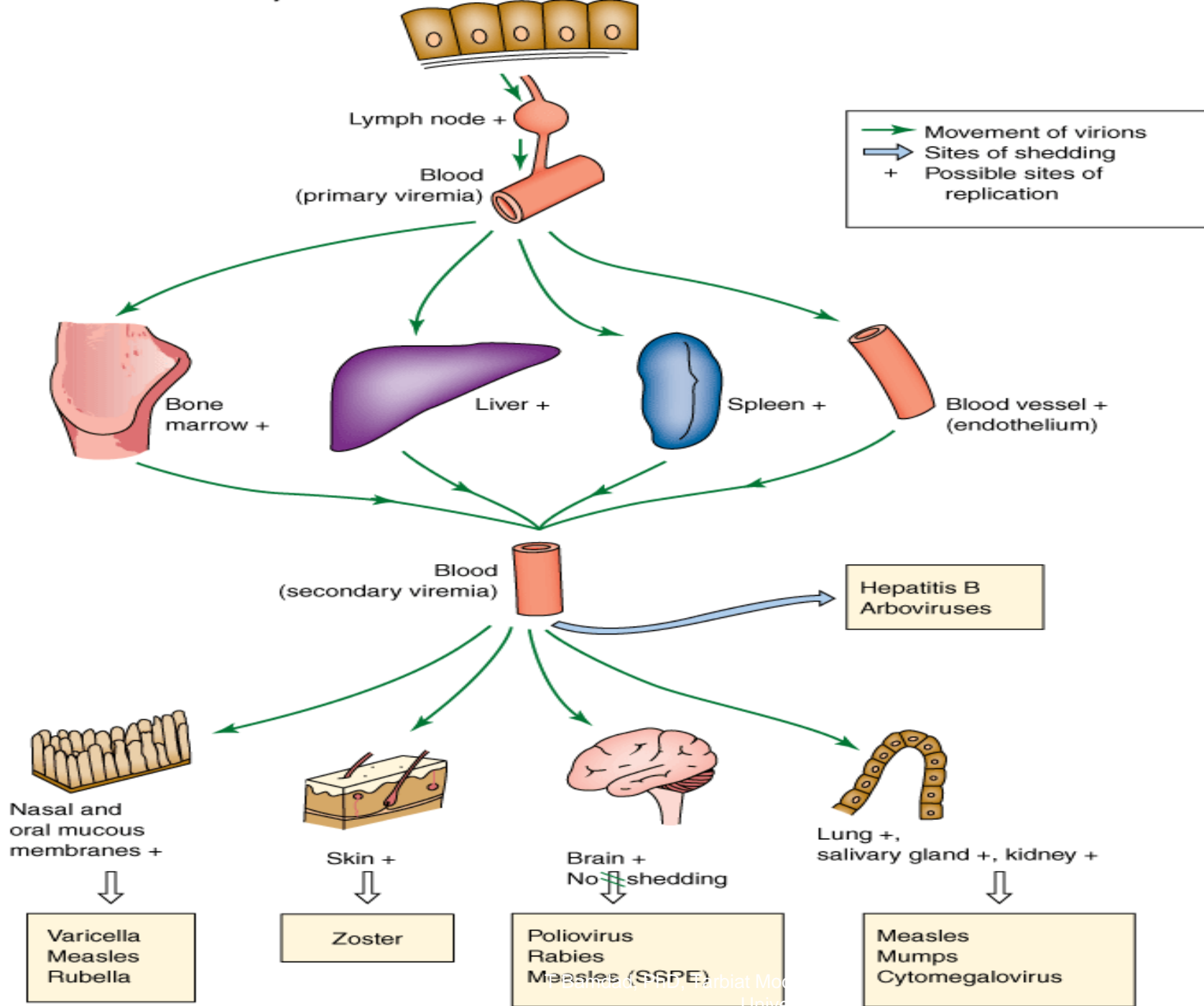


Viral Diseases

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Types of Viral Disorders

- ▶ Categorizing viral infections by the organ system most commonly affected (eg, lungs, GI tract, skin, liver, CNS, mucous membranes) can be clinically useful, although certain viral disorders (eg, mumps) are hard to categorize.



