
بسم الله الرحمن الرحیم
به نام خدای بخشاینده مهربان
In the name of Allah the Compassionate the Merciful

VIRAL HEPATITIS

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VIRAL HEPATITIS

- Hepatitis
  - Liver inflammaion
- Caused by **Viral** Iefction
  - ACUTE
  - CHRONIC
- Five important causes
  - Hepatitis A B C D E
- Other agents, such as **CMV**, **EBV**, **adenovirus**, and the **hemorrhagic fever viruses**, produce hepatitis as part of a systemic or disseminated illness

Viral CAUSES

PRIMARY HEPATOTROPIC

- Hepatitis A virus
- Hepatitis B virus
- Hepatitis C virus
- Hepatitis D virus
- Hepatitis E virus

RNA VIRUSES

- **Enteroviruses**
- **Hemorrhagic fever viruses**
- **Human immunodeficiency virus**
- **Measles virus**
- **Rubella virus**
- **Syncytial giant-cell hepatitis**

DNA VIRUSES

- **Adenovirus**
- **Cytomegalovirus**
- **Epstein-Barr virus**
- **Erythrovirus (human parvovirus B-19)**
- **Herpes B virus**
- **Herpes simplex viruses 1 and 2**
- **Human herpesviruses 6, 7, and 8**
- **Varicella zoster virus**

- **ACUTE**
  - < 6 months
  - Nausea , Vomiting & RUQ Pain
  - ↑↑↑ Bilirubin :
    - Jaundice
    - Pruritus
    - Dark Urine
    - **Clay-Colored Stools**
  - **P/E** : HEPATOMEALY

- **CHRONIC**
  - > 6 months
  - Sometimes ASYMTOMATIC
  - Fever , fatigue & loss of appetite
  - Extrahepatic symptoms :
    - Arthralgias
    - Skin rashes
  - **P/E** :
    - liver may feel **Normal**
    - If cirrhosis
      - LOWER MARGIN can FEEL **IRRIGULAR**

DIGNOSIS

Dignostic w/u :	ACUTE	CHRONIC
CBC	THROMBOCYTOPENIA	THROMBOCYTOPENIA
AST , ALT	> 100 IU/L	↑ > 6MONTHS (USUALLY < 400IU/L)
Total Bilirubin (+Unconjugated)	↑ (>2mg/dl ➔ JAUNDICE)	↑
ALK phosphatase	↑	↑
PT	PROLONGED	PROLONGED
PTT	PROLONGED	PROLONGED
INR	**INR↑**	**INR↑**

PRIMARY HEPATOTROPIC

	HEPATITIS A	HEPATITIS B	HEPATITIS C	HEPATITIS E
TYPE	RNA	DNA	RNA	RNA
INCUBATION PERIOD	**30** DAYS	**90** DAYS	**40** DAYS	**50** DAYS
ROUTE	FECAL-ORAL	PARENTERAL	PARENTERAL	FECAL-ORAL
SEVERITY	MILD	SEVER	MILD	MILD
CHRONICTY	NONE	10%	50-60%	NONE

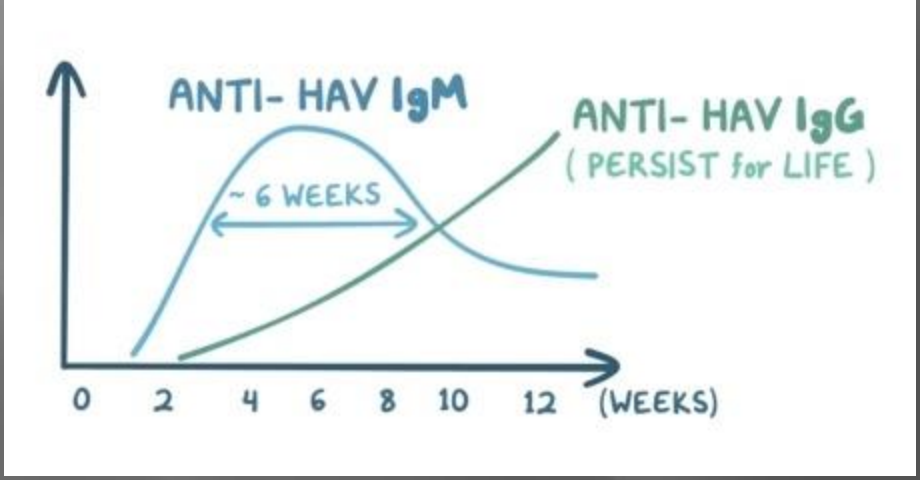
- **HAV** causes approximately **half of all cases** of viral hepatitis in the United States.

