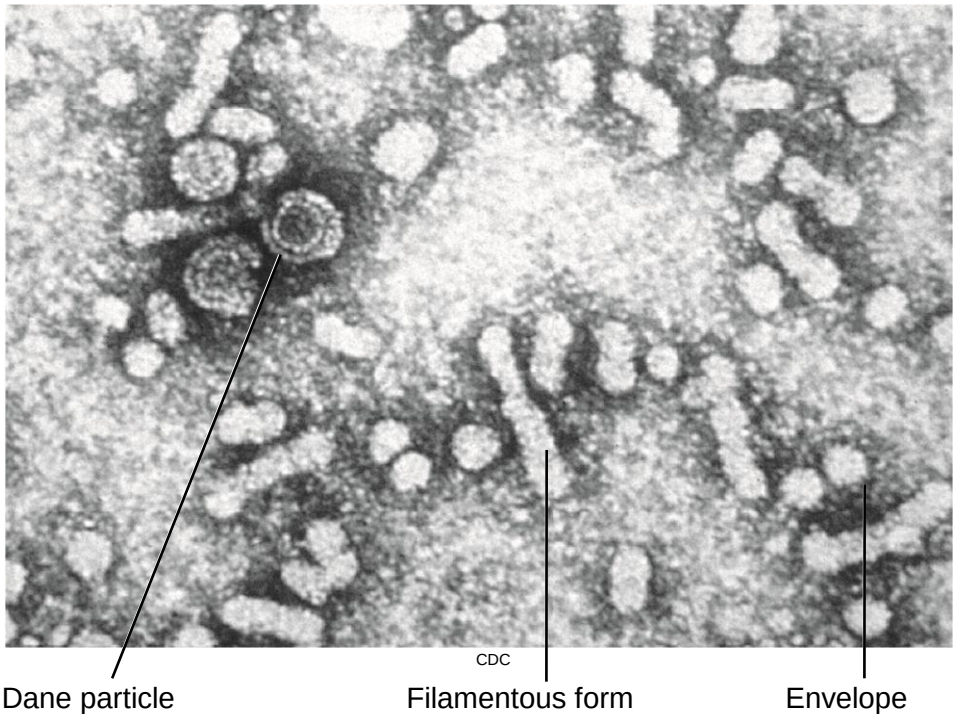
24.4 The Viral Agents of Hepatitis

- **Hepatitis** – an inflammatory disease of liver cells that may result from several viruses
- Interferes with liver's excretion of bile pigments, bilirubin accumulates in blood and tissues causing jaundice, a yellow tinge in skin and eyes
- 3 principal viruses involved in hepatitis:
  - **Hepatitis B, hepatitis A (RNA virus – Ch. 25), hepatitis C (RNA virus – Ch. 25)**

Hepadnaviruses

- Enveloped DNA viruses
- Never been grown in tissue culture
- Unusual genome containing both double- and single-stranded DNA
- Tropism for liver

