Viral Infection in Gastrointestinal System

Enteroviruses
Gastroenteritis viruses
Hepatitis viruses

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Fundamental of Medical Science 1
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Virtues transmitted by fecal-oral route

**Enteroviruses** are a group of (+)ssRNA viruses associated with several human and mammalian diseases, for examples hand, foot and mouth disease, acute hemorrhagic conjunctivitis, aseptic meningitis, myocarditis, paralysis. **Enteroviruses:** Poliovirus, Coxsackievirus A, Coxsackievirus B, Echovirus, New enterovirus. **Enteroviruses** do not cause enteric disease but are transmitted by the fecal-oral route.

**Gastroenteritis viruses** are a variety of viruses that cause inflammation of stomach and small and large intestines resulting in vomiting or diarrhea. **Gastroenteritis viruses:** Rotavirus, Norovirus, Sapovirus, Astrovirus, Adenovirus, Coronavirus, Aichi virus, Parechovirus.

**Hepatitis viruses** are a variety of viruses that cause liver inflammation. They may present in acute (recent infection, relatively rapid onset) or chronic infection. **Hepatitis viruses:** Hepatitis A virus (HAV), HBV, HCV, HDV and HEV. HAV and HEV are transmitted by the fecal-oral route.
Properties of Enteroviruses

- Family *Picornaviridae*
- Small, 25-30 nm in diameter
- A positive ss-RNA genome
- Non-enveloped virus
- Icosahedral capsid: are very resistant to harsh environmental conditions and the conditions in the GI tract.
- Acid-stable virus (~pH 3)
- Replicates in cytoplasm of infected cells
- Cytolytic virus
Classification of Enteroviruses

<table>
<thead>
<tr>
<th>Species</th>
<th>Number of serotype</th>
<th>Serotypes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Poliovirus</td>
<td>3</td>
<td>1-3</td>
</tr>
<tr>
<td>Coxsackievirus A</td>
<td>23</td>
<td>1-22, 24&lt;br&gt;Coxsackievirus A23 = Echovirus 9</td>
</tr>
<tr>
<td>Coxsackievirus B</td>
<td>6</td>
<td>1-6</td>
</tr>
<tr>
<td>Echovirus</td>
<td>30</td>
<td>1-9, 11-27, 29-33&lt;br&gt;Echovirus 10 = Reovirus 1&lt;br&gt;Echovirus 28 = Rhinovirus 1A&lt;br&gt;Echovirus 34 = variant of Coxsackievirus A24</td>
</tr>
<tr>
<td>New enterovirus</td>
<td>68-71</td>
<td></td>
</tr>
</tbody>
</table>

Murry P.R., et al. Medical Microbiology, 2005
Pathogenesis of Enterovirus Infection
Transmission: fecal-oral route, respiratory route and direct contact

Echovirus, Coxsackievirus, Enterovirus

Viruses replicate at mucosa and lymph node of oropharynx and intestine

Primary viremia

Secondary viremia

Target tissues

Skin
Echo, CVA
Hand-foot-and-mouth disease
Rash, herpangina

Muscle
Echo, CVA, CVB

Brain
Polio, Coxsackie

Meninges
Echo, polio coxsackie

Virus shed in stool

Heart
Thorax

Myocarditis, pericarditis
Pleurodyinia

Meningitis
Encephalitis
Paralytic disease

Modified from Murray P.R., et. al., Medical Microbiology, 2005
Coxsackieviruses

They are divided into 2 groups, A and B, on the basis of certain biologic and antigenic differences.

