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)**

1

Positive-strand RNA viruses

	Picornaviridae	Caliciviridae	Togaviridae	Flaviviridae	Coronaviridae
Genome size (kb)	7.2–8.4	8	12	10	16–21
Envelope	No	No	Yes	Yes	Yes
Capsid symmetry	Icosahedral	Icosahedral	Icosahedral	Icosahedral	Helical

Negative-strand RNA viruses

	Rhabdoviridae	Filoviridae	Paramyxoviridae
Genome size (kb)	13–16	13	16–20
Envelope	Yes	Yes	Yes
Capsid symmetry	Helical	Helical	Helical

Segmented negative-strand RNA viruses

	Orthomyxoviridae	Bunyaviridae	Arenaviridae
Genome size (kb)	14	13–21	10–14
Envelope	Yes	Yes	Yes
Capsid symmetry	Helical	Helical	Helical

Segmented double-strand RNA viruses

	Reoviridae
Genome size (kb)	16–27
Envelope	No
Capsid symmetry	Icosahedral

Retroviruses

	Retroviridae
Genome size (kb)	3–9
Envelope	Yes
Capsid symmetry	Icosahedral

DNA viruses

100 nm

	Parvoviridae	Papillomaviridae Polyomaviridae	Hepadnaviridae	Adenoviridae	Herpesviridae	Poxviridae
Genome size (kb)	5	5–9	3*	36–38	100–250	240
Envelope	No	No	Yes	No	Yes	Yes
Capsid symmetry	Icosahedral	Icosahedral	Icosahedral	Icosahedral	Icosahedral	Complex

*partial RNA genome

Viral Gastroenteritis

TABLE 227-1 VIRAL CAUSES OF GASTROENTERITIS AMONG HUMANS

Virus	Family	Genome	Primary Age Group at Risk	Clinical Severity	Detection Assays
Group A rotavirus	Reoviridae	Double-strand segmented RNA	Children <5 years	+++	EM, EIA (commercial), PAGE, RT-PCR
Norovirus	Caliciviridae	Positive-sense single-strand RNA	All ages	++	EM, RT-PCR
Sapovirus	Caliciviridae	Positive-sense single-strand RNA	Children <5 years	+	EM, RT-PCR
Astrovirus	Astroviridae	Positive-sense single-strand RNA	Children <5 years	+	EM, EIA, RT-PCR
Adenovirus (mainly types 40 and 41)	Adenoviridae	Double-strand DNA	Children <5 years	+/++	EM, EIA (commercial), PCR

- Norovirus may be the second **most common viral agent** (after rotavirus) among young children
- By the **fecal-oral route** but can occur by aerosolization, by contact with contaminated fomites, and by person-to-person contact
- The stools are characteristically **loose and watery, without** blood, mucus, or leukocytes

