Infectious diseases

	4/5th Semester Classes on Infectious Diseases, 8-9AM, Tuesdays (LT-1)
	Topics
1	Approach to Infectious Diseases and their prevention
2	Antibiotic stewardship practices
3	Community-Acquired Infections
4	Health Care–Associated Infections
5	Gram-Positive Bacteria (part-1)
6	Gram-Positive Bacteria (part-2)
7	Gram-Negative Bacteria (part-1)
8	Gram-Negative Bacteria (part-2)
9	Spirochetal Diseases
10	Diseases Caused by Atypical/Miscellaneous Bacterial Infections
11	**Revision-cum-exam on bacteria (Must to know type)**
12	Infections Due to DNA Viruses
13	Infections Due to RNA Viruses (part 1)
14	Infections Due to RNA Viruses (part 2)
15	HIV/AIDS – part 1
16	HIV/AIDS – part 2
17	Fungal Infections
18	Parasitic Infections (part 1)
19	Parasitic Infections (part 2)
20	**Revision-cum-exam on Virus, Fungal, and Parasite (Must to know type)**

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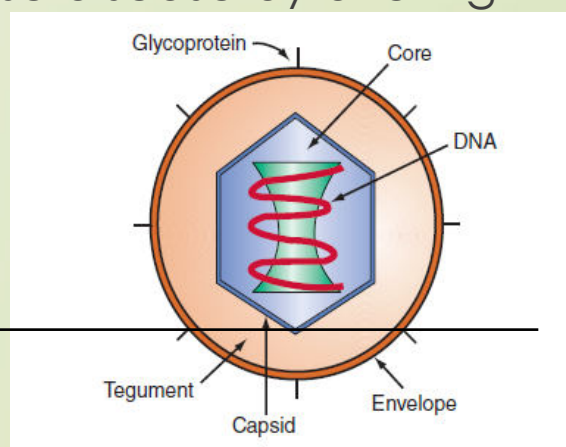
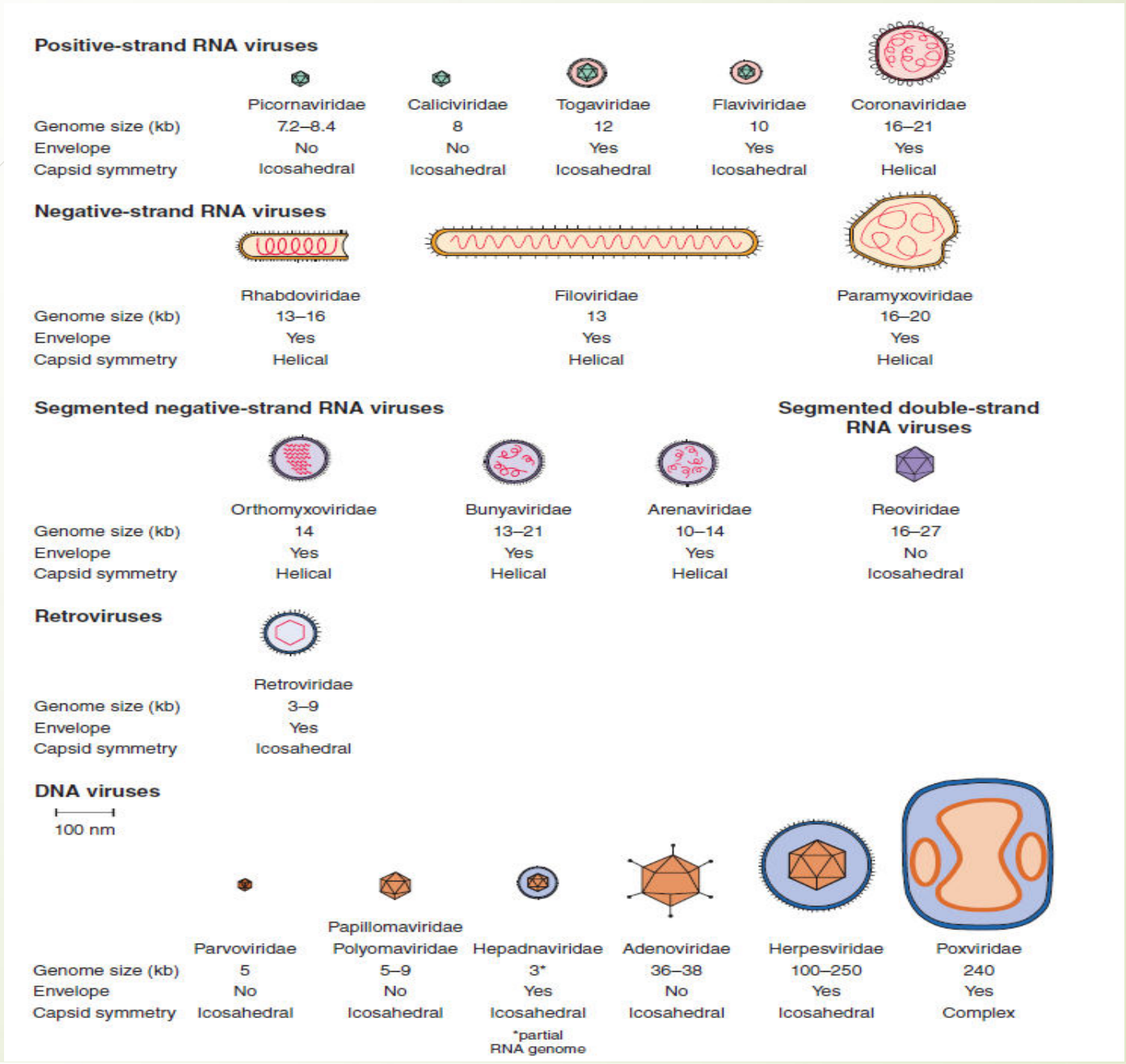
- **Viruses** are obligate intracellular parasites
- **Virusoids** are nucleic acids that depend on cells and helper viruses for packaging their nucleic acids into virus-like particles.
- **Viroids** are naked, cyclical, mostly double-strand small RNAs that appear to be restricted to plants, spread from cell to cell, and are replicated by cellular RNA polymerase II.
- **Prions** are abnormal proteins that propagate and cause disease by altering the structure of a normal cell protein.