- **Coxsackievirus group A (CVA):**
  - first isolated in 1948 from the feces of paralyzed children in Coxsackie, New York
  - CVA $\rightarrow$ newborn mice $\rightarrow$ flaccid paralysis

*CVA* is associated with diseases involving vesicular lesions (e.g., herpangina).
COXSACKIEVIRUSES

- **Coxsackievirus group B (CVB):**
  - isolated in 1949 from the feces of aseptic meningitis patient

  CVB → newborn mice → spastic paralysis and generalized infection (virus spreads to brain, pancreas and heart)

CVB (B for body) are most frequently associated with myocarditis and pleurodynia.
Diseases caused by Coxsackieviruses

1. Herpangina (Vesicular pharyngitis)
   - fever, sore throat, pain on swallowing, anorexia, vesicular ulcerated lesions around the soft palate and uvula (self-limited)

2. Hand, Foot and Mouth Disease (HFMD): CVA16
   - a vesicular examthem: versicular lesions on the hand, feet, mouth and tongue (self-limited)
Diseases caused by Coxsackie viruses

**CVA**
3. Exanthematous fever (ไข้ออกผื่น)

**CVB**
4. Pueurodynia (อาการปวดกล้ามเนื้อระหว่างซี่โครงที่ทรงอก)

**CVB5**
5. Aseptic meningitis, encephalitis (เยื่อหุ้มสมองอักเสบ) (สมองอักเสบ)

**CVB5**
6. Paralysis

**CVB**
7. Pericarditis, myocarditis

**CVB**
8. Diabetes mellitus

**CVA24 variant**
9. Acute hemorrhagic conjunctivitis (AHC)* (โรคตาแดง, เยื่อตาขาวอักเสบเฉียบพลัน)

*highly contagious conjunctivitis virus, otherwise known as pink eye*

http://www.uic.edu/depts/mcpt/curriculum/ppt/oral_mc/img040.jpg
ECHOVIRUSES

Enteric Cytopathogenic Human Orphans

In 1951, echoviruses were isolated from the stool of asymptomatic individuals. Echoviruses received their name because they were enteric isolates, cytopathogenic in tissue culture, isolated from humans, and orphans (i.e., unassociated with a known clinical disease).

Diseases caused by Echoviruses

1. Aseptic meningitis, encephalitis, paralysis
2. Myocardiopathy
3. Pleurodynia
4. Exanthematous fever
5. Common cold
6. Diarrhea
7. Acute hemorrhagic conjunctivitis
NEW ENTEROVIRUSES

Enterovirus 68: Bronchiolitis, pneumonia
(หลอดลมฝอยอักเสบ)

Enterovirus 69: None

Enterovirus 70: Acute hemorrhagic conjunctivitis

Enterovirus 71*: Hand, foot and mouth disease (HFMD) and sometimes associated with severe CNS (meningitis, encephalitis, paralysis)

- Children < 5 years old

* EV71 เป็น Enterovirus ที่มีความรุนแรงต่อระบบประสาทรองจาก Poliovirus
Hand, Foot and Mouth disease (HFMD)
โรครู้มือ - เท้า และปาก (เปื่อย)

Mostly caused by
- Coxsackievirus A16 (CVA16)
- Enterovirus 71 (EV71)

- found mainly in young children (< 5 years old)
- fever, sore throat, vesicles and ulcers in the anterior part of mouth, followed by a vesicular rash on hands and feet
- supportive treatment, no anti-viral drug available
- if it is not severe, patients will recover and have immunity
Herpangina (Vesicular pharyngitis)  
[โรคแผลในปาก (ร้อนใน)]
Mostly caused by - Coxsackievirus A 
- Echovirus 
- young children, 1-7 years old 
- fever, sore throat, difficulty in swallowing 
- vesicles on the soft palate, uvula, and posterior wall of the pharynx

Acute hemorrhagic conjunctivitis
Mostly caused by - Coxsackievirus A24 variant 
- Enterovirus 70 
- Adenovirus 11: swimming pool conjunctivitis
Laboratory Diagnosis of Enteroviruses

1. **Virus isolation:** Specimens - *feces*, rectal swab (5 weeks) - throat swab (10-14 days)
   Culture - cell culture (CPE)

2. **Serology:** Specimens - paired sera (acute and convalescent sera)
   Detection - neutralization (NT)
   [rising antibody titer (> 4 fold)]

3. **Viral genome:** Specimens - feces, rectal swab, throat swab
   Detection - RT-PCR
   (reverse transcription-polymerase chain reaction)
Gastroenteritis viruses

- Gastroenteritis means inflammation of the stomach and small and large intestines.

- Acute gastroenteritis is the major cause of morbidity and mortality worldwide (infants and children less than 5 years of age).

