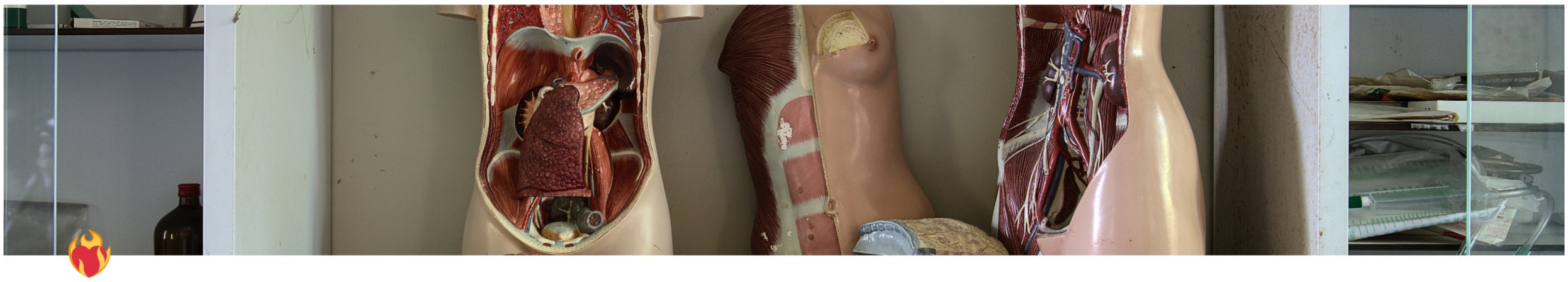


M16 - Viral hepatitis & HIV/AIDS

3 more properties

Learning Objectives

- Basic virology of the hepatitis viruses (hepatitis A to E) and human immunodeficiency viruses (HIV).
- Epidemiology and transmission of the different types of viral hepatitis and HIV infection.
- Clinical courses of viral hepatitis and HIV infection.
- HIV infection versus AIDS; AIDS-defining illnesses.
- Principles of diagnosis and management of viral hepatitis and HIV infection.
- Principles of prevention of viral hepatitis and HIV infection.

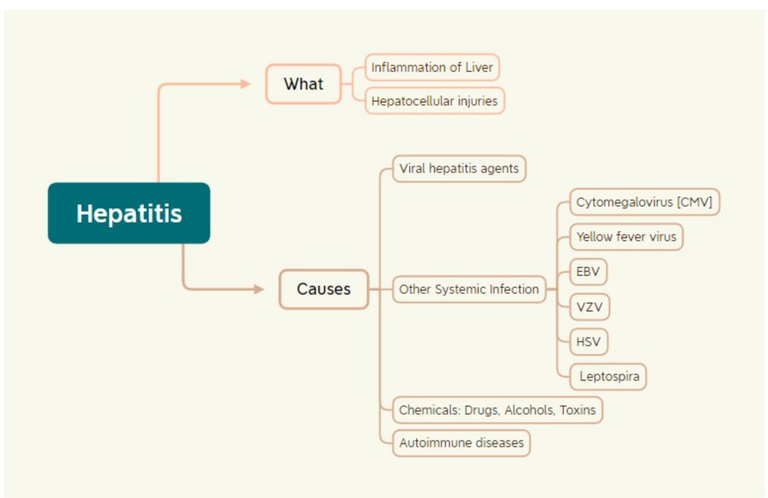
Clinical Precaution: HIV v.s. Viral Hepatitis

Risk of transmission after needlestick injury:

HBeAg+	30%
HBeAg-	1-6%
HCV	1.8%
HIV	0.3%

Introduction to the Hepatitis

Characteristic of Hepatitis - Not State in Learning Objectives



- "Classical" viral hepatitis agents
  - Hepatitis A, B, C, D, E viruses
- Hepatotropic viruses (hepatitis viruses A to E) that have a specific affinity for the liver
- Liver damage occurring as a result of other systemic infections

Yellow fever virus	Cytomegalovirus (CMV)	Epstein-Barr virus (EBV)
Varicella-zoster virus (VZV)	Herpes simplex virus (HSV)	Leptospira