Categorizing viral infections by the organ affected

Group	Tissues Affected	Important Diseases
Pneumotropic	Respiratory system	Influenza, Respiratory Syncytial Disease, Adenovirus Infection, Rhinovirus Infection
Dermotropic	Skin and Subcutaneous Tissues	Chicken Pox, Herpes Simplex, Measles, Mumps, Small Pox, Molluscum Contagiosum, German Measles
Viscerotropic	Blood and Visceral Organs	Yellow Fever, Dengue Fever, Infectious Mononucleosis, Cytomegalovirus Disease, Infectious Hepatitis, Serum Hepatitis, Sandfly Fever, Colorado Tick Fever
Neurotropic	Central nervous system	Rabies, Polio, Encephalitis, Slow Virus Disease

Respiratory infections (RIs)

- ▶ The most common viral infections are probably URIs. Respiratory infections are more likely to cause severe symptoms in infants, the elderly, and patients with a lung or heart disorder.
- ▶ Respiratory viruses include influenza viruses (A, B, C), parainfluenza viruses 1 through 4, adenoviruses, respiratory syncytial virus, and rhinoviruses. They are typically spread from person to person by contact with infected respiratory droplets.

Summary OR List of Pneumotropic Viral Diseases of Human

Disease	Transmission	Organs Affected	Vaccine
Influenza	Droplets	Respiratory Tract	Available for high risk
Adenovirus Infections	Droplets, Contact	Lungs, Eyes	Not Available
Respiratory Syncytial Disease	Droplets	Respiratory Tract	Not Available
Rhinovirous Infections	Droplets, Contact	Upper Respiratory Tract	Not Available
Corona virus	Droplets	Upper Respiratory Tract	

Viral Infections of the Respiratory Tract

		Most Common Viral Causes		
Syndromes	Main Symptoms	Infants	Children	Adults
Common cold	Nasal obstruction, nasal discharge	Rhino	Rhino	Rhino
		Adeno	Adeno	Corona
Pharyngitis	Sore throat	Adeno	Adeno	Adeno
		Herpes simplex	Coxsackie	Coxsackie
Laryngitis/croup	Hoarseness, "barking" cough	Parainfluenza	Parainfluenza	Parainfluenza
		Influenza	Influenza	Influenza
Tracheobronchitis	Cough	Parainfluenza	Parainfluenza	Influenza
		Influenza	Influenza	Adeno
Bronchiolitis	Cough, dyspnea	Respiratory syncytial	Rare	Rare
		Parainfluenza		
Pneumonia	Cough, chest pain	Respiratory syncytial	Influenza	Influenza
		Influenza	Parainfluenza	Adeno

Differentiation based on the symptoms

Influenza infection (acute and severe symptoms are characteristic), Rhino virus infection (rhinitis like), RS virus infection (also rhinitis like) and Parainfluenza virus infection are commonly prevalent in **winter and spring**. Adenovirus infection, Enterovirus infection, Coxsackie virus infection and ECHO virus infection are commonly seen in **summer** (it is called hot weather cold). Every virus has an affinity with the infection region of the respiratory organs to some degree, but it is difficult to identify the caused virus only by clinical symptoms, and it needs to segregate each virus by genetic diagnosis procedure such as PCR or by immuno-serological examination etc using nasal secretion or tissue from throat and serum in order to identify the virus exactly. However, it is not significant to identify the caused virus except Influenza virus and Adenovirus in daily medical work.

Differentiation based on the prevalence

Rhino viruses are the most commonly viral agents of upper respiratory infections.

Corona viruses are responsible for about 10-20% of viral URIs.

Parainfluenza viruses are responsible for about 5% of viral URIs.

Adenoviruses are responsible for about 3-5% of viral URIs.

- ▶ 2006 National Hospital Ambulatory Medical Care Survey showed:
 - most common ED diagnosis for
 - kids <1 = upper respiratory infection
 - kids 2–12 = otitis media/ear disorders
- ▶ In all, fever is the **most common** chief complaint of kids presenting to the ED (about 20–30% all peds visits)

Multisystem diseases:

- ▶ Enteroviruses, which include coxsackieviruses and echoviruses can cause various multisystem syndromes, as can cytomegaloviruses, EBV,....