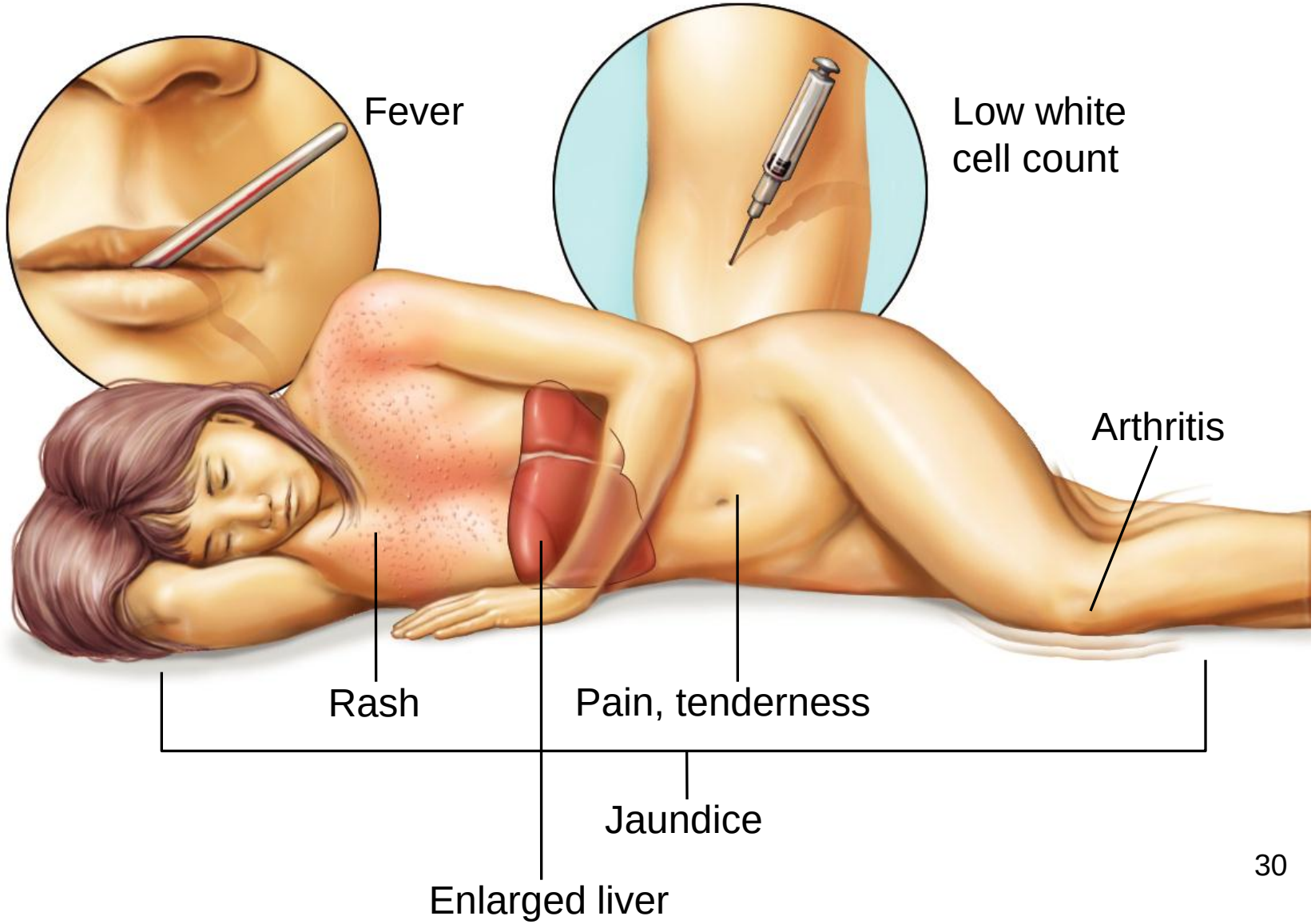
Figure 24.18 blood from hepatitis B virus infected patient



Hepatitis B Virus and Disease

- Multiplies exclusively in the liver, which continuously seeds blood with viruses – chronic
- 10^7 virions/mL blood
- Minute amounts of blood, blood products can transmit infection; sexually transmitted
- High incidence among homosexuals and drug addicts
- Can become a chronic infection
- Increases risk of liver cancer – **hepatocellular carcinoma**

The Clinical Features of Hepatitis B



Pathogenesis of Hepatitis B Virus

- Virus enters through break in skin or mucous membrane or by injection into bloodstream
- Reaches liver cells, multiplies, and releases viruses into blood; average 7 week incubation Most exhibit few overt symptoms and eventually develop HBV immunity
- Some experience malaise, fever, chills, anorexia, abdominal discomfort, and diarrhea
- Fever, jaundice, rash, and arthritis in more severe disease cases
- Small number of patients develop chronic liver disease – Necrosis and cirrhosis

Diagnosis and Management of Hepatitis B

- Diagnosis based on examination of risk factors, serological tests to detect viral antibodies or antigen; radioimmunoassay and ELISA tests for surface antigens
- Screening of blood for transfusion, semen for sperm banks, organs for transplant, and routine prenatal testing of all pregnant women
- Mild cases managed by treatment of symptoms and supportive care; chronic infections treated with interferon

Prevention of Hepatitis B

- Passive immunization with HBIG for persons exposed, or possibly exposed, including neonates born to infected mothers

- Primary prevention is vaccination for high risk individuals and encouraged for all newborns and infants
  - Vaccines derived from surface antigen from cloned yeast – 3 doses with boosters
  - Vaccine derived from purified sterile antigen extracted from carrier blood; mainly for people who have yeast allergies