TABLE 227-2 CHARACTERISTICS OF GASTROENTERITIS CAUSED BY VIRAL AND BACTERIAL AGENTS

Feature	Viral Gastroenteritis	Bacterial Gastroenteritis
Setting	Incidence similar in developing and developed countries	More common in settings with poor hygiene and sanitation
Infectious dose	Low (10–100 viral particles) for most agents	High (>10^5 bacteria) for *Escherichia coli, Salmonella, Vibrio;* medium (10^2–10^5 bacteria) for *Campylobacter jejuni;* low (10–100 bacteria) for *Shigella*
Seasonality	In temperate climates, winter seasonality for most agents; year-round occurrence in tropical areas	More common in summer or rainy months, particularly in developing countries with a high disease burden
Incubation period	1–3 days for most agents; can be shorter for norovirus	1–7 days for common agents (e.g., *Campylobacter, E. coli, Shigella, Salmonella);* a few hours for bacteria producing preformed toxins (e.g., *Staphylococcus aureus, Bacillus cereus*)
Reservoir	Primarily humans	Depending on species, human (e.g., *Shigella, Salmonella*), animal (e.g., *Campylobacter, Salmonella, E. coli*), and water (e.g., *Vibrio*) reservoirs exist
Fever	Common with rotavirus and norovirus; uncommon with other agents	Common with agents causing inflammatory diarrhea (e.g., *Salmonella, Shigella*)
Vomiting	Prominent and can be the only presenting feature, especially in children	Common with bacteria producing preformed toxins; less prominent in diarrhea due to other agents
Diarrhea	Common; nonbloody in almost all cases	Prominent and occasionally bloody with agents causing inflammatory diarrhea
Duration	1–3 days for norovirus and sapovirus; 2–8 days for other viruses	1–2 days for bacteria producing preformed toxins; 2–8 days for most other bacteria
Diagnosis	This is often a diagnosis of exclusion in clinical practice. Commercial enzyme immunoassays are available for detection of rotavirus and adenovirus, but identification of other agents is limited to research and public health laboratories.	Fecal examination for leukocytes and blood is helpful in differential diagnosis. Culture of stool specimens, sometimes on special media, can identify several pathogens. Molecular techniques are useful epidemiologic tools but are not routinely used in most laboratories.
Treatment	Supportive therapy to maintain adequate hydration and nutrition should be given. Antibiotics and antimotility agents are contraindicated.	Supportive hydration therapy is adequate for most patients. Antibiotics are recommended for patients with dysentery caused by *Shigella* or diarrhea caused by *Vibrio cholerae* and for some patients with *Clostridium difficile* colitis.

Enterovirus

- These viruses **are not a** prominent cause of gastroenteritis.
  - 3 serotypes of poliovirus,
  - 21 serotypes of coxsackievirus A,
  - 6 serotypes of **coxsackievirus B1**,
  - 28 serotypes of echovirus,
  - enteroviruses 68–71, and
  - multiple new enteroviruses (beginning with enterovirus 73)
- Infection is more common in **socioeconomically disadvantaged areas**, especially in those where hygiene is poor
- Transmitted primarily by the **fecal-oral or oral-oral route,** other rare route also
- IP; 2 to 14 days but usually **is <1 week**
- After ingestion, it infect epithelial cells in the mucosa of the gastrointestinal tract and then to spread to and replicate in the submucosal lymphoid tissue, then to the regional lymph nodes, a viremic phase ensues, and the virus replicates in **organs of the reticuloendothelial system**

Most common clinical manifestation is a nonspecific febrile illness

Poliovirus Infection:

- Abortive poliomyelitis
- Nonparalytic poliomyelitis
- Paralytic poliomyelitis - it is more common among older individuals, pregnant women, and persons exercising trenuously or undergoing trauma
- Vaccine-associated poliomyelitis
- Postpolio syndrome - a new onset of weakness, fatigue, fasciculations, and pain with additional atrophy of the muscle group involved during the initial paralytic disease **20–40 years earlier**

Manifestation	Serotype(s) of Indicated Virus: Coxsackievirus	Serotype(s) of Indicated Virus: Echovirus (E) and Enterovirus (Ent)
Acute hemorrhagic conjunctivitis	A24	E70
Aseptic meningitis	A2, 4, 7, 9, 10; B1–5	E4, 6, 7, 9, 11, 13, 16, 18, 19, 30, 33; Ent70, 71
Encephalitis	A9; B1–5	E3, 4, 6, 7, 9, 11, 18, 25, 30; Ent71
Exanthem	A4, 5, 9, 10, 16; B1, 3–5	E4–7, 9, 11, 16–19, 25, 30; Ent71
Generalized disease of the newborn	B1–5	E4–7, 9, 11, 14, 16, 18, 19
Hand-foot-and-mouth disease	A5–7, 9, 10, 16; B1, 2, 5	Ent71
Herpangina	A1–10, 16, 22; B1–5	E6, 9, 11, 16, 17, 25, 30; Ent71
Myocarditis, pericarditis	A4, 9, 16; B1–5	E6, 9, 11, 22
Paralysis	A4, 7, 9; B1–5	E2–4, 6, 7, 9, 11, 18, 30; Ent70, 71
Pleurodynia	A1, 2, 4, 6, 9, 10, 16; B1–6	E1–3, 6, 7, 9, 11, 12, 14, 16, 19, 24, 25, 30
Pneumonia	A9, 16; B1–5	E6, 7, 9, 11, 12, 19, 20, 30; Ent-D68, 71