- Chemicals, drugs, alcohols, toxins
- Autoimmune diseases

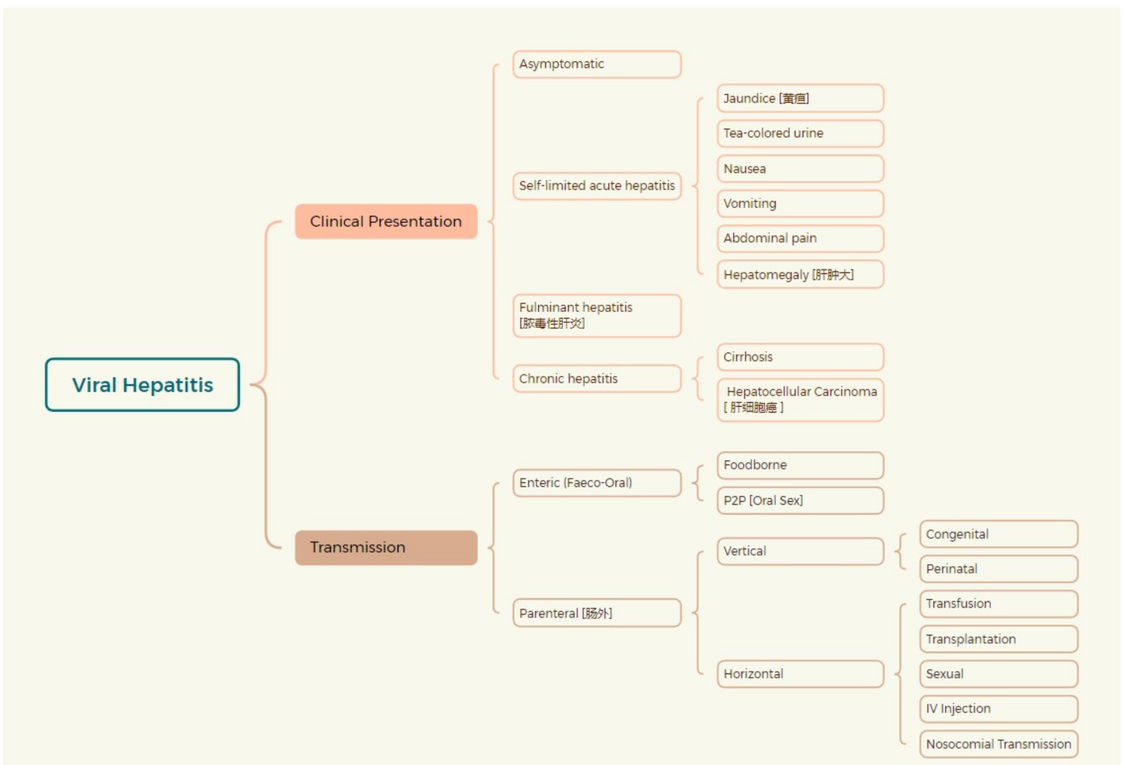
More about Viral Hepatitis

Introduction to Viral Hepatitis - Text Version

Clinical Presentation	
Asymptomatic	No Symptoms
Self-limited acute hepatitis	Jaundice [黄疸]
	Tea-colored urine
	Nausea
	Vomiting
	Abdominal pain
	Hepatomegaly [肝肿大]
Fulminant hepatitis	[脓毒性肝炎]
Chronic hepatitis	Cirrhosis
	Hepatocellular Carcinoma [肝细胞癌]

Transmission	
Enteric (Faeco-Oral)	Foodborne
	P2P [Oral Sex]
Parenteral [肠外]	
Vertical	Congenital
	Perinatal
Horizontal	Transfusion
	Transplantation
	Sexual
	IV Injection
	Nosocomial Transmission [Exp.: HAV]

> Remarks:
> - Fulminant hepatitis [acute liver failure] is severe and rapidly progressing
>   - Massive liver cell death and failure.



Diagnosis

- Serology
  - Commonest method for diagnosis
  - Antibody detection
- Clinical suspicion
  - Clinical manifestations
  - Epidemiology
- Nucleic acid amplification
  - PCR/RT-PCR of feces, blood, etc. for viral DNA/RNA

Treatment - Supportive

- Supportive treatment

	HBV	HCV [DAA use > 1 Antiviral]	HDV	HEV	HBV + HDV [Fulminant liver failure]
Treatment	**Entecavir**	Interferon-alpha + ribavirin	Interferon-alpha	Ribavirin	Liver transplantation
	Tenofovir	**Direct-acting antivirals (DAA)**	bulevirtide		
	Lamivudine	sofosbuvir			
	Adefovir	simeprevir			
	Telbivudine	ledipasvir			

Prevention of Viral Hepatitis

> 1. Interruption of the routes of transmission.
> 2. Vaccines
> 3. Post-exposure prophylaxis - 接触后预防

Comparison of Viral Hepatitis Vaccines

Vaccine	Type
Hepatitis A vaccine	Inactivated vaccine
Hepatitis B vaccine	Plasma-derived → Recombinant HBsAg
Hepatitis C vaccine	Recombinant viral capsid protein

More about Post-exposure prophylaxis

- HAV & HBV: **Vaccination [Given when unvaccinated before] + Ig Treatment**
- HCV: Monitor recipient at **baseline**, **6 weeks**, and **6 months** after exposure.
  - Liver function
  - Serology (antibody seroconversion)
  - RT-PCR for HCV RNA

Characteristic of Viral Hepatitis

Text version - Characteristic of Viral Hepatitis

Type	Family	Genus	Characteristic
HAV	Picornaviridae	Hepatovirus	Non-enveloped, ssRNA
HBV	Hepadnaviridae	Orthohepadnavirus	Enveloped, dsDNA
HDV	—	Deltavirus	ssRNA(-)
HCV	Flaviviridae	Hepacivirus	Enveloped, ssRNA (+)
HEV	Hepeviridae	Hepevirus	ssRNA (+)

💡 Hepatitis A

- Environment

Destroy	Stable
Heat [100℃] - 5mins	Low pH
NaOCl	Heat [-60℃]
Ultraviolet Irradiation	
Food [85 ℃] w/ 1mins	

💡 Hepatitis B - 3 Morphological Form

Morphological Form	Size	Composition
42 nm Dane particles	-	HBcAg in the core, HBsAg in the envelope
22 nm diameter tubular	-	Most common, made up of HBsAg
22 nm spherical particles	Length: >200 nm	made up of HBsAg