DNA Viruses		
Hepadnaviridae	Hepatitis B virus	ds DNA with ss portions
Parvoviridae	Parvovirus B19	ss DNA
Papillomaviridae	Human papillomaviruses	ds DNA
Polyomaviridae	JC virus	
	BK virus	
	Merkel cell polyoma virus	
Adenoviridae	Human adenoviruses	ds DNA
Herpesviridae	Herpes simplex virus types 1 and 2[b]	ds DNA
	Varicella-zoster virus[c]	
	Epstein-Barr virus[d]	
	Cytomegalovirus[e]	
	Human herpesvirus 6	
	Human herpesvirus 7	
	Kaposi's sarcoma–associated herpesvirus[f]	
Poxviridae	Variola (smallpox) virus	ds DNA
	Orf virus	
	Molluscum contagiosum virus	

Herpes Simplex Virus Infections

- Herpes simplex viruses (HSV-1, HSV-2; Herpesvirus hominis) produce a variety of infections involving mucocutaneous surfaces, the central nervous system (CNS), and—on occasion—visceral organs
- The clinical manifestations and course of HSV infection depend on the anatomic site involved, the age and immune status of the host, and the antigenic type of the virus.
- Genital HSV-2 infection is twice as likely to reactivate and recurs 8–10 times more frequently than genital HSV-1 infection. Conversely, oral-labial HSV-1 infection recurs more frequently than oral-labial HSV-2 infection.

I. Mucocutaneous HSV infections

A. *Infections in immunosuppressed patients*

1. *Acute symptomatic first or recurrent episodes:* IV acyclovir (5 mg/kg q8h) or oral acyclovir (400 mg qid), famciclovir (500 mg bid or tid), or valacyclovir (500 mg bid) is effective. Treatment duration may vary from 7 to 14 days.
2. *Suppression of reactivation disease (genital or oral-labial):* IV acyclovir (5 mg/kg q8h) or oral valacyclovir (500 mg bid) or acyclovir (400–800 mg 3–5 times per day) prevents recurrences during the 30-day period immediately after transplantation. Longer-term HSV suppression is often used for persons with continued immunosuppression. In bone marrow and renal transplant recipients, oral valacyclovir (2 g/d) is also effective in reducing cytomegalovirus infection. Oral valacyclovir at a dose of 4 g/d has been associated with thrombotic thrombocytopenic purpura after extended use in HIV-positive persons. In HIV-infected persons, oral acyclovir (400–800 mg bid), valacyclovir (500 mg bid), or famciclovir (500 mg bid) is effective in reducing clinical and subclinical reactivations of HSV-1 and HSV-2.