- **Isolation of enterovirus in cell culture** is the traditional diagnostic procedure
- Identification of the enterovirus serotype is useful primarily for epidemiologic studies
- **A pan-enterovirus PCR assay** can detect all human enteroviruses
- **Intensive supportive care** may be needed for cardiac, hepatic, or CNS disease.
- IV, intrathecal, or intraventricular **immunoglobulin** has been used with apparent success in some cases for the treatment of **chronic enterovirus meningoencephalitis and dermatomyositis** in patients with hypogammaglobulinemia or agammaglobulinemia.
- Poliovirus is shed from some immunocompromised persons **for >10 years,** discontinuing vaccinations is difficult to decide

TABLE 228-3 RECOMMENDATIONS FOR POLIOVIRUS VACCINATION OF ADULTS

1. Most adults in the United States have been vaccinated during childhood and are at little risk of exposure to wild-type virus in the United States. Immunization is recommended for those with a higher risk of exposure than the general population, including:
   a. travelers to areas where poliovirus is or may be epidemic or endemic;
   b. members of communities or population groups with disease caused by wild-type polioviruses;
   c. laboratory workers handling specimens that may contain wild-type polioviruses; and
   d. health care workers in close contact with patients who may be excreting wild-type polioviruses.
2. Three doses of IPV are recommended for adults who need to be immunized. The second dose should be given 1–2 months after the first dose; the third dose should be given 6–12 months after the second dose.
3. Adults who are at increased risk of exposure to wild-type poliovirus and who have previously completed primary immunization should receive a single dose of IPV. Adults who did not complete primary immunization should receive the remaining required doses of IPV.

Viral Respiratory Infections

TABLE 223-1 ILLNESSES ASSOCIATED WITH RESPIRATORY VIRUSES

	Frequency of Respiratory Syndromes		
Virus	**Most Frequent**	**Occasional**	**Infrequent**
Rhinoviruses	Common cold	Exacerbation of chronic bronchitis and asthma	Pneumonia in children
Coronaviruses[a,b]	Common cold	Exacerbation of chronic bronchitis and asthma	Pneumonia and bronchiolitis
Human respiratory syncytial virus	Pneumonia and bronchiolitis in young children	Common cold in adults	Pneumonia in elderly and immunosuppressed patients
Parainfluenza viruses	Croup and lower respiratory tract disease in young children	Pharyngitis and common cold	Tracheobronchitis in adults; lower respiratory tract disease in immunosuppressed patients
Adenoviruses	Common cold and pharyngitis in children	Outbreaks of acute respiratory disease in military recruits[c]	Pneumonia in children; lower respiratory tract and disseminated disease in immunosuppressed patients
Influenza A viruses	Influenza[d]	Pneumonia and excess mortality in high-risk patients	Pneumonia in healthy individuals
Influenza B viruses	Influenza[d]	Rhinitis or pharyngitis alone	Pneumonia
Enteroviruses	Acute undifferentiated febrile illnesses[e]	Rhinitis or pharyngitis alone	Pneumonia
Herpes simplex viruses	Gingivostomatitis in children; pharyngotonsilitis in adults	Tracheitis and pneumonia in immunocompromised patients	Disseminated infection in immunocompromised patients
Human metapneumoviruses	Upper and lower respiratory tract disease in children	Upper respiratory tract illness in adults	Pneumonia in elderly and immunosuppressed patients