💡 Hepatitis D [Delta Agent]

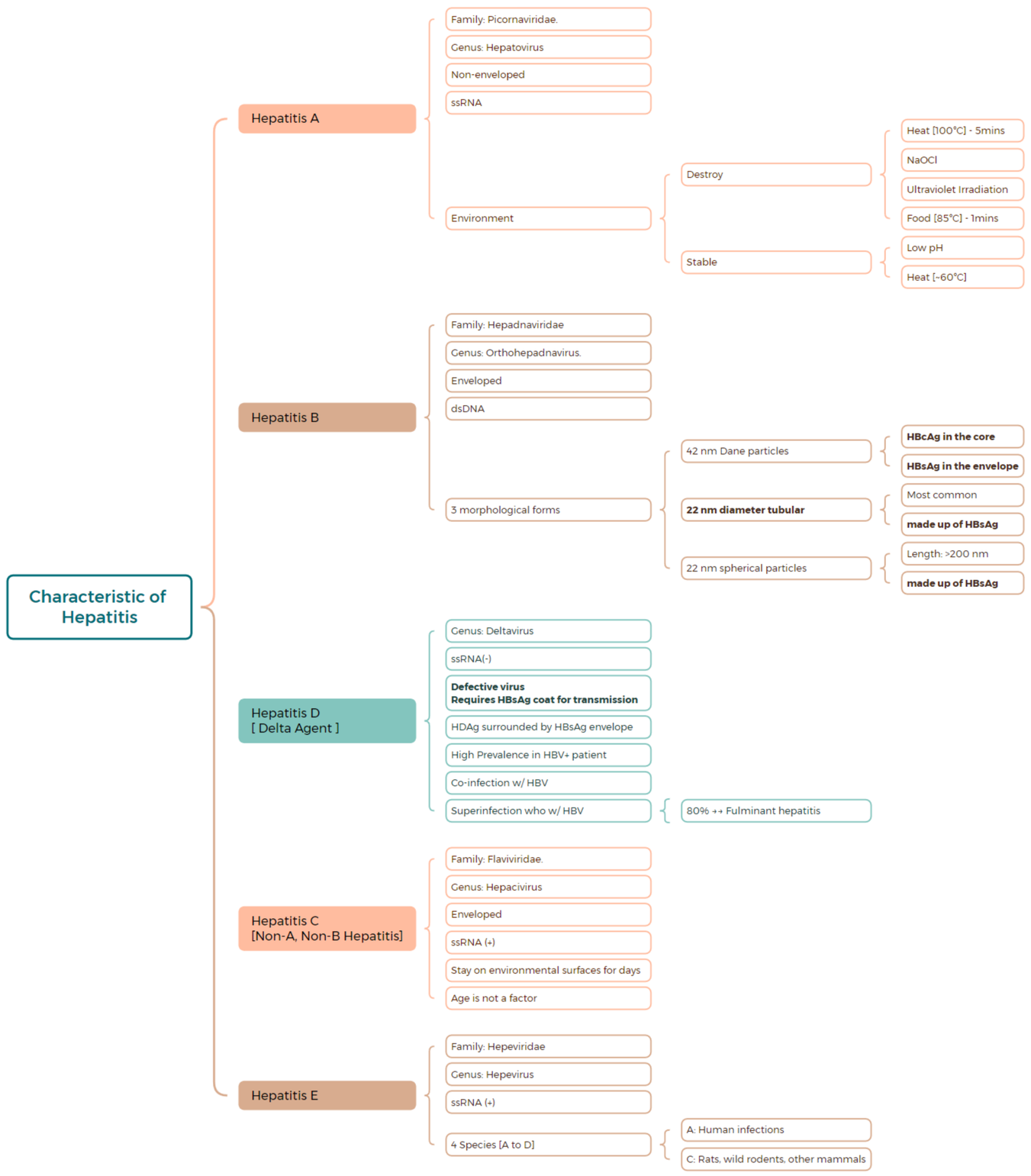
- **Defective virus - Requires HBsAg coat for transmission**
- HDAg surrounded by HBsAg envelope
- High Prevalence in HBV+ patient
- Co-infection w/ HBV
- Superinfection who w/ HBV
  - 80% → Fulminant hepatitis

💡 Hepatitis C [Non-A, Non-B Hepatitis]