B. *Infections in immunocompetent patients*

1. *Genital herpes*
   a. *First episodes:* Oral acyclovir (200 mg 5 times per day or 400 mg tid), valacyclovir (1 g bid), or famciclovir (250 mg bid) for 7–14 days is effective. IV acyclovir (5 mg/kg q8h for 5 days) is given for severe disease or neurologic complications such as aseptic meningitis.
   b. *Symptomatic recurrent genital herpes:* Short-course (1- to 3-day) regimens are preferred because of low cost, likelihood of adherence, and convenience. Oral acyclovir (800 mg tid for 2 days), valacyclovir (500 mg bid for 3 days), or famciclovir (750 or 1000 mg bid for 1 day, a 1500-mg single dose, or 500 mg stat followed by 250 mg q12h for 3 days) effectively shortens lesion duration. Other options include oral acyclovir (200 mg 5 times per day), valacyclovir (500 mg bid), and famciclovir (125 mg bid for 5 days).
   c. *Suppression of recurrent genital herpes:* Oral acyclovir (400–800 mg bid) or valacyclovir (500 mg daily) is given. Patients with >9 episodes per year should take oral valacyclovir (1 g daily or 500 mg bid) or famciclovir (250 mg bid or 500 mg bid).
2. *Oral-labial HSV infections*
   a. *First episode:* Oral acyclovir is given (200 mg 5 times per day or 400 mg tid); an oral acyclovir suspension can be used (600 mg/m^2 qid). Oral famciclovir (250 mg bid) or valacyclovir (1 g bid) has been used clinically. The duration of therapy is 5–10 days.
   b. *Recurrent episodes:* If initiated at the onset of the prodrome, single-dose or 1-day therapy effectively reduces pain and speeds healing. Regimens include oral famciclovir (a 1500-mg single dose or 750 mg bid for 1 day) or valacyclovir (a 2-g single dose or 2 g bid for 1 day). Self-initiated therapy with 6-times-daily topical penciclovir cream effectively speeds healing of oral-labial HSV. Topical acyclovir cream has also been shown to speed healing.
   c. *Suppression of reactivation of oral-labial HSV:* If started before exposure and continued for the duration of exposure (usually 5–10 days), oral acyclovir (400 mg bid) prevents reactivation of recurrent oral-labial HSV infection associated with severe sun exposure.
3. *Surgical prophylaxis of oral or genital HSV infection:* Several surgical procedures, such as laser skin resurfacing, trigeminal nerve-root decompression, and lumbar disk surgery, have been associated with HSV reactivation. IV acyclovir (3–5 mg/kg q8h) or oral acyclovir (800 mg bid), valacyclovir (500 mg bid), or famciclovir (250 mg bid) effectively reduces reactivation. Therapy should be initiated 48 h before surgery and continued for 3–7 days.
4. *Herpetic whitlow:* Oral acyclovir (200 mg) is given 5 times daily (alternative: 400 mg tid) for 7–10 days.
5. *HSV proctitis:* Oral acyclovir (400 mg 5 times per day) is useful in shortening the course of infection. In immunosuppressed patients or in patients with severe infection, IV acyclovir (5 mg/kg q8h) may be useful.
6. *Herpetic eye infections:* In acute keratitis, topical trifluorothymidine, vidarabine, idoxuridine, acyclovir, penciclovir, and interferon are all beneficial.

II. Central nervous system HSV infections

A. *HSV encephalitis:* IV acyclovir (10 mg/kg q8h; 30 mg/kg per day) is given for 10 days or until HSV DNA is no longer detected in cerebrospinal fluid.

B. *HSV aseptic meningitis:* No studies of systemic antiviral chemotherapy exist. If therapy is to be given, IV acyclovir (15–30 mg/kg per day) should be used.

C. *Autonomic radiculopathy:* No studies are available. Most authorities recommend a trial of IV acyclovir.

III. Neonatal HSV infections: Oral acyclovir (60 mg/kg per day, divided into 3 doses) is given. The recommended duration of IV treatment is 21 days. Monitoring for relapse should be undertaken. Continued suppression with oral acyclovir suspension should be given for 3–4 months.

IV. Visceral HSV infections

A. *HSV esophagitis:* IV acyclovir (15 mg/kg per day) is given. In some patients with milder forms of immunosuppression, oral therapy with valacyclovir or famciclovir is effective.