- In developing countries, there are more than 1.5 billion cases and 3 million deaths per year.

- Viral gastroenteritis is an infection caused by a variety of viruses that results in vomiting or diarrhea.
Rotaviruses

- Family Reoviridae
- Non-enveloped virus
- 60-80 nm in diameter
- Wheel-like spherical particle
- dsRNA genome, 11 segments

- Triple-layered capsid
  - outer capsid (VP7, VP4-spike)
  - middle capsid (VP6)
  - inner capsid (VP2-core, VP1/3)
Rotaviruses

Classification: 7 groups (A-G) and 2 subgroups (I and II) based on VP6 differences

- **Rotavirus group A**: the most common species, causes more than 90% of infections in humans (age < 5 years)
- **Rotavirus group B**: adult diarrhea rotavirus (outbreaks in China)
- **Rotavirus group C**: rare (worldwide)

<table>
<thead>
<tr>
<th>Group</th>
<th>Host or Reservoirs</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>human, horse, pig, dog, cat, goat</td>
</tr>
<tr>
<td>B</td>
<td>human, cow, pig, sheep, rat</td>
</tr>
<tr>
<td>C</td>
<td>human, pig, ferret</td>
</tr>
<tr>
<td>D</td>
<td>chicken</td>
</tr>
<tr>
<td>E</td>
<td>pig</td>
</tr>
<tr>
<td>F</td>
<td>chicken</td>
</tr>
<tr>
<td>G</td>
<td>chicken</td>
</tr>
</tbody>
</table>
Pathogenesis of Rota Gastroenteritis

- The most common cause of severe diarrhea among infants and young children
- Asymptomatic infection: all ages
- Symptomatic infection: infants and small children (< 5 years old)
- The most severe symptoms tend to occur in children six months to two years of age.
- Immunity develops with each infection, so subsequent infections are less severe; adults are rarely affected.
Pathogenesis of Rota Gastroenteritis

- Rotavirus gastroenteritis is a mild to severe disease with vomiting, watery diarrhea, and low-grade fever.

- Once a child is infected by the virus, there is an incubation of about 1-3 days before symptoms appear.

- Symptoms often start with vomiting followed by 4-5 days of profuse diarrhea (7-10 days in some cases).

- The feces of an infected person can contain more than 10 trillion infectious particles \((10^{12})\) per gram.

- Fewer than 100 of infectious Rotavirus particles are required to transmit infection to another person.

- **Dehydration** is more common in rotavirus infection than in most of those caused by bacterial pathogens, and is the most common cause of death related to rotavirus infection.
**Pathogenesis of rotavirus diarrhea**

**Ingested virus:**
- Infected cell at tip of villi in small intestine
- Spreads to infect large numbers of these cells
- Release of virus particles into lumen
- Infected cells damaged and lost, leaving immature cells with reduced absorptive capacity for sugar, water, salts
- Fluid accumulation in lumen
- Diarrhea
- Dehydration
- Virus replication ceases due to
  - Antibody
  - Interferon
  - Infection of all susceptible cells
- Crypt cells repopulate villi
- Normal appearances regained

Mims’ Medical Microbiology, 5th edition, 2013
**Mechanism of Rotavirus Diarrhea**

- Rotaviruses infect, multiply and destroy columnar epithelial cells, near apex of villi.
- Malabsorption secondary to destruction of enterocytes results in osmotic diarrhea.
- Rotavirus encodes a viral enterotoxin (NSP4) causing diarrhea.

*Enterocytes secrete lactase into the small intestine.*

Laboratory diagnosis of rotavirus infection

1. Detection of viral antigen (viral protein)
   - ELISA
   - Immunochromatography (IC) strip test

2. Detection of viral genome
   - RT-PCR (reverse transcription-polymerase chain reaction)
   - PAGE (polyacrylamide gel electrophoresis)

3. Virus isolation
   - Difficult to culture rotavirus isolated from specimen in monkey kidney cell line
Rotavirus

- The most common cause of serious viral diarrhea in young children (<5 years old) worldwide.