RHINOVIRUS - In contrast to other picornavirus, rhinoviruses are acid-labile and are almost completely inactivated at pH ≤3

- Seasonal peaks in **early fall and spring**; spread through direct contact with infected secretions, usually **respiratory droplets**; IP- 1-2 DAYS
- Antibacterial agents **should be used only if** bacterial complications such as otitis media or sinusitis develop

CORONAVIRUS - that infect humans (HCoVs) fall into two genera: *Alphacoronavirus* (***common cold***) and *Betacoronavirus* (**SARS-CoV and MERS-CoV**) - it is suspected that **bats** may be the animal reservoir

- Person-to-person transmission has been documented; IP – 2-7DAYS
- SARS usually begins as a systemic illness marked by the onset of fever, which is often accompanied by malaise, headache, and myalgias and is followed in 1–2 days by a nonproductive cough and dyspnea, then ARDS in second week

HUMAN RESPIRATORY SYNCYTIAL VIRUS - (HRSV)- A common cold–like syndrome is the illness most commonly associated with HRSV infection in adults (both upper and lower respiratory tract illnesses, such as bronchiolitis, croup, and pneumonia)

HUMAN METAPNEUMOVIRUS - (HMPV) - similar to that associated with HRSV

PARAINFLUENZA VIRUS - In older children and adults, parainfluenza infections tend to be milder, presenting most frequently as a common cold or as hoarseness, with or without cough

Influenza

- **Hemagglutinin** is the site by which the virus binds to sialic acid cell receptors, whereas the **neuraminidase** degrades the receptor and plays a role in the release of the virus from infected cells after replication has taken place
- **Influenza A** viruses are further subdivided (subtyped) on the basis of the surface hemagglutinin (H) and neuraminidase (N)

TABLE 224-1 EMERGENCE OF ANTIGENIC SUBTYPES OF INFLUENZA A VIRUS ASSOCIATED WITH PANDEMIC OR EPIDEMIC DISEASE

Years	Subtype	Extent of Outbreak
1889–1890	H2N8[a]	Severe pandemic
1900–1903	H3N8[a]	?Moderate epidemic
1918–1919	H1N1[b] (formerly HswN1)	Severe pandemic
1933–1935	H1N1[b] (formerly H0N1)	Mild epidemic
1946–1947	H1N1	Mild epidemic
1957–1958	H2N2	Severe pandemic
1968–1969	H3N2	Moderate pandemic
1977–1978[c]	H1N1	Mild pandemic
2009–2010[d]	H1N1	Pandemic

- Because the genome is **segmented**, the opportunity for gene reassortment during infection is high; reassortment often takes place during infection of cells with more than one influenza A virus
- Major antigenic variations, called ***antigenic shifts***, are seen only with influenza A viruses and may be associated with pandemics; Minor variations are called ***antigenic drifts***
- **Interpandemic influenza** A outbreaks usually begin abruptly, peak over a 2- to 3-week period, generally last for 2–3 months, and often subside almost as rapidly as they began
- In contrast, **pandemic influenza** may begin with rapid transmission at multiple locations, have high attack rates, and extend beyond the usual seasonality, with multiple waves of attack before or after the main outbreak
- Aquatic birds are **the largest reservoir** of influenza A viruses; pandemic strains resulted from **reassortment of gene segments between human and avian viruses**
- Whereas **humans primarily have a-2,6-galactose receptors** for hemagglutinins and **birds primarily have a-2,3-galactose receptors**, swine have **both types** of receptors
- Influenza is most frequently described as a respiratory illness; severe with **risk factors**
- Pulmonary Complications as ***PNEUMONIA***: "primary" influenza viral pneumonia, secondary bacterial pneumonia, or mixed viral and bacterial pneumonia
- Myositis, rhabdomyolysis, and myoglobinuria are occasional complications