- Stay on environmental surfaces for days
- Age is not a factor

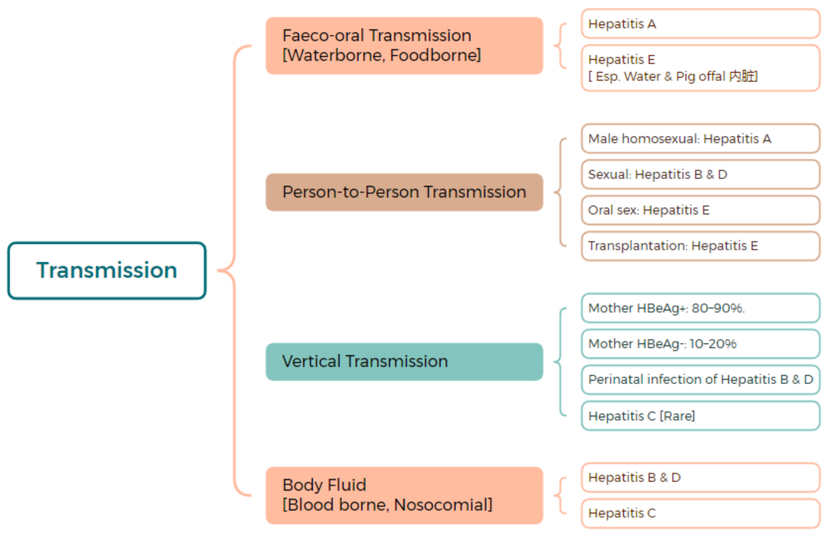
💡 Hepatitis E

- 4 Species [A to D]
  - A: Human infections
  - C: Rats, wild rodents, other mammals



Transmission of Viral Hepatitis

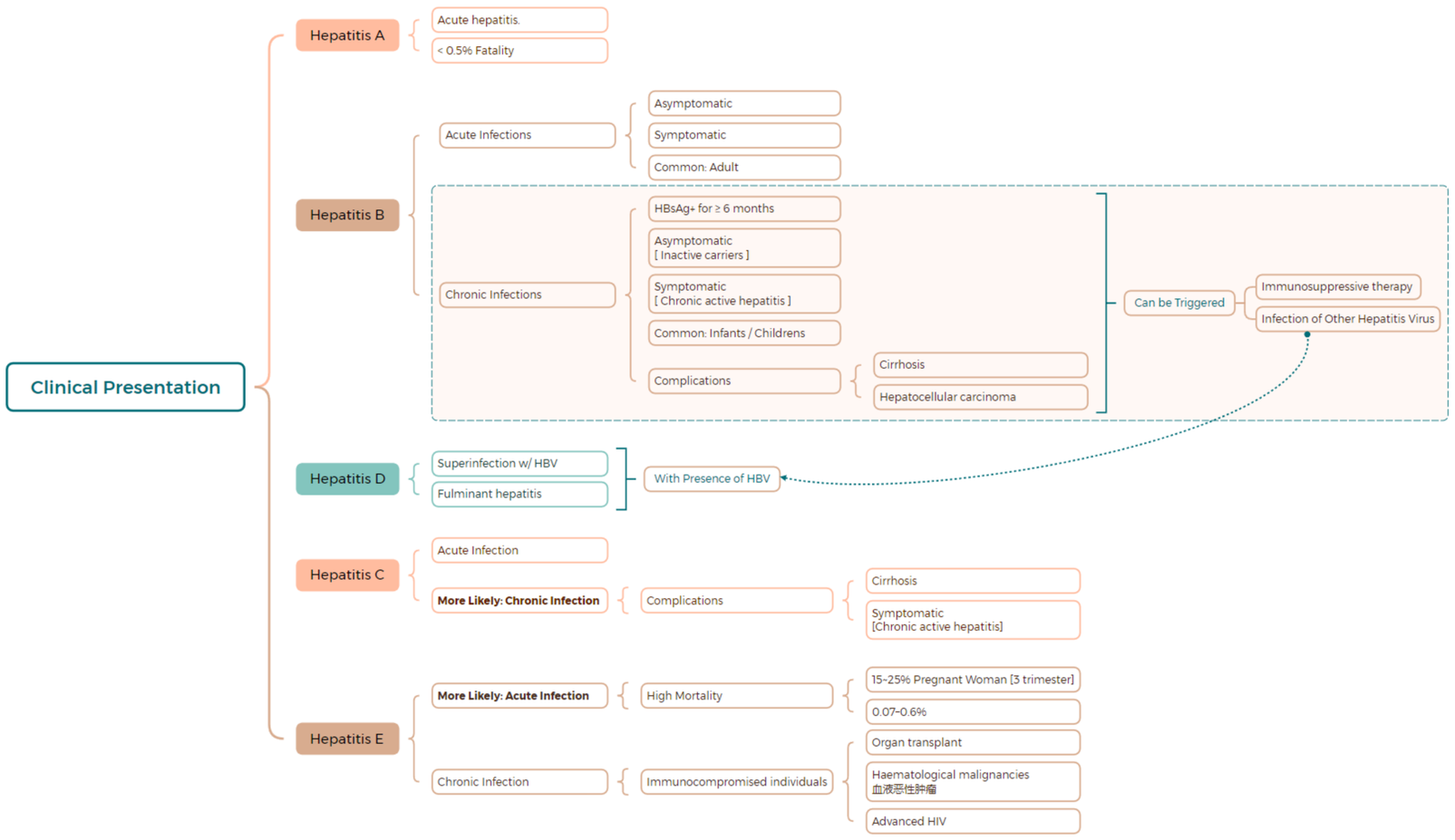
Faeco-oral Transmission [Waterborne, Foodborne]	Hepatitis A
	Hepatitis E [Esp. Water & Pig offal 内脏]
Person-to-Person Transmission	Male homosexual: Hepatitis A
	Sexual: Hepatitis B & D
	Oral sex: Hepatitis E
	Transplantation: Hepatitis E
Vertical Transmission	Mother HBeAg+: 80-90%.
	Mother HBeAg-: 10-20%
	Perinatal infection of Hepatitis B & D
	Hepatitis C [Rare]
Body Fluid [Blood borne, Nosocomial]	Hepatitis B & D
	Hepatitis C



> Remarks:
>
> - Infectivity of HBV depends on viral load and HBeAg status.