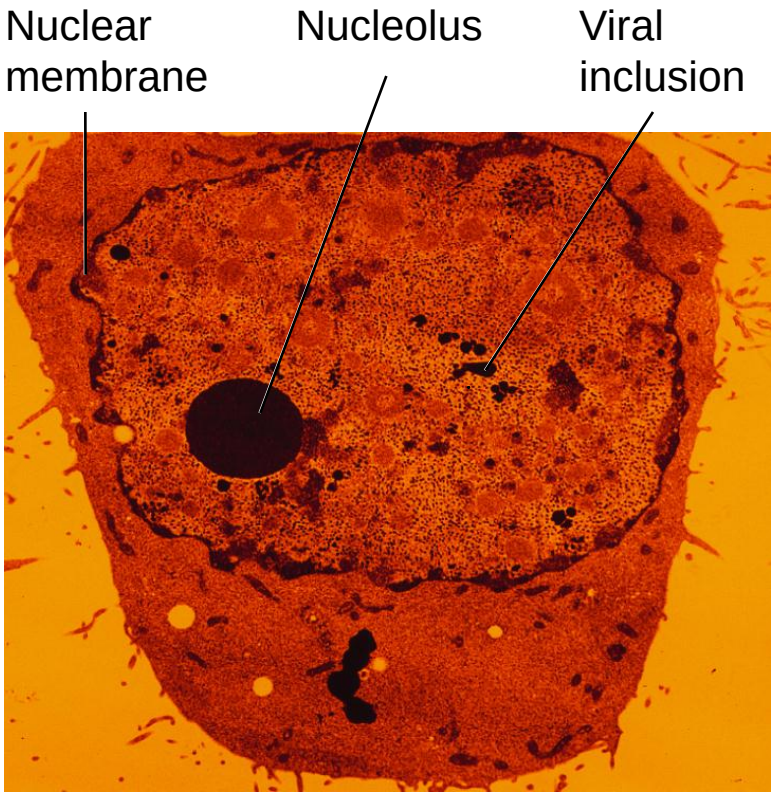
24.5 Nonenveloped DNA Viruses

- **Adenoviruses**
- **Papillomaviruses**

The Adenoviruses

- Nonenveloped, dsDNA
- 30 types associated with human disease

Cellular and nuclear alterations



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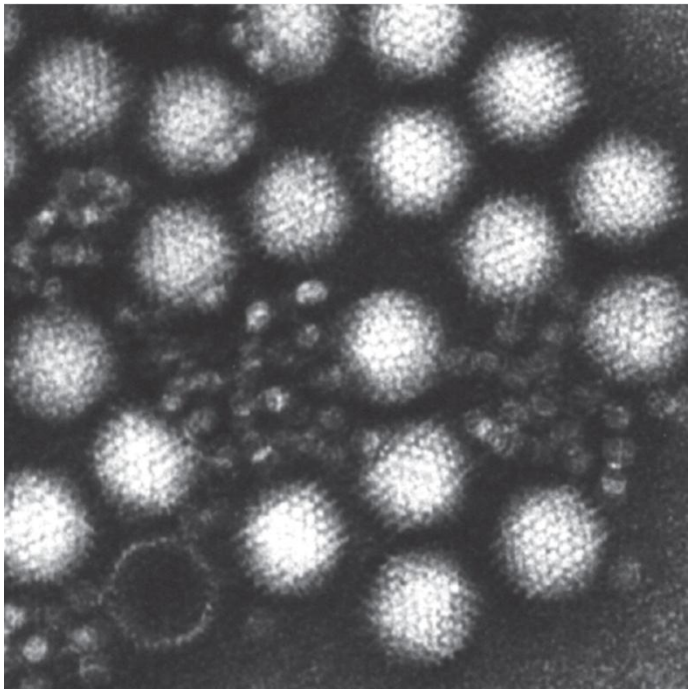
Magnification of viruses, 220,000X



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The Adenoviruses

- Infect lymphoid tissue, respiratory and intestinal epithelia and conjunctiva
- Oncogenic in animals, not in humans
- Spread by respiratory and ocular secretions
- Causes colds, pharyngitis, conjunctivitis, keratoconjunctivitis, acute hemorrhagic cystitis
- Severe cases treated with interferon
- Inactivated polyvalent vaccine

Papilloma Virus

- Small, nonenveloped dsDNA
- Circular DNA
- Cause persistent infections and tumors