Summary OR List of Viscerotropic Viral Diseases of Human

Disease	Transmission	Organs Affected	Vaccine
Yellow Fever	Aedes (Mosquito)	Agypti Liver,Blood	Inactivated Viruses
Dengue Fever	Aedes (Mosquito)	Aegypti Blood, Muscles	Not Available
Infectious Mononucleosis	Saliva Droplet	Contact, Blood,Lymph nodes,Spleen	Not Available
Cytomegalovirus Disease	Contact, Congenital Transfer	Blood,Spleen	Not Available
Heaptitis A	Food,Water,Contact	Liver	Not Available
Hepatitis B	Contact with body Fluids	Liver	HBsAg Fragments
NANB Hepatitis	Contact with body fluids	Liver	Not Available
Viral Gastroenteritis	Food, Water	Intestine	Not Available
Viral Fevers	Contact,Arthropods, Animals	Blood	Not Available
AIDS	Contact with body Fluids	T- lymphocytes	Not Available

Gastrointestinal infections (GI)

- ▶ GI infections: Gastroenteritis is usually caused by viruses and transmitted from person-to person by the oral-fecal route. Age group primarily affected depends on the virus:
- ▶ **Rotavirus:** Children
- ▶ **Norovirus:** Older children and adults
- ▶ **Astrovirus:** Usually infants and young children
- ▶ **Adenovirus 40 and 41:** Infants
- ▶ **Coronavirus-like agents:** Infants
- ▶ Local epidemics may occur in children, particularly during colder months.
- ▶ The main symptoms are vomiting and diarrhea.
- ▶ No specific treatment is recommended, but supportive care, particularly rehydration, is important.

Rotaviruses have been estimated to cause 30-50% of all cases of severe diarrhoeal disease in man. **Seasons:** In temperate '1st world' populations rota virus is the main cause of **winter gastroenteritis** .

In tropical and developing countries, rotavirus diarrhoea occurs all the year round ,but with a **peak in summer**.

NORWALK agent

'*Common source*' type of explosive outbreaks of gastroenteritis, with limited secondary spread to household contacts, have been described. These often occur in institutions, or follow common source ingestion episodes e.g. celebratory feasts.

Vomiting with cramps are more common symptoms than the diarrhoea.

Hepatic infections

- ▶ At least 5 specific viruses (hepatitis A, B, C, D, and E viruses) can cause hepatitis; each causes a specific type of hepatitis. Hepatitis D virus can infect only when hepatitis B is present. Transmission is from person to person by contact with infected blood or body secretions or by the fecal-oral route for hepatitis A and E.
- ▶ Other viruses can affect the liver as part of their disease process. Common examples are cytomegalovirus, Epstein-Barr virus, and yellow fever virus. Less common examples are echovirus, coxsackievirus, and herpes simplex, rubeola, rubella, and varicella viruses

Exanthematous infections

- ▶ Some viruses cause only skin lesions (as in molluscum contagiosum and warts—others also cause systemic manifestations or lesions elsewhere in the body. Transmission is typically from person to person; alphaviruses have a mosquito vector.

Summary OR List of Dermotropic Viral Diseases of Human

Disease	Transmission	Organs Affected	Vaccine
Chicken Pox (Varicella)	Contact, Droplets	Skin, Nervous System	Not Available
Herpes Simplex	Contact	Skin, Pharynx, Genital Organs	Not Available
Measles (Rubeola)	Contact, Droplets	Skin, Respiratory Tract	Attenuated Viruses
Mumps (Epidemic Parotitis)	Droplets	Salivary Glands, Blood	Attenuated Viruses
Small Pox (Variola)	Contact, Droplets	Skin, Blood	Cowpox Viruses
Molluscum Contagiosum	Contact	Skin	Not Available
German Measles (Rubella)	Contact, Droplets	Skin	Attenuated Viruses

Herpes whitlow



HSV-1



VZV



Measles



B19



Papilloma



Rubella



COXSACKIE VIRUSES
Hand, foot and mouth disease



Dengue Hemorrhagic Fever (DHF)