- Fecal-oral route transmission

- Prevention and control
  - no anti-Rotavirus agent available
  - maintenance of hydration: oral rehydration solution (ORS)

- Rotavirus vaccination
  1. **Rotarix** (Glaxo Smith Klin, Belgium):
     - Live-attenuated monovalent vaccine, G1P[8]
     - Oral vaccine, 2 doses at the ages 2 and 4 months

  2. **RotaTeq** (Merck & Co., Inc., USA):
     - Live-attenuated pentavalent vaccine,
     - Oral vaccine, 3 doses at the ages 2, 4 and 6 months old
Norovirus

- Family *Caliciviridae*
- Genus *Norovirus*
- Small, 27 nm in diameter
- Non-enveloped (+) ssRNA viruses
- Icosahedral capsid
- Can not be grown in cell culture
- 5 genogroups (GI-GV)
- GI, GII (19 genotypes) and GIV: causes diarrhea in humans
- Genogroup GII, genotype 4 (GII.4): majority of adult outbreaks of gastroenteritis in USA and Europe

*Norwalk virus*, the prototypical norovirus, was discovered during an epidemic of acute gastroenteritis in Norwalk, Ohio in 1968 upon electron microscopic examination of stool samples from adults.
Norovirus

- Incubation period: 12-48 hours
- Clinical symptoms: acute onset of nausea, forceful vomiting, watery diarrhea, and abdominal cramps.
- The illness usually resolves within 1 to 3 days without problems but can last up to 6 days. The disease is usually self-limiting, and severe illness is rare.
- Immunity is generally short lived at best and may not be protective. The large number of strain and high rate of mutation allows reinfection despite antibodies from a previous exposure.
- The virus affects around 267 million people and causes over 200,000 deaths each year; these deaths are usually in less developed countries and in the very young, elderly and immuno-suppressed people.
Norovirus

- **Shellfish (oyster)** and salad ingredients are the foods most often implicated in norovirus outbreaks.

- As few as 10 virions of Norovirus will initiate disease in humans.

- Infected individuals shed large amounts of virus upon onset of symptoms and up to 4 weeks after recovery.

- During peak shedding, 100 billion virions are released per gram of feces.

**Laboratory diagnosis**

- Viral antigen: ELISA
- Viral genome: RT-PCR
- Antibody: ELISA
Gastroenteritis Viruses

- Rotavirus (dsRNA, 11 segments, Triple shell capsid)
- Norovirus (ssRNA)
- Sapovirus (ssRNA)
- Astrovirus (ssRNA)
- Enteric adenovirus (dsDNA)
  - Non-enveloped viruses

Prevention and control
- No specific anti-viral drug
- Universal precaution
- Supportive treatment: ORS
- Vaccine (Rotavirus)

Laboratory diagnosis
- Ag: ELISA
- Genome: RT-PCR, PCR
- Ab: ELISA
Hepatitis viruses: cause viral Hepatitis

- Hepatitis A virus
- Hepatitis B virus
- Hepatitis C virus
- Hepatitis D virus
- Hepatitis E virus
Hepatitis A virus (HAV)

- **Family** Picornaviridae
- **Genus** Hepatovirus
- Icosahedral capsid (25–27 nm)
- Non-enveloped virus
- A (+) ssRNA genome
- 1 serotype
- Stable at pH 1 for 5 hours, and at 60°C for 10–12 hours
- Cytolytic virus
- Transmitted by fecal-oral route
- Incubation period: 2–6 weeks (average: 30 days)
- Adults experience signs and symptoms more often than children
Hepatitis and jaundice

- **Preicteric phase**
  - Fatigue, abdominal pain, loss of appetite, nausea and vomiting

- **Icteric phase, jaundice**
  - High levels of ALT (Alanine aminotransferase) and bilirubin, jaundice (yellow color of the skin, mucous membranes, or eyes) and dark urine

- **Convalescent phase**
  - Usually recover in 2 weeks (ALT and AST ↓)
  - About 0.5% of HAV-infected patients: fulminant hepatitis
  - Self-limited disease that does not result in chronic infection or chronic liver disease
  - Last-long immunity, no carrier

Asymptomatic infection: 90% of HAV-infected children (age < 5 years old)
Clinical symptom, virus levels, immune responses of hepatitis A virus infection

Hollinger FB and Emerson SU, 2001
Liver function test
- ALT, serum bilirubin, etc.