B. *HSV pneumonitis:* No controlled studies exist. IV acyclovir (15 mg/kg per day) should be considered.

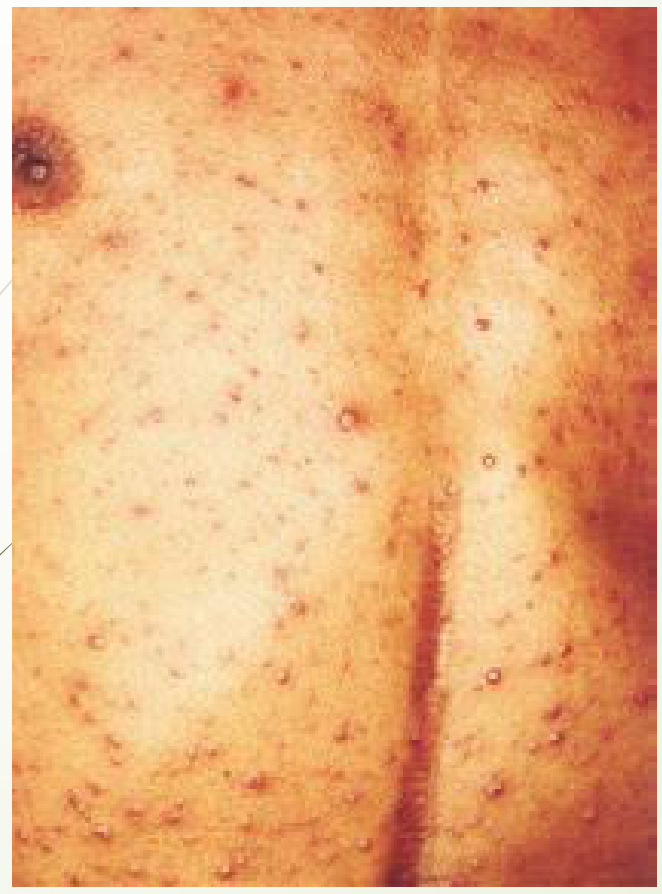
V. Disseminated HSV infections: No controlled studies exist. IV acyclovir (5 mg/kg q8h) should be tried. Adjustments for renal insufficiency may be needed. No definite evidence indicates that therapy will decrease the risk of death.

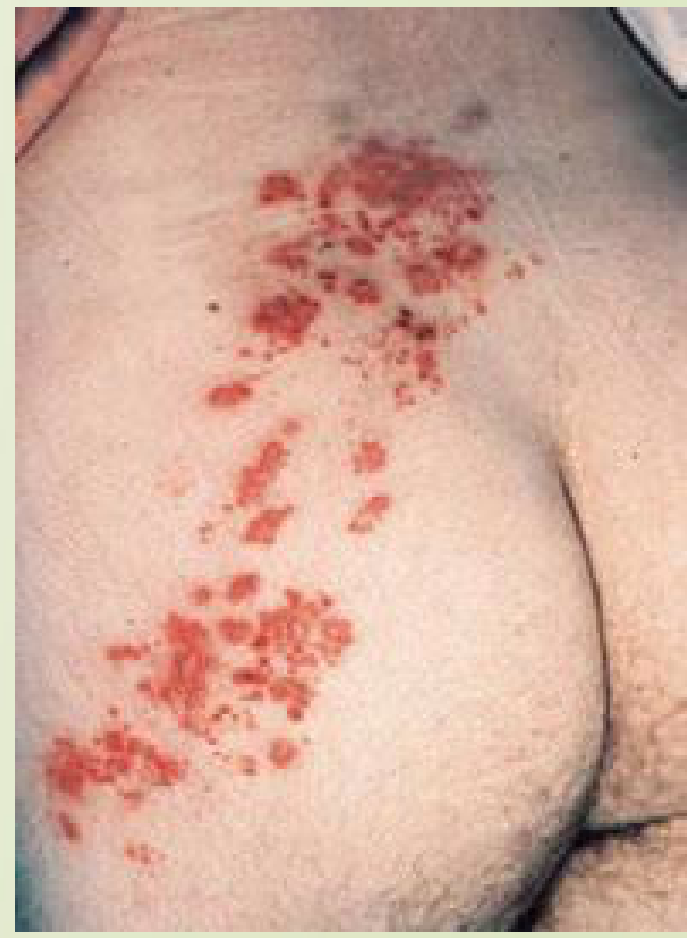
VI. Erythema multiforme associated with HSV: Anecdotal observations suggest that oral acyclovir (400 mg bid or tid) or valacyclovir (500 mg bid) will suppress erythema multiforme.