Clinical Presentation of Viral Hepatitis

- Hepatitis A
  - Acute hepatitis.
  - < 0.5% Fatality
- Hepatitis B
  - Acute Infections
    - Asymptomatic / Symptomatic
    - Common: Adult
  - Chronic Infections
    - HBsAg+ for ≥ 6 months
    - Asymptomatic - Inactive carriers
    - Symptomatic - Chronic active hepatitis
    - Common: Infants / Childrens
    - Complications
      - Cirrhosis
      - Hepatocellular carcinoma
- Hepatitis D
  - Superinfection w/ HBV
  - Fulminant hepatitis
- Hepatitis C
  - Acute Infection
  - More Likely: Chronic Infection
    - Complications
      - Cirrhosis
      - Symptomatic - [Chronic active hepatitis]
- Hepatitis E
  - More Likely: Acute Infection
    - High Mortality
      - 15~25% Pregnant Woman [3 trimester]
      - 0.07~0.6%
  - Chronic Infection
    - Immunocompromised individuals

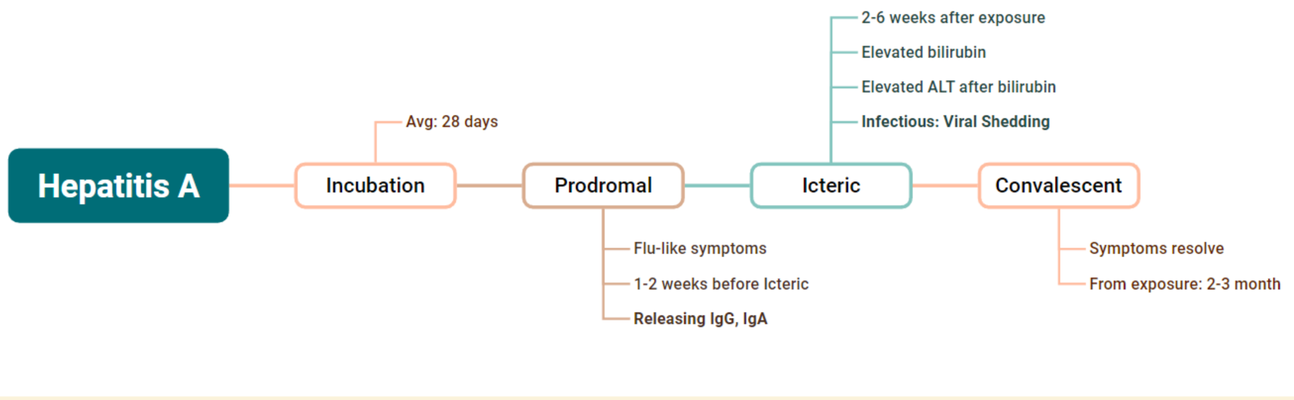


> Remarks:
> - Manifestation and course depends on age of infection.

Serology & Clinical Course of Hepatitis Virus

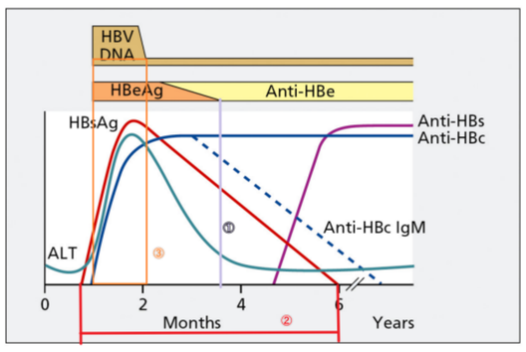
> Several Indicators in Hepatitis Serology:
>
> 1. ALT:
>   Enzymes in Liver cell. When the liver is injured or inflamed, **ALT is released into the bloodstream.**
> 2. Bilirubin:
>   Yellowish pigment that is **formed during the normal breakdown of red blood cells.**
>   Elevated bilirubin levels can indicate **liver dysfunction or damage.**

- Acute Hepatitis - HAV:
  - Incubation
    - **Avg: 28 days**
  - Prodromal
    - Flu-like symptoms
    - **1-2 weeks before Icteric**
    - Releasing IgG, IgA
  - Icteric
    - **2-6 weeks after exposure**
    - Elevated bilirubin & Elevated ALT after bilirubin
    - Infectious: Viral Shedding
  - Convalescent
    - **Symptoms resolve From exposure: 2-3 month**



Remarks: Anti-HAV IgM [Last For 3-6 Months]