Detection of anti-HAV antibody
- acute infection: anti-HAV IgM = diagnostic marker by ELISA
Prevention and control

- No specific treatment available
- Supportive management
- Good hygiene and sanitation
- HAV vaccines
  - Killed vaccine
  - Live-attenuated vaccine
  - Two doses (0 and 6 months)
- HAV vaccination protects against HAV in more than 95% of cases for longer than 25 years
- Passive immunization will be given to individuals who likely had been exposed to or in close contact with HAV-infected patients by intramuscular injection with anti-HAV antibodies
Hepatitis B virus (HBV)

- Family *Hepadnaviridae*
- Enveloped virus (42 nm)
- A partially circular double-stranded DNA (dsDNA)
- Contain reverse transcriptase (RT) within particle
- 8 genotypes, 24 subtypes
Hepatitis B virion (Dane particle)

- **Hepatitis B surface antigen (HBsAg)**
- **Core (c) and e antigens**
- **DNA polymerase**
- **Partially circular ds-DNA**

- **Surface/envelope:** HBsAg
- **Capsid:** HBcAg and HBeAg
- **Core:** partially circular dsDNA genome and RNA-dependent DNA polymerase (Reverse transcriptase)
Antigens of HBV particle

1. Hepatitis B surface antigen (HBsAg)
   - Bind to specific receptor on target cell
   - HBsAg present in plasma of infected patient

2. Hepatitis B core antigen (HBCAg)
   - Found only in HBV virion (Dane particle)
   - HBCAg present on cell membrane and nuclear membrane of infected hepatocyte
   - Not detected in plasma/serum of infected patient
   - Activate cytotoxic T-cells
Antigens of HBV particle

3. Hepatitis B e antigen (HBeAg)

- Found only in HBV virion (Dane particle)
- HBeAg present in plasma/serum of active HBV patient
  - contagiousness
  - chronicity (chronic carrier, chronic hepatitis, cirrhosis)
  - vertical transmission (mother → baby)

HBeAg = Prognostic marker
Transmission of HBV

1. Vertical transmission
   - Carrier mother to infant (blood from infected mother enters the uninfected fetus or during childbirth)

2. Horizontal transmission
   - High-risk groups: intravenous drug users
   - Hemodialysis patients
   - share items such as razors and toothbrushes with infected person
   - have been exposed to sharp instruments contaminated with infected blood, such as needles used for tattooing, body piercing and acupuncture

3. Sexual transmission
   - have sex with HBV-infected person

Incubation period: 6 - 26 weeks (average: 80 days)
Hepatitis B virus (HBV)

- More than 90% of healthy adults who are infected with HBV will recover naturally from the virus within the first year.
- Chronic hepatitis B: depends upon the age at which a person becomes infected.

- **In infants and children:**
  - 80-90% of infants infected during the first year of life develop chronic infections.
  - 30-50% of children infected before the age of 6 years develop chronic infections.

- **In adults:**
  - <5% of otherwise healthy persons who are infected as adults will develop chronic infection.
  - 20-30% of adults who are chronically infected will develop cirrhosis and/or liver cancer.
HBV serological markers: HBsAg / HBeAg / anti-HBc / (anti-HBe), anti-HBs

Acute infection

Core window period

Anti-HBc * IgM = Diagnostic marker for HBV acute infection
Progression to Chronic HBV Infection