Human Papillomavirus

- **Papilloma** – squamous epithelial growth, wart, or verruca
- Caused by 100 different strains of HPV
- Transmissible through direct contact or contaminated fomites; incubation – 2 weeks to more than a year
- Most common warts regress over time; they can be removed by direct chemical application of podophyllin and physical removal by cauterization, freezing, or laser surgery
- Warts can recur

Human Papillomavirus

- **Common seed warts** – painless, elevated, rough growth; on fingers, etc.
- **Plantar warts** – deep, painful; on soles of feet
- **Genital warts** – most common STD in U.S.; morphology ranges from tiny, flat, inconspicuous bumps to extensive, branching, cauliflower-like masses

Figure 24.14 (a) common warts

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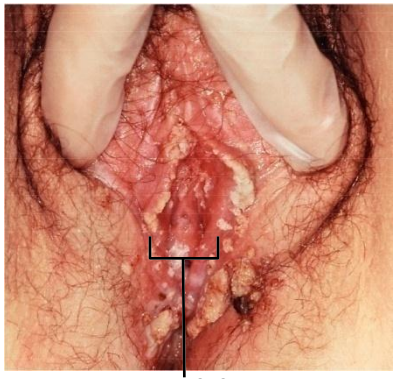


CDC

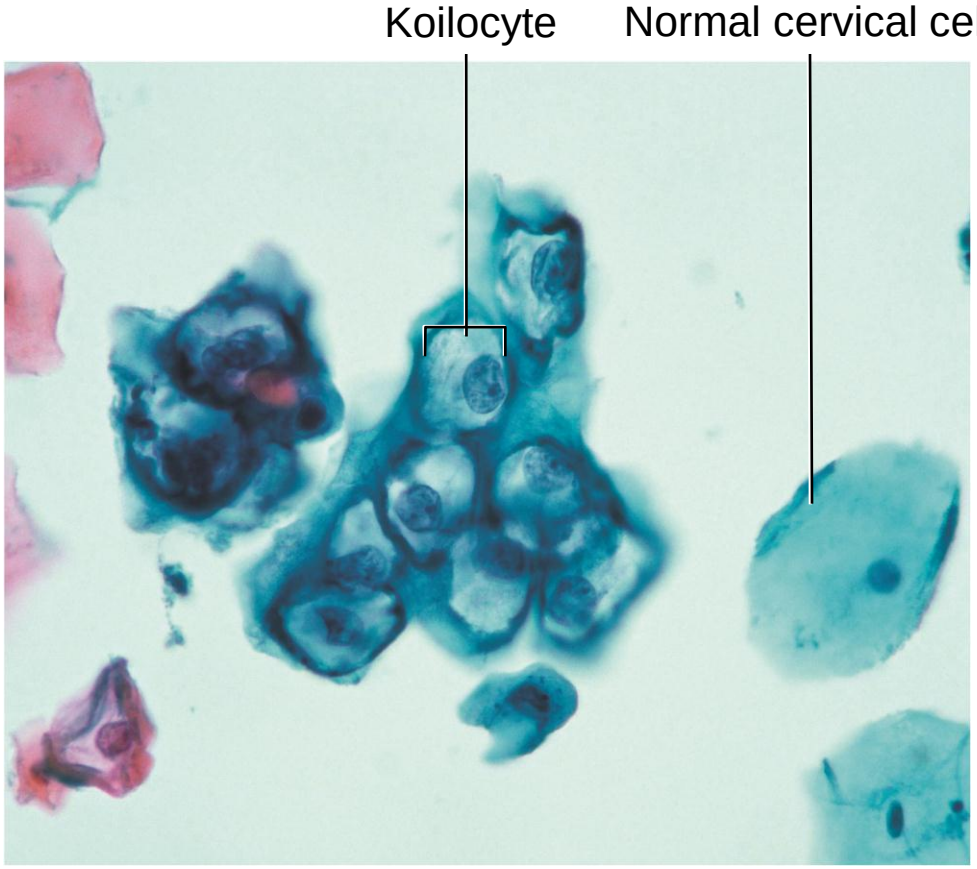
Condylomata acuminata

Figure 24.14 (b) chronic genital warts

Human Papillomavirus

- Nine HPV types increase risk for developing reproductive cancer; 2 account for 70% of metastatic tumors
- Early detection through inspection of genitals, women Pap smear to screen for abnormal cervical cells
- Two effective HPV vaccines

Figure 24.22 Pap smear of cervix in patient with HPV



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