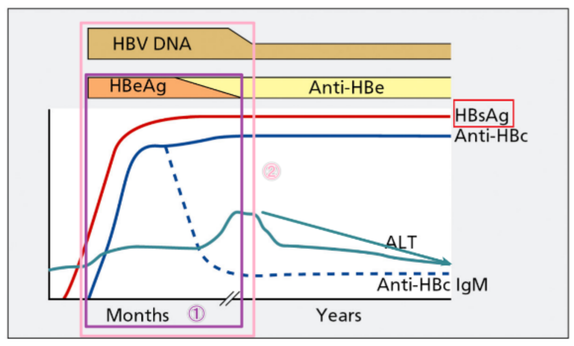
- Acute Hepatitis - HBV [**1 month Incubation Period**]:
  1. The Conc. HBeAg drops to zero → Stop high viral replication activity
     - From exposure: **around 4 months**
     - Symptoms are improved
  2. The duration of infection:
     - From Incubation Period → Fully Recovery [incl: ALT level]
  3. **Presence of Symptoms (1 Months):**
     - Prodromal Phase
     - Icteric Phase



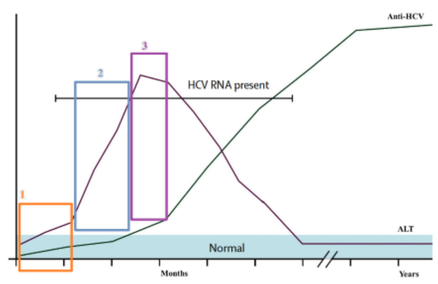
- Chronic Hepatitis -HBV [Fluctuates - Similar to other Chronic Viral Hepatitis]:

Clinical Course	DNA	ALT	Inflammation	Symptoms	HBsAg
Immune tolerant	High	Normal	No or minimal	None	High
Immune active	**Fluctuates**	**Elevated**	**Moderate/severe**	**Most symptomatic**	**High**
Inactive carrier	Low	Normal	Mild or none	None	High

  - Usually **ABSENCE OF Anti-HBs** → **HBsAg** are in High Lv.
  - In "**Immune active**":
    - **Anti-HBc IgM drops**
    - **Anti-HBc IgG raises**

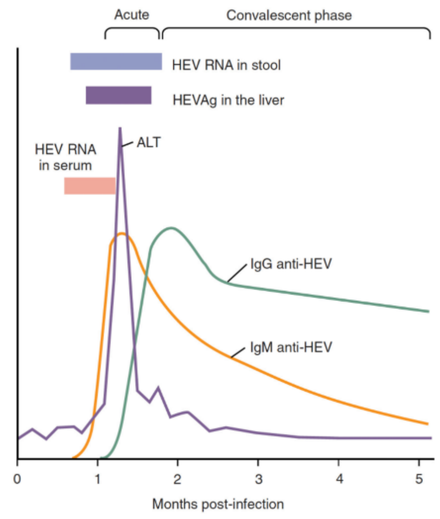


- Acute Hepatitis - HCV:
  1. **Incubation period - 6 Weeks**
  2. Prodromal phase - 5~6 Weeks
     - Non-specific flu-like symptoms
  3. Icteric phase - 1-3 Weeks
     - Jaundice
  4. **Full Recovery - 6 Months**



Acute Hepatitis - HEV:

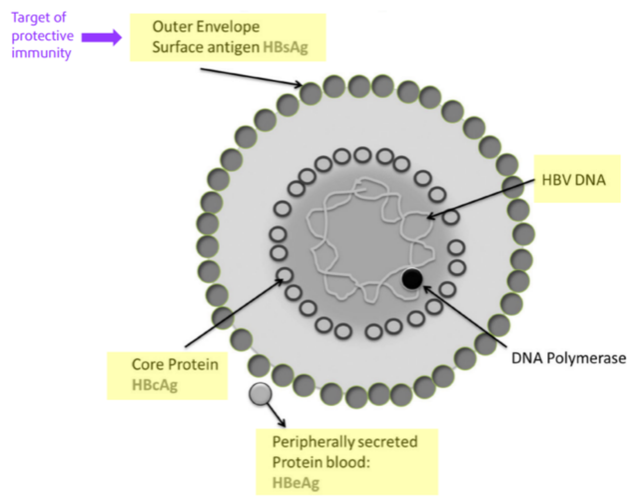
1. **Incubation period - 2~3 Weeks**
2. Prodromal phase - 3 Weeks
   - Non-specific flu-like symptoms
3. Icteric Phase -3 Weeks
   - Jaundice
4. **Full Recovery - 10 Weeks**