Eye infections

Adenovirus (**Epidemic Keratoconjunctivitis**) is by far the most common cause, and **herpes simplex virus** (**Herpes keratitis**) is the most problematic. Less common causes include **varicella-zoster virus** (VZV), **picornavirus** (enterovirus 70, Coxsackie A24), **poxvirus** (molluscum contagiosum, vaccinia), and **human immunodeficiency virus** (HIV). Rarely, conjunctivitis is seen during systemic infection with influenza virus, **Epstein-Barr virus**, paramyxovirus (**measles**, **mumps**, Newcastle), and **rubella**.

Neurologic infections

- ▶ Most cases of encephalitis are caused by viruses. Many of these viruses are transmitted to humans by blood-eating arthropods, mainly mosquitoes and ticks (Arboviridae, Arenaviridae, and Filoviridae, ...); these viruses are called arboviruses (arthropod-borne viruses). For such infections, prevention includes avoiding mosquito and tick bites. Meningitis is also caused by different viruses.

Summary OR List of Neurotropic Viral Diseases of Human

Disease	Transmission	Organs Affected	Vaccine
Rabies	Contact with body Fluids	Brain, Spinal Cord	Inactivated Viruses
Lymphocytic choriomeningitis	Dust, Contact	Brain, Meninges	Not Available Inactivated
Polio	Food, Water, Contact	Intestine, Spinal Cord, Brain	Viruses, Attenuated Viruses
Arboreal Encephalitis	Arthropods	Brain	Not Available
Slow Disease	Virus Not Established	Brain	Not Available

Incidence of meningitis based on different viruses

- Enteroviruses 40%
- Mumps 15%
- Lymphocytic choriomeningitis 5%
- Other 10%
- Unknown 30%

Severe and Fatal Encephalitis

- Arthropod-borne viruses
- Herpes simplex viruses

Other viruses:

chickenpox

measles

mumps

Epstein-Barr virus (EBV)

cytomegalovirus infection

HIV

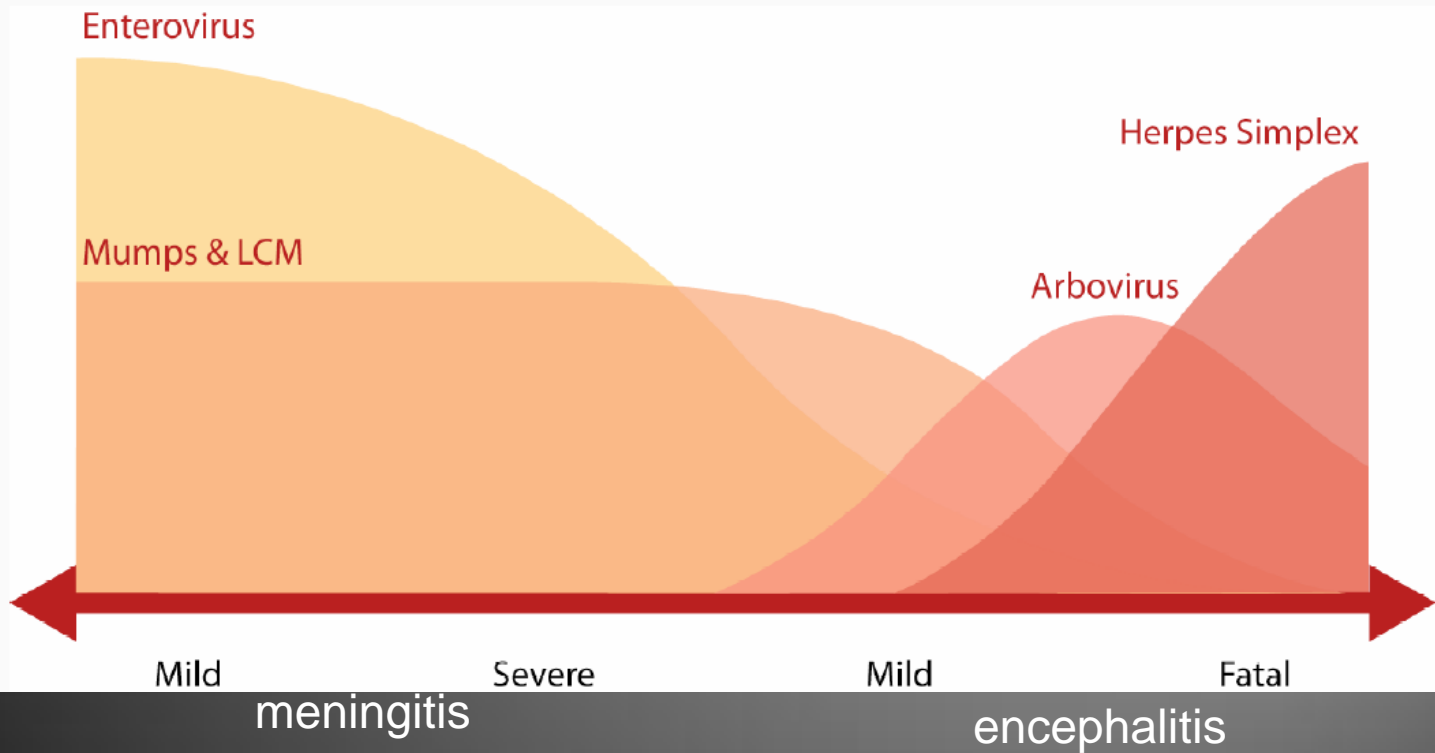
herpes zoster (shingles)