VII. Infections due to acyclovir-resistant HSV: IV foscarnet (40 mg/kg IV q8h) should be given until lesions heal. The optimal duration of therapy and the usefulness of its continuation to suppress lesions are unclear. Some patients may benefit from cutaneous application of trifluorothymidine or 5% cidofovir gel.

Varicella-Zoster Virus Infections

- VZV causes two distinct clinical entities: varicella (chickenpox) and herpes zoster (shingles).
- Chickenpox, a ubiquitous and extremely contagious infection, is usually a benign illness of childhood characterized by an exanthematous vesicular rash.
- With reactivation of latent VZV (which is most common after the sixth decade of life), herpes zoster presents as a dermatomal vesicular rash, usually associated with severe pain.
- Humans are the only known reservoir for VZV.





Varicella pneumonia, the most serious complication following chickenpox, develops more often in adults (up to 20% of cases) than in children and is particularly severe in pregnant women. Pneumonia usually has its onset 3–5 days into the illness

Medical management of chickenpox in the immunologically normal host is directed toward the prevention of avoidable complications

Acyclovir (800 mg by mouth five times daily), valacyclovir (1 g three times daily), or famciclovir (250 mg three times daily) for 5–7 days is recommended for adolescents and adults with chickenpox of ≤24 h duration.

Three methods are used for the prevention of VZV infections.

- First, a live attenuated varicella vaccine (Oka)
- to administer varicella-zoster immune globulin (VZIG)
- antiviral therapy can be given as prophylaxis to individuals at high risk who are ineligible for vaccine or who are beyond the 96-h window after direct contact.

TABLE 217-1 RECOMMENDATIONS FOR VZIG ADMINISTRATION

Exposure Criteria

1. Exposure to a person with chickenpox or zoster
   a. Household: residence in the same household
   b. Playmate: face-to-face indoor play
   c. Hospital

      Varicella: same 2- to 4-bed room or adjacent beds in large ward, face-to-face contact with infectious staff member or patient, visit by a person deemed contagious

      Zoster: intimate contact (e.g., touching or hugging) with a person deemed contagious
   d. Newborn infant: onset of varicella in the mother ≤5 days before delivery or ≤48 h after delivery; VZIG not indicated if the mother has zoster
2. Patient should receive VZIG as soon as possible but not >96 h after exposure

Candidates (Provided They Have Significant Exposure) Include:

1. Immunocompromised susceptible children without a history of varicella or varicella immunization
2. Susceptible pregnant women
3. Newborn infants whose mother had onset of chickenpox within 5 days before or within 48 h after delivery
4. Hospitalized premature infant (≥28 weeks of gestation) whose mother lacks a reliable history of chickenpox or serologic evidence of protection against varicella
5. Hospitalized premature infant (<28 weeks of gestation or ≤1000-g birth weight), regardless of maternal history of varicella or VZV serologic status

Epstein-Barr Virus Infections

EBV is the cause of heterophile-positive infectious mononucleosis (IM), which is characterized by fever, sore throat, lymphadenopathy, and atypical lymphocytosis.

EBV is also associated with several tumors, including nasopharyngeal and gastric carcinoma, Burkitt's lymphoma, Hodgkin's disease, and (in patients with immunodeficiencies) B cell lymphoma.

EBV is spread by contact with oral secretions

TABLE 218-1 SIGNS AND SYMPTOMS OF INFECTIOUS MONONUCLEOSIS

Manifestation	Median Percentage of Patients (Range)
Symptoms	
Sore throat	75 (50–87)
Malaise	47 (42–76)
Headache	38 (22–67)
Abdominal pain, nausea, or vomiting	17 (5–25)
Chills	10 (9–11)
Signs	
Lymphadenopathy	95 (83–100)
Fever	93 (60–100)
Pharyngitis or tonsillitis	82 (68–90)
Splenomegaly	51 (43–64)
Hepatomegaly	11 (6–15)
Rash	10 (0–25)
Periorbital edema	13 (2–34)
Palatal enanthem	7 (3–13)
Jaundice	5 (2–10)