TABLE 224-2 PERSONS AT HIGHER RISK FOR COMPLICATIONS OF INFLUENZA OR FOR INFLUENZA-RELATED VISITS TO HEALTH CARE FACILITIES

All children from birth to <5 years, especially <2 years

All persons ≥50 years old

Pregnant women

Adults and children who have chronic pulmonary (including asthma) or cardiovascular (except isolated hypertension), renal, hepatic, neurologic, hematologic, or metabolic disorders (including diabetes mellitus)

Persons who have immunosuppression (including that caused by medications or by HIV infection)

Children and adolescents (6 months to 18 years old) who are receiving long-term aspirin therapy and who might be at risk for Reye's syndrome after influenza virus infection

Residents of nursing homes and other long-term care facilities

Native Americans/Alaska Natives

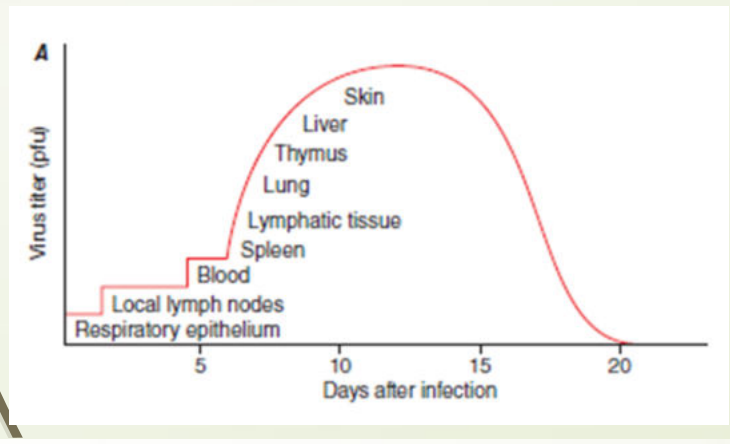
Persons who are morbidly obese (body mass index ≥40 kg/m^2)