herpes B

polio

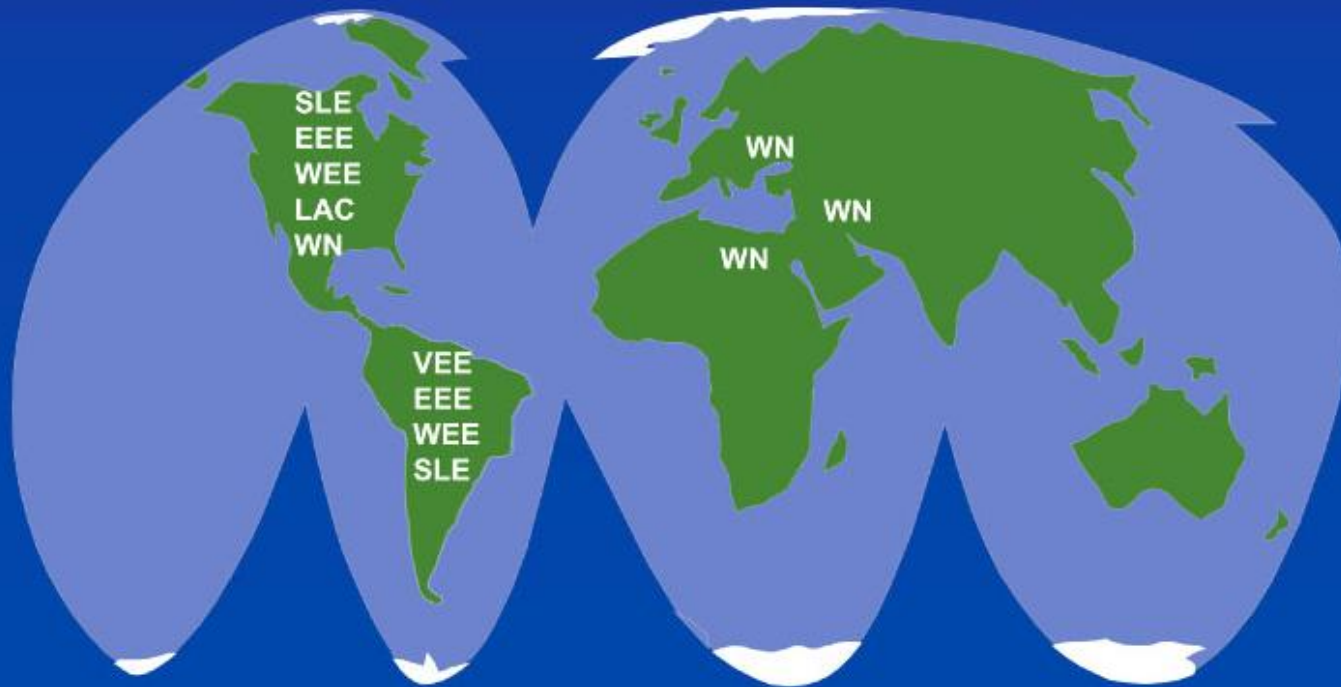
rabies

Viruses and Severity of Disease



Arboviral encephalitis is prevalent worldwide

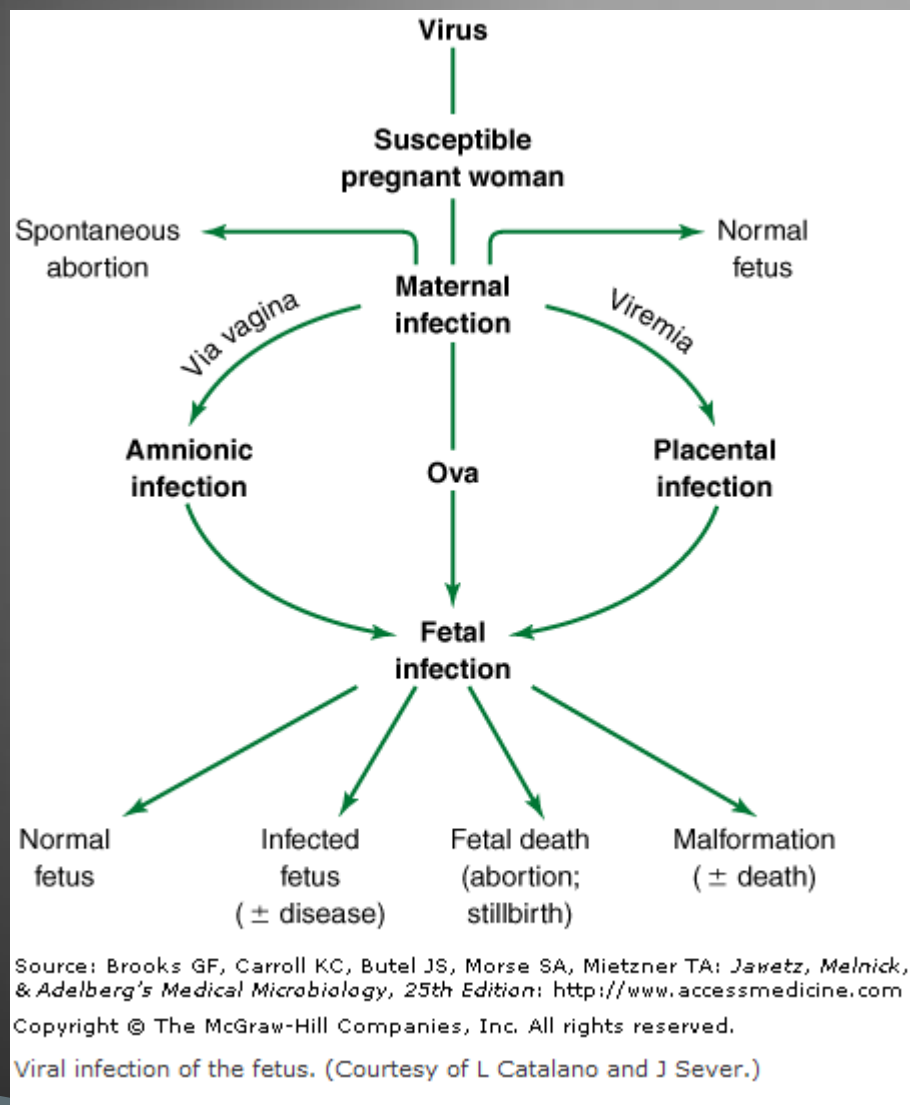
Worldwide Distribution of Major Arboviral Encephalitides



EEE: Eastern equine encephalitis
LAC: LaCrosse encephalitis
SLE: St. Louis encephalitis

WEE: Western equine encephalitis
WN: West Nile encephalitis
VEE: Venezuelan equine encephalitis