TABLE 218-2 DIFFERENTIAL DIAGNOSIS OF INFECTIOUS MONONUCLEOSIS

	Sign or Symptom				
Etiology	**Fever**	**Adenopathy**	**Sore Throat**	**Atypical Lymphocytes**	**Differences from EBV Mononucleosis**
EBV infection	+	+	+	+	—
CMV infection	+	±	±	+	Older age at presentation, longer duration of fever
HIV infection	+	+	+	±	Diffuse rash, oral/genital ulcers, aseptic meningitis
Toxoplasmosis	+	+	±	±	Less splenomegaly, exposure to cats or raw meat
HHV-6	+	+	+	+	Older age at presentation
Streptococcal pharyngitis	+	+	+	–	No splenomegaly, less fatigue
Viral hepatitis	+	±	–	±	Higher aminotransferase levels
Rubella	+	+	±	±	Maculopapular rash, no splenomegaly
Lymphoma	+	+	+	+	Fixed, nontender lymph nodes
Drugs[a]	+	+	–	±	Occurs at any age

- Therapy for IM consists of supportive measures, with rest and analgesia.
- Prednisone (40–60 mg/d for 2–3 days, with subsequent tapering of the dose over 1–2 weeks) has been used for the prevention of airway obstruction in patients with severe tonsillar hypertrophy, for autoimmune hemolytic anemia, for hemophagocytic lymphohistiocytosis, and for severe thrombocytopenia.
- Glucocorticoids have also been administered to rare patients with severe malaise and fever and to patients with severe CNS or cardiac disease.

Cytomegalovirus and Human Herpesvirus Types 6, 7, and 8

Cytomegalovirus (CMV); In addition to inducing severe birth defects, CMV causes a wide spectrum of disorders in older children and adults, ranging from an asymptomatic subclinical infection to a mononucleosis syndrome in healthy individuals to disseminated disease in immunocompromised patients. Human CMV is one of severa related species-specific viruses that cause similar diseases in various animals.

All are associated with the production of characteristic enlarged cells—hence the name cytomegalovirus. CMV, a β-herpesvirus, has double-stranded

TABLE 219-1 CMV DISEASE IN THE IMMUNOCOMPROMISED HOST

Population	Risk Factors	Principal Syndromes	Treatment	Prevention
Fetus	Primary maternal infection/early pregnancy	Cytomegalic inclusion disease	Ganciclovir for symptomatic neonates	Avoidance of exposure; possibly, maternal treatment with CMV immunoglobulin during pregnancy
Organ transplant recipient	Seropositivity of donor and/or recipient; potent immunosuppressive regimen; treatment of rejection	Febrile leukopenia; gastrointestinal disease; pneumonia	Ganciclovir or valganciclovir	Prophylaxis or preemptive therapy with ganciclovir or valganciclovir
Hematopoietic stem cell transplant recipient	Graft-vs.-host disease; older age of recipient; seropositive recipient; viremia	Pneumonia; gastrointestinal disease	Ganciclovir or valganciclovir or foscarnet, ± CMV immunoglobulin	Prophylaxis or preemptive therapy with ganciclovir or valganciclovir
Person with AIDS	<100 CD4+ T cells/μL; CMV seropositivity	Retinitis; gastrointestinal disease; neurologic disease	Ganciclovir, valganciclovir, foscarnet, or cidofovir	Oral valganciclovir

Parvovirus Infections

TABLE 221-1 DISEASES ASSOCIATED WITH HUMAN PARVOVIRUS B19 INFECTION AND METHODS OF DIAGNOSIS

Disease	Host(s)	IgM	IgG	PCR	Quantitative PCR
Fifth disease	Healthy children	Positive	Positive	Positive	$>10^4$ IU/mL
Polyarthropathy syndrome	Healthy adults (more often women)	Positive within 3 months of onset	Positive	Positive	$>10^4$ IU/mL
Transient aplastic crisis	Patients with increased erythropoiesis	Negative/positive	Negative/positive	Positive	Often $>10^{12}$ IU/mL, but rapidly decreases
Persistent anemia/pure red-cell aplasia	Immunodeficient or immunocompetent patients	Negative/weakly positive	Negative/weakly positive	Positive	Often $>10^{12}$ IU/mL, but should be $>10^6$ in the absence of treatment
Hydrops fetalis/congenital anemia	Fetus (<20 weeks)	Negative/positive	Positive	Positive amniotic fluid or tissue	n/a

Thank you