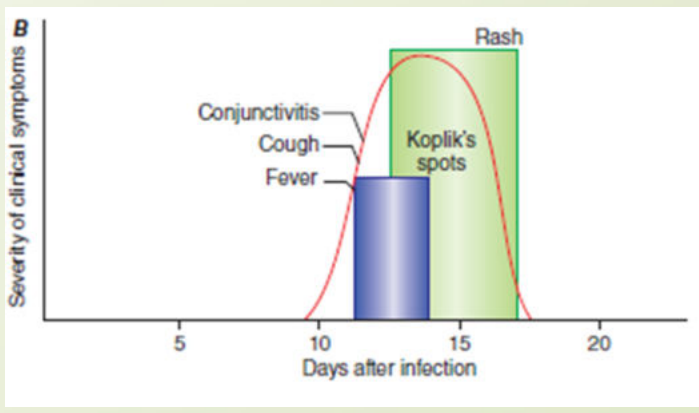
TABLE 224-3 ANTIVIRAL MEDICATIONS FOR TREATMENT AND PROPHYLAXIS OF INFLUENZA

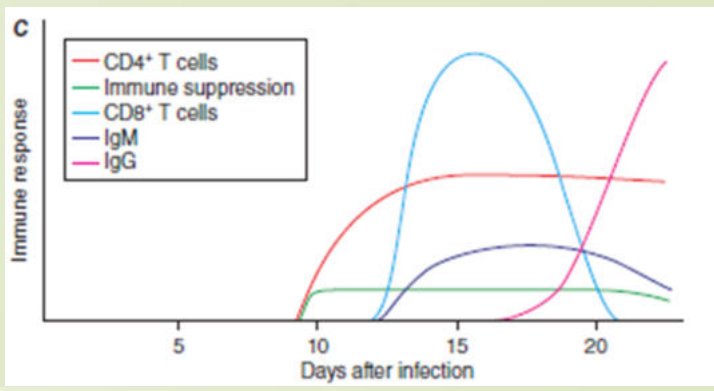
	Age Group (Years)		
Antiviral Drug	**Children (≤12)**	**13–64**	**≥65**
Oseltamivir			
Treatment, Influenza A and B	Age 1–12, dose varies by weight[a]	75 mg PO bid	75 mg PO bid
Prophylaxis, Influenza A and B	Age 1–12, dose varies by weight[b]	75 mg PO qd	75 mg PO qd
Zanamivir			
Treatment, Influenza A and B	Age 7–12, 10 mg bid by inhalation	10 mg bid by inhalation	10 mg bid by inhalation
Prophylaxis, Influenza A and B	Age 5–12, 10 mg qd by inhalation	10 mg qd by inhalation	10 mg qd by inhalation
Amantadine[c]			
Treatment, Influenza A	Age 1–9, 5 mg/kg in 2 divided doses, up to 150 mg/d	Age ≥10, 100 mg PO bid	≤100 mg/d
Prophylaxis, Influenza A	Age 1–9, 5 mg/kg in 2 divided doses, up to 150 mg/d	Age ≥10, 100 mg PO bid	≤100 mg/d
Rimantadine[c]			
Treatment, Influenza A	Not approved	100 mg PO bid	100–200 mg/d
Prophylaxis, Influenza A	Age 1–9, 5 mg/kg in 2 divided doses, up to 150 mg/d	Age ≥10, 100 mg PO bid	100–200 mg/d

Measles (Rubeola)

- CDC case definition for measles requires
  - (1) a generalized maculopapular rash of at least 3 days' duration;
  - (2) fever of at least 38.3°C (101°F); and
  - (3) cough, coryza, or conjunctivitis
- IP: is **10 days to fever onset and 14 days to rash onset** with **Airborne** transmission
- **D/D:** rubella, Kawasaki disease, infectious mononucleosis, roseola, scarlet fever, Rocky Mountain spotted fever, enterovirus or adenovirus infection, and drug sensitivity
- Serology is the most common method of laboratory diagnosis
- **Paradoxically** associated with depressed immune responses to unrelated antigens, which persist for several weeks to months that enhances susceptibility to **secondary infections** with bacteria and viruses that cause pneumonia and diarrhea







Rubella (German Measles)

- Spread from person to person via respiratory droplets
- Primary implantation and replication in the **nasopharynx** are followed by spread to the lymph nodes, then other organs or placenta in congenital rubella syndrome
- The pathology of CRS in the infected fetus is well defined, with almost **all organs found to be infected**; however, the pathogenesis of CRS is only poorly delineated
- Acquired rubella commonly presents a subclinical and mild disease: a generalized maculopapular **rash** that usually lasts for up to 3 days; **Lymphadenopathy**, particularly occipital and postauricular, may be noted during the second week after exposure
- The hallmark of fetal infection is **chronicity**, with persistence throughout fetal development in utero and for up to 1 year after birth

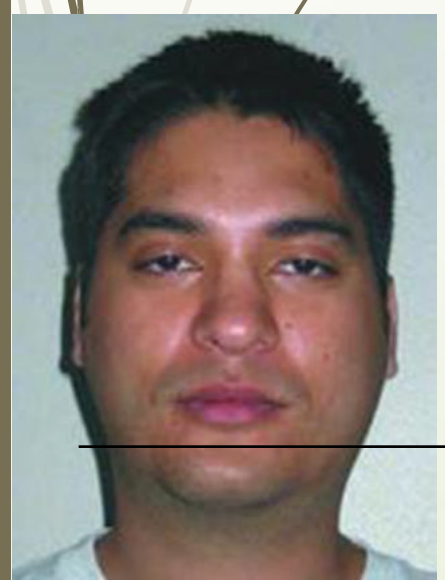
TABLE 230e-1 COMMON TRANSIENT AND PERMANENT MANIFESTATIONS IN INFANTS WITH CONGENITAL RUBELLA SYNDROME