Congenital Viral Infections



Acquisition of Significant Perinatal Viral Infections

	Frequency of Time of Infection			
Virus	Prenatal (In Utero)	Natal (during Delivery)	Postnatal (after Delivery)	Neonatal Incidence (Per 1000 Live Births)
Rubella	+	-	Rare	0.1-0.7
Cytomegalovirus	+	++	+	5-25
Herpes simplex	+	++	+	0.03-0.5
Varicella-zoster	+	Rare	Rare	Rare
Hepatitis B	+	++	+	0-7
Enterovirus	+	++	+	Uncommon
HIV	+	++	Rare	Variable
Parvovirus B19	+	-	Rare	Rare

common infectious pathogens in the neonate

AGE	BACTERIAL	VIRAL	OTHER
0–28 days	Group B <i>Strep</i> <i>Listeria</i> <i>E. Coli</i> <i>C. trachomatis</i> <i>N. gonorrhoeae</i>	Herpes simplex Varicella Enterovirus RSV Flu	Bundling environment
1–3 months	<i>H. flu</i> <i>S. pneumo</i> <i>N. meningitidis</i> <i>E. coli</i>	Varicella Enterovirus RSV flu	Bundling environment

common infectious pathogens in the young child

AGE	BACTERIAL	VIRAL	OTHER
3-36 months	<i>S. pneumo</i> <i>N. meningiditis</i> <i>E. coli</i>	Varicella Enterovirus RSV Flu Mono Roseola Adenovirus Norwalk Coxsackie	Leukemia Lumphoma Neuroblastoma Wilms' tumor

Diagnostic assays for central nervous system viral infections

No.	Organism	Specimen(s)	Suggested methodology	Comments
1.	<i>Herpesviridae</i> (HSV 1 and 2, CMV, VZV, EBV, HHV 6)	CSF and paired serum specimens	Isolation using cell culture, antigen detection and PCR, antibody detection	PCR has replaced culture as the "Gold standard"
2.	<i>Enteroviruses</i>	CSF and paired serum specimens	Isolation using cell culture, detection of rising antibody titres and PCR	PCR using genus-specific conserved primers has proved most sensitive
3.	<i>Flaviviridae</i> (JEV, West Nile, dengue)	CSF and paired serum specimens	Detection of IgM antibodies in CSF and sera, virus isolation	Utility of PCR has not been comprehensively evaluated
4.	<i>Paramyxoviridae</i> (mumps, measles, Nipah)	CSF and paired serum specimens	Detection of IgM antibodies in CSF and sera, virus isolation	Utility of PCR has not been comprehensively evaluated

Diagnostic assays for central nervous system viral infections

6.	<i>Papovaviridae</i> (JC virus)	CSF and paired serum specimens	Virus isolation and PCR	PCR has proved more sensitive
7.	<i>Rhabdoviridae</i> (rabies, ...)	Brain(post-mortem) CSF	Virus isolation, immuno-fluorescence	PCR has not been extensively evaluated

Diagnostic assays for Respiratory viral infections

No.	Organism	Specimens(s)	Suggested methodology	Comments
1.	Influenza viruses (Influenza virutypes A, B and C, avian influenza virus)	Nasopharyngeal aspirates, throat swab, paired serum samples collected at 7 and 14 days after onset of symptoms	Isolation using cell culture, antigen detection by immuno-fluorescence, antibody detection by neutralization, and nucleic acid detection by PCR	PCR using genus-specific conserved primers has proved most sensitive
2.	Para-influenza viruses (PI types 1-3)	Nasopharyngeal aspirates, throat swab, paired serum samples collected at 7 and 14 days after onset of symptoms	Isolation using cell culture, antigen detection by immuno-fluorescence, and nucleic acid detection by PCR	PCR using genus specific conserved primers has proved most sensitive
3.	Respiratory syncytial virus	Nasopharyngeal aspirates, throat	Isolation using cell culture, antigen	Utility of PCR has not been
4.	Paramyxoviridae (mumps, measles, Nipah)	Nasopharyngeal aspirates, throat swab, single serum samples	Isolation using cell culture, antigen detection by immuno-fluorescence, antibody detection by ELISA IgM, and nucleic acid detection by PCR	Utility of PCR has not been comprehensively evaluated