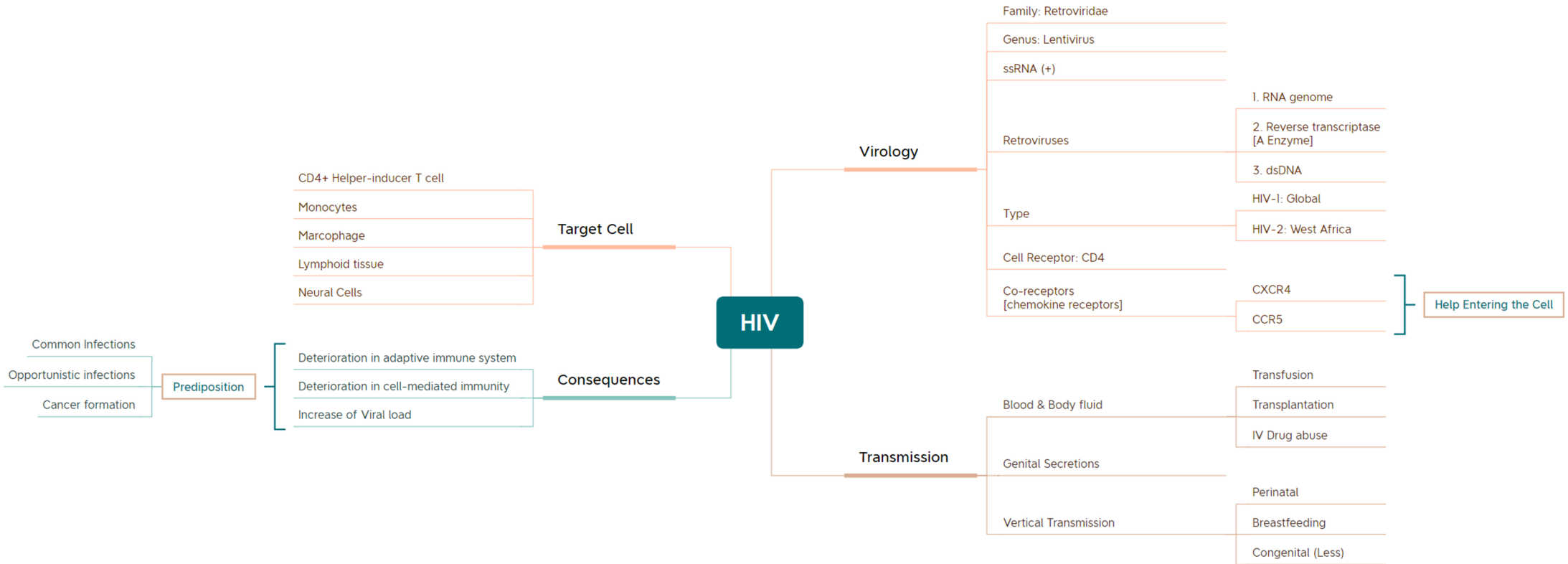
More about HBV antigens & Serological diagnosis

HBsAg	Total anti-HBc	IgM anti-HBc	Anti-HBs	Interpretation
–	–	–	–	Never infected or vaccinated; susceptible.
+	–	–	–	Early acute infection; transient (up to 18–21 days) after vaccination.
+	+	+	–	Acute infection.
–	+	+	–	Acute resolving infection.
–	+	–	+	Past infection; recovered; immune (protected).
+	+	–	–	Chronic infection.
–	+	–	–	False positive; past infection; low-level chronic infection; passive transfer to infant born to HBsAg-positive mother.
–	–	–	+	Response to vaccine; immune if antibody >10 mIU/mL; passive transfer after HBIG.

	Name	Description
HBcAg	Core antigen	Persist life-long → **Indicate history of infection.**
HBsAg	Surface antigen	On surface of viral envelope and circulating.
		Indicates active infection (acute and chronic).
		Antibodies (anti-HBs) are protective.
		The coat of HBsAg can facilitate HDV transmission
HBV DNA	DNA	**Indicates active infection (acute and chronic).**
		Quantification possible.
HBeAg	E antigen	A truncated derivative of HBcAg / NOT ALL patient has this antigen
		A marker of high viral replication activity → Correlates Infectivity.



Introduction to HIV / AIDS



▼ Text version - Introduction to HIV

Virology

- Family: Retroviridae
- Genus: Lentivirus
- ssRNA (+)
- Retroviruses
  - RNA genome + Reverse transcriptase → dsDNA
- Type
  - HIV-1: Global
  - HIV-2: West Africa
- Cell Receptor: CD4
- Co-receptors - [chemokine receptors]
  - CXCR4
  - CCR5

Transmission

- Blood & Body fluid
  - Transfusion
  - Transplantation
  - IV Drug abuse
- Genital Secretions
- Vertical Transmission
  - Perinatal
  - Breastfeeding
  - Congenital (Less)

Target Cell

- CD4+ Helper-inducer T cell
- Monocytes
- Marcophage
- Lymphoid tissue
- Neural Cells

Consequences

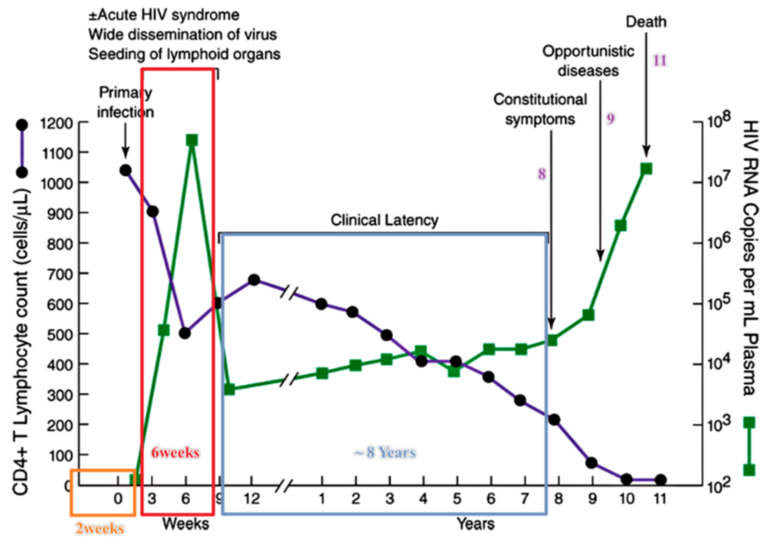
- Deterioration in adaptive immune system
- Deterioration in cell-mediated immunity
- Increase of Viral load

More about HIV - Clinical Course

1. **Incubation period - 2 Weeks**
2. **Primary infection - 6 Weeks**
   - Acute (primary) HIV syndrome

Fever	Skin rash
Pharyngitis	Myalgia
Enlarge lymph nodes	Arthralgia

3. Dissemination to lymphoid organs.
4. Latency (2–15 y: Median [8~10y]).
5. Elevated HIV expression.
6. Clinical disease.
7. Death.