Transient Manifestations	Permanent Manifestations
Hepatosplenomegaly	Hearing impairment/deafness
Interstitial pneumonitis	Congenital heart defects (patent ductus arteriosus, pulmonary arterial stenosis)
Thrombocytopenia with purpura/petechiae (e.g., dermal erythropoiesis, or "blueberry muffin syndrome")	Eye defects (cataracts, cloudy cornea, microphthalmos, pigmentary retinopathy, congenital glaucoma)
Hemolytic anemia	Microcephaly
Bony radiolucencies	Central nervous system sequelae (mental and motor delay, autism)
Intrauterine growth retardation	
Adenopathy	
Meningoencephalitis	

- Laboratory assessment of rubella infection is conducted by serologic and virologic methods
- Demonstration of **IgM antibodies in an acute-phase serum specimen or a fourfold rise in IgG antibody (**the acute-phase serum specimen should be collected within 7–10 days after onset of illness and the convalescent-phase specimen ~14–21 days after the first specimen)
- **Mature (high-avidity) IgG antibodies** most likely indicate an infection occurring at least 2 months previously (This test helps **distinguish primary infection from reinfection**)
- Symptom based treatment for various manifestations, such as fever and arthralgia, is appropriate
- Administration of **immunoglobulin** should be considered **only if** a pregnant woman who has been exposed to rubella will not consider termination of the pregnancy under any circumstance
- The most effective method of preventing acquired rubella and CRS is through **vaccination with an MMR/MMRV (**globally RA27/3 virus strain)

Mumps

- Illness characterized by acute-onset unilateral or bilateral tender, self-limited swelling of the parotid or other salivary gland(s) that lasts at least 2 days and has no other apparent cause
- Now frequently occurs in older age groups—primarily college students, most of whom **were vaccinated** in early childhood
- IP: **19 days** (range, 7–23 days); transmitted by the **respiratory route** via droplets, saliva, and fomites
- Primary replication likely occurs in the nasal mucosa or upper respiratory mucosal epithelium; THEN **salivary glands, testes, pancreas, ovaries, mammary glands, and central nervous system (CNS**); Other unusual complications include thyroiditis, nephritis, arthritis, hepatic disease, keratouveitis, and thrombocytopenic purpura
- Typical mumps encephalitis appears to be secondary to respiratory spread and is probably a **parainfectious** process
- Mumps parotidits, usually **within 24 h of prodromal viral symptoms**
- Detection of viral RNA by RT-PCR or on serology



- Therapy for parotitis and other clinical manifestations is **symptom based** and supportive

- Treatment consists of general **supportive measures**, such as hydration and administration of antipyretic agents
- Prompt **antibiotic treatment** for patients who have clinical evidence of bacterial infection; *Streptococcus pneumoniae* and *Haemophilus influenzae* type b are common causes of bacterial pneumonia following measles
- Once-daily doses of **200,000 IU of vitamin A for 2** consecutive days to all children with mea
- Most **complications** of measles involve the respiratory tract (croup, Giant-cell pneumonitis, Otitis media, and bronchopneumonia) and include the effects of measles virus replication itself and secondary bacterial infectionsles who are ≥12 months of age
- **Postmeasles encephalomyelitis -** within 2 weeks of rash onset and is characterized by fever, seizures, and a variety of neurologic abnormalities
- **Measles inclusion body encephalitis (MIBE-** occurs months after infection**) and subacute sclerosing panencephalitis (SSPE- o**ccurring 5–15 years after measles**)**
- Prophylaxis with **immunoglobulin** is recommended for susceptible household and nosocomial contacts who are at risk of developing severe measles, particularly children <1 year of age, immunocompromised persons (including HIVinfected persons previously immunized with live attenuated measles vaccine), and pregnant women

Thank you