Diagnostic assays for gastroenteritis viruses

No.	Organism	Specimens(s)	Suggested methodology
1.	Reoviruses (Rotaviruses)	Stool	Antigen detection by ELISA, electron microscopy, and PCR
2.	Enteroviruses	Stool	Antigen detection by ELISA, electron microscopy, and PCR
3.	Astroviruses	Stool	Electron microscopy, virus antigen detection and PCR
4.	Caliciviruses	Stool	Electron microscopy, virus antigen detection and PCR

Diagnostic assays for viruses that cause fever with rash or haemorrhage

No.	Organism	Specimens(s)	Suggested methodology
1.	Measles virus	Nasal aspirates, throat washings urine whole blood, single serum samples	Virus isolation, IgM antibody detection by ELISA and nucleic acid detection by PCR
2.	Rubella	Nasal aspirates, throat washings, single serum samples	
3.	Flaviviruses (dengue virus serotypes 1-4, West Nile virus)	Paired serum samples	
4.	Alphaviruses (chikungunya)	Paired serum samples	
5.	Enteroviruses (coxsackie and ECHO viruses)	Stool specimens, throat washings, paired serum samples	
6.	Filoviridae	Paired serum samples	

Appropriate Specimens For Virus Culture

Organ system involved	Agent suspected	Appropriate specimens
Respiratory (upper respiratory, tracheobronchitis, pneumonitis)	rhinovirus, RSV influenza, parainfluenza	NP, BAL, OTHER RESP FLD, NW NP, BAL, LUNG BX, NW
	cytomegalovirus adenovirus, enterovirus	BAL, LUNG BX, BLD, THRT THRT, BAL, STOOL
Central Nervous System (encephalitis, encephalomyelitis, meningitis, neuritis, polyradiculo-encephalopathy)	enterovirus cytomegalovirus	THRT, STOOL, CSF CSF, BLD
Skin, Mucous Membrane, Eye	varicella-zoster verpes simplex enterovirus adenovirus	VESICL VESICL, THRT, EYE SWB VESICL, THRT, STOOL EYE SWB
Urogenital	herpes simplex adenovirus enterovirus cytomegalovirus chlamydia	GENSWB, URN THRT, URN THRT, URN, STOOL URN, BLD, THRT GENSWB, URN
Gastrointestinal	adenovirus enterovirus	STOOL, THRT, BX
	cytomegalovirus herpes simplex	STOOL, BX, BLD STOOL, BX, BLD
Cardiovascular (Pericarditis, myocarditis)	influenza enterovirus	NP, NW STOOL, THRT, PERICD
Mononucleosis	cytomegalovirus	BLD, THRT, URN

BAL: bronchoalveolar lavage; BLD: blood; BX: biopsy; CSF: cerebrospinal fluid; GENSWB: genital swab; PERICD: pericardial fluid; THRT: throat wab; THRW: throat wash; URN: urine; VESICL: vesicle/cyst aspirate or fluid; vesicle scraping; NW: nasal wash; NP: nasopharyngeal swab

Sampling examples

Virus agent	Nature of test	Specimen	Amount and Handling
HSV 1 and 2	DFA	Swab or scraping of vesicle or base of lesion	Use a special Syva Micro Trak HSV1/HSV2 collection kit available to UPMC clinicians from the virology lab or may be purchased from Syva (2 kits if both VZV and HSV are requested)
VZV	DFA	Swab or scraping of vesicle or base of lesion	Use a special Syva Micro Trak HSV1/HSV2 collection kit available to UPMC clinicians from the virology lab or may be purchased from Syva (2 kits if both VZV and HSV are requested)
rotavirus	antigen EIA	Stool	Collect in a sterile container without any preservatives; keep cool on ice for transport

Optimal time for collection of specimens

Specimen	Optimal time after onset of symptoms in days within which sample should be collected (days)
CSF and plasma	7
Stool, Urine	14
Nasopharyngeal swab, nasal washings	5
Throat washings, buffy coat for CMV	As early as possible
Vesicular fluid (fluid/scraping), genital swab	
Post-mortem specimens	