More about AIDS & AIDS-defining illness

AIDS

> An advanced stage of HIV infection
> **Immune system is severely compromised.**

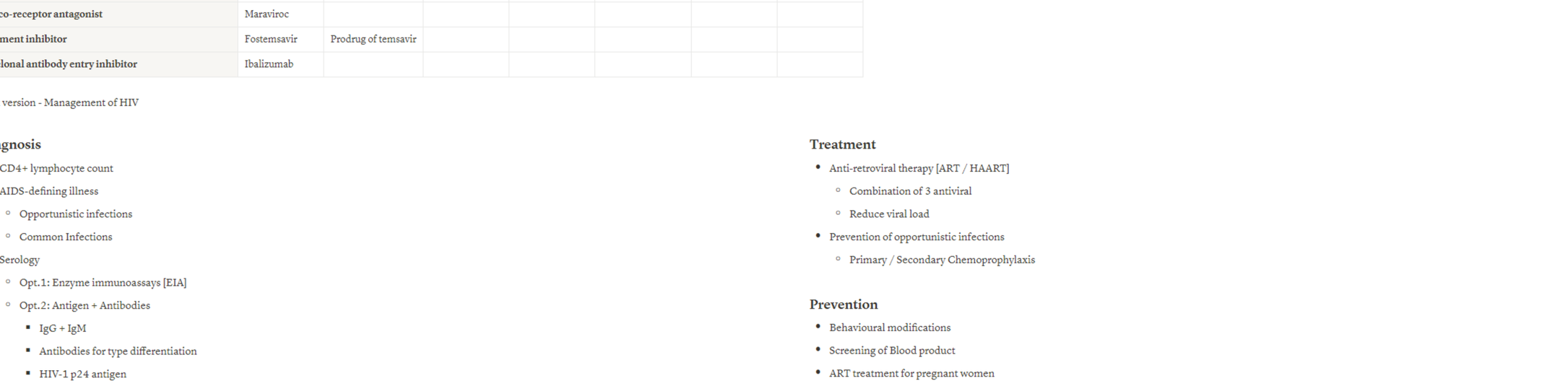
- Without treatment, appears 8–10 years later
- Diagnosis: Documented HIV infection + presence of AIDS-defining illness.
  - CD4+ cell count <200/μL

AIDS-defining illness

> Most of them are fungi - Molds, Yeast, Parasites

- Commonest ADI in Hong Kong
  - **Pneumocystis jirovecii pneumonia**
  - Tuberculosis
  - Other fungal infections
  - Talaromycosis - Commonest ADI in SEA
    - Penicilliosis
    - Talaromyces marneffei / Penicillium marneffei
  - Cytomegalovirus disease [CMV]

Management of HIV Infection - Diagnosis, Treatment & Prevention



Anti-retroviral agents for ART

Groups	Examples						
Nucleoside reverse transcriptase inhibitors (NRTI)	Abacavir	Didanosine	Emtricitabine	Lamivudine	Stavudine	Zidovudine	
Nucleotide reverse transcriptase inhibitors (NtRTI)	Tenofovir						
Non-nucleoside reverse transcriptase inhibitors (NNRTI)	Efavirenz	Etravirine	Rilpivirine	Nevirapine			
Protease inhibitors (PI)	Atazanavir	Darunavir	Saquinavir	Nelfinavir	Lopinavir/ritonavir	Indinavir	Fosamprenavir
Integrase inhibitors (INSTI)	Dolutegravir	Cabotegravir	Bictegravir	Raltegravir	Elvitegravir		
Fusion inhibitor (FI)	Enfuvirtide						
CCR5 co-receptor antagonist	Maraviroc						
Attachment inhibitor	Fostemsavir	Prodrug of temsavir					
Monoclonal antibody entry inhibitor	Ibalizumab						

▼ Text version - Management of HIV

Diagnosis

- CD4+ lymphocyte count
- AIDS-defining illness
  - Opportunistic infections
  - Common Infections
- Serology
  - Opt.1: Enzyme immunoassays [EIA]
  - Opt.2: Antigen + Antibodies
    - IgG + IgM
    - Antibodies for type differentiation
    - HIV-1 p24 antigen
- Nucleic acid amplification
  - Quantification of viral load
  - Detection of resistance to antivirals

Treatment

- Anti-retroviral therapy [ART / HAART]
  - Combination of 3 antiviral
  - Reduce viral load
- Prevention of opportunistic infections
  - Primary / Secondary Chemoprophylaxis

Prevention

- Behavioural modifications
- Screening of Blood product
- ART treatment for pregnant women
- Post-exposure prophylaxis
- Pre-exposure prophylaxis