Chronic infection: HBsAg is present longer than 6 months

- Chronic infection: HBsAg+, anti-HBc total+, and anti-HBc IgM-
- Therapy: Chronic hepatitis: Pegylated interferon-alpha and Lamivudine or adofovir
<table>
<thead>
<tr>
<th>Assay Results</th>
<th>Interpretation</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>HBsAg</strong></td>
<td><strong>Anti-HBs</strong></td>
</tr>
<tr>
<td>Positive</td>
<td>Negative</td>
</tr>
</tbody>
</table>
| Positive     | Negative     | Positive                         | HBV infection, either acute or chronic.  
- Differentiate with IgM anti-HBc.  
- Determine level of replicative activity (infectivity) with HBeAg or HBV DNA |
<p>| Negative     | Positive     | Positive                         | Indicates previous HBV infection and immunity to hepatitis B. |
| Negative     | Negative     | Positive                         | Possibilities include: HBV infection in remote past; “low-level” HBV carrier; “window” between disappearance of HBsAg and appearance of anti-HBs; or false-positive or nonspecific reaction. |
| Negative     | Negative     | Negative                         | Another infectious agent, toxic injury to liver, disorder of immunity, hereditary disease of the liver, or disease of the biliary tract. |
| <strong>Negative</strong> | <strong>Positive</strong> | <strong>Negative</strong>                     | Vaccine-type response |</p>
<table>
<thead>
<tr>
<th>Markers</th>
<th>Interpretation</th>
</tr>
</thead>
<tbody>
<tr>
<td>HBsAg</td>
<td>Active infection (acute or chronic carrier state)</td>
</tr>
</tbody>
</table>
| Anti-HBs   | Past infection Immunity  
Positive after successful hepatitis B vaccination |
| Anti-HBc Total | Current or past infection, Measures all antibody classes  
Not present after hepatitis B vaccination |
| Anti-HBc IgM | Recent infection  
Occasionally present at low levels in chronic carriers |
| HBeAg      | Active infection, Present in some HBsAg positive individuals  
Relatively high level of viral replication, with greater risk of progression and contagion |
| Anti-HBe   | Lower level of viral replication, with lower risk of progression and contagion |
| HBV DNA    | Detectable in some HBsAg-positive individuals  
Quantitative information on level of viral replication |
Prevention and control

1. Hepatitis B immunoglobulin + vaccine
   - Baby born from HBV carrier mother
   - HBV exposed individuals

2. Vaccine (recombinant DNA vaccine)
   - HBsAg (subunit vaccine)
     - HBsAg gene recombinant plasmid $\rightarrow$ expression of HBsAg protein in yeast
   - Health care workers: physician, nurse, dentist, hemodialysis patient, blood-transfusion recipient

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Baby from HBV carrier mother</th>
<th>Healthy baby</th>
<th>Adult</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dose#1</td>
<td>In 12 hours after birth + HBIG</td>
<td>In 2 months after birth</td>
<td>anytime</td>
</tr>
<tr>
<td>Dose#2</td>
<td>1-2 months after 1\textsuperscript{st} injection</td>
<td>1 month after 1\textsuperscript{st} injection</td>
<td>1 month after 1\textsuperscript{st} injection</td>
</tr>
<tr>
<td>Dose#3</td>
<td>6 months after 1\textsuperscript{st} injection</td>
<td>6 months after 1\textsuperscript{st} injection</td>
<td>6 months after 1\textsuperscript{st} injection</td>
</tr>
</tbody>
</table>
There are three types of viral particles in HBV-infected sera.

- **HBV virion (Dane particle)**: Filamentous spherical particle
- **Incomplete particles**: Subviral particle containing only envelope + HBsAg
- **Virion**: Contains viral DNA and core

$10^3$- to $10^6$-fold excess over Dane particles
Replication cycle of hepadnavirus
**Hepatitis C virus (HCV)**

- **Family** *Flaviviridae*
- **Genus** *Hepacivirus*
- Enveloped virus (40-50 nm)
- Icosahedral capsid
- A (+) ssRNA genome
- 7 genotypes and > 71 subtypes
- Incubation period: 2-26 weeks
  (average: 6-7 weeks)
Transmission of HCV infection

- HCV is predominantly a blood-borne virus, very low risk of sexual or vertical transmission
  - Intravenous drug users
  - Transfusion
  - Hemodialysis

HCV infection

- About 80% of HCV-infected individuals have no signs or symptoms.
- Between 55% and 85% of infected persons experience a chronic infection.
- Chronic infection can lead to cirrhosis of the liver and hepatocellular carcinoma in 5% to 20% of persons.
Clinical symptoms and immune responses to HCV infection

A: Acute Hepatitis C

- ALT (U/L)
- HCV RNA
- Anti-HCV
- Symptoms

B: Chronic Hepatitis C

- ALT (U/L)
- HCV RNA
- Anti-HCV
- Symptoms
Laboratory diagnosis of HCV infection

- Detection of anti-HCV antibodies by ELISA
- Detection of viral genome (RNA) by RT-PCR
- Identification of HCV genotypes (RNA) by RT-PCR → therapy

Prevention and control

- No vaccine available
- Chronic infection: Pegylated interferon and ribavirin
Hepatitis delta virus (HDV)

- Enveloped virus
- (-) circular ssRNA virus with nucleocapsid protein (δAg)
- Defective virus
  (require co-infection with HBV for virion assembly but not for replication)
- 8 genotypes
- Transmission: similar to HBV infection
# Hepatitis Delta virus (HDV)

<table>
<thead>
<tr>
<th>HDV/HBV</th>
<th>Incubation period</th>
<th>Acute infection</th>
<th>Chronic infection</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Coinfection</strong> (simultaneous onset of infection)</td>
<td>6 weeks – 6 months</td>
<td><strong>Majority: acute infection</strong> anti-HBc IgM + anti-HD IgM</td>
<td>5 %</td>
</tr>
<tr>
<td><strong>Super Infection</strong> (HBV chronic carrier infected with HDV)</td>
<td>≤ 3 weeks</td>
<td><strong>Severe</strong> anti-HBc IgG + anti-HD IgM</td>
<td>75% (chronic hepatitis --&gt; cirrhosis)</td>
</tr>
</tbody>
</table>

**Laboratory diagnosis:** anti-HDV IgM  
**Prevention:** HBV vaccine  
**Therapy:** Pegylated interferon-alpha
Hepatitis E virus (HEV)

- Family *Hepeviridae*
- Genus *Hepevirus*
- A (+) ssRNA genome
- Non-enveloped virus
- Icosahedral capsid
- 1 serotype
- Fecal-oral transmission
- Incubation period: 2-9 weeks
- Asymptomatic infection in children
- High mortality rate in pregnancy women (10-20%)
- Anti-HEV IgM: Diagnostic marker

(E = enteric, eat)
# Viral Hepatitis in Humans

<table>
<thead>
<tr>
<th>Virus</th>
<th>Family/genus</th>
<th>Genome</th>
<th>Transmission</th>
<th>Chronicity?</th>
</tr>
</thead>
<tbody>
<tr>
<td>HAV</td>
<td>Picornaviridae/ Hepatovirus</td>
<td>(+)ssRNA Naked</td>
<td>Fecal-oral</td>
<td>Very little</td>
</tr>
<tr>
<td>HBV</td>
<td>Hepadnaviridae/ Orthohepadnovirus</td>
<td>dsDNA (RT) Enveloped</td>
<td>Parenteral, sexual, vertical</td>
<td>10% of adults, 90% of neonates</td>
</tr>
<tr>
<td>HCV</td>
<td>Flaviviridae/ Hepacivirus</td>
<td>(+)ssRNA Enveloped</td>
<td>Parenteral, sexual, vertical</td>
<td>&gt;50%</td>
</tr>
<tr>
<td>HDV</td>
<td>Deltavirus</td>
<td>Circular ssRNA Enveloped</td>
<td>Parenteral, (sexual, vertical?)</td>
<td>Yes</td>
</tr>
<tr>
<td>HEV</td>
<td>Hepeviridae/ Hepevirus</td>
<td>(+)ssRNA Naked</td>
<td>Fecal-oral</td>
<td>No</td>
</tr>
</tbody>
</table>
Laboratory diagnosis of acute viral hepatitis

Hepatitis A: Anti-HAV IgM (HAV vaccine)
Hepatitis B: Anti-HBc IgM (HBV vaccine)
Hepatitis C: Anti-HCV, Viral genome
Hepatitis D: Anti-HDV IgM (HBV vaccine)
Hepatitis E: Anti-HEV IgM
Good Luck for your FMS1 exam

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