- new cases of viral hepatitis are caused
  - 70% to 80% by HAV
  - 5%to 30% by HBV
  - 5% to 15% by HCV

Hepatitis A

- ONLY causes ACUTE Hepatitis
- CONTAMINATED FOOD & WATER

- IgG ANTIBODIES with NO IgM :
- **VACCINATED** or **PRIOR INFECTION**



- **Symptomatic** → **≈ 30% of** infected < 6 yrs
- **Few** of these have **jaundice**.

- OLDER age → infection usually is **symptomatic**
- Typically Lasts **Several Weeks**
- **Jaundice** Occurring In **70%** Or More Of Cases

- Signs and symptoms typically last less than 2 months
- **10% to 15%** of symptomatic →

prolonged or **relapsing** disease lasting as long as **6 months**

- **Fulminant hepatitis** → if underlying liver disease

- Hepatits A usually **resolves** within a few weeks
  - **TREATMENT**
    - **FLUIDS**

- **PREVENTION**
  - **VACCINATION**
  - **2 DOSES**
  - **6 MONTHS APART**

Table 3.13. Recommendations for Preexposure Immunoprophylaxis of Hepatitis A Virus (HAV) for Travelers to Countries With High or Intermediate Hepatitis A Endemicity[a]

Age	Recommended Prophylaxis	Notes
Younger than 12 mo	IGIM	0.02 triL/kg[b] protects for up to 3 mo. For trips of 3 mo or longer, 0.06 mL/kgb should be given at departure and every 5 mo if exposure to HAV continues.
12 mo through 40 y	HepA vaccine	
41 y or older	HepA vaccine, with or without IGIM	If departure is in less than 2 wk, older adults, immunocompromised people, and people with chronic liver disease or other chronic medical conditions can receive IGIM with the initial dose of HepA vaccine to ensure optimal protection.

Table 3.14. Recommendations for Postexposure Immunoprophylaxis of Hepatitis A Virus (HAV)

Time Since Exposure	Age of Patient	Recommended Prophylaxis
2 wk or less	Younger than 12 mo	IGIM, 0.02 mL/kga
	12 mo through 40 y	HepA vaccineb
	41 y or older	IGIM, 0.02 mL/kg,a but HepA vaccineb can be used if IGIM is unavailablea
	People of any age who are immunocompromised, have chronic liver disease, or contraindication to vaccination	IGIM, 0.02 mL/kga
More than 2 wk	Younger than 12 mo	No prophylaxis
	12 mo or older	No prophylaxis, but HepA vaccine may be indicated for ongoing exposure"

Hepatitis E

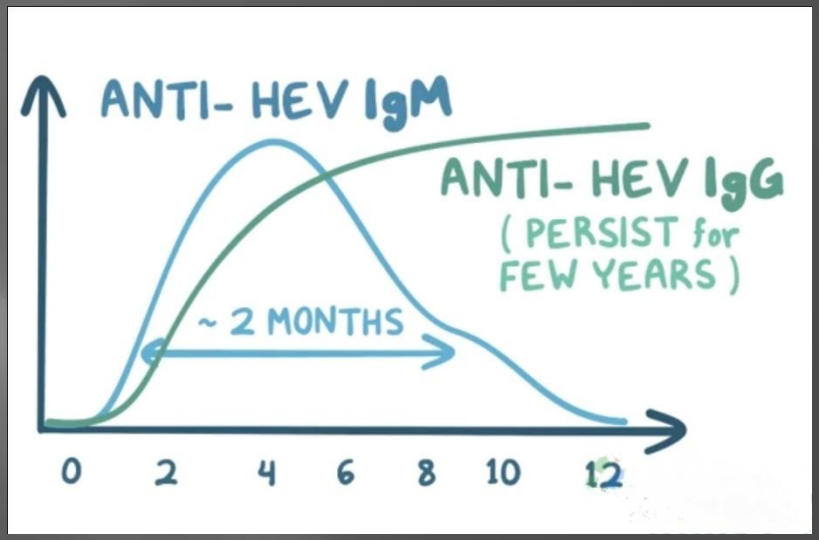
- **TYPICALLY ACUTE** Hepatitis
  - CHRONIC in IMMUNOCOMPROMISED
- CAUSED BY:
  - CONTAMINATED FOOD & WATER
  - MOTHER ➔ ➔ CHILD during BIRTH
- SYMPTOMS
  - USUALLY MILD
    - In PREGNANCY ➔ SEVER
      - ACUTE LIVER FAILURE

- **ACUTE** Hepatitis E

  HEV RNA ↑ ↑ ↑

  - check in
    - STOOL
    - SERUM
- **Chronic** Hepatitis E

  HEV RNA detected > 6 MON



TREATMENT

- **ACUTE Hepatitis E**
  - usually **resolves** within a few weeks
  - **TREATMENT**
    - **FLUIDS (in case of dehydration)**
    - **LIVER Tx** ► in acute liver failure
- **Chronic Hepatitis E**
  - In immuncompromised person
    - **↓↓↓ Immunosuppressants dose**
    - **RIBAVIRIN (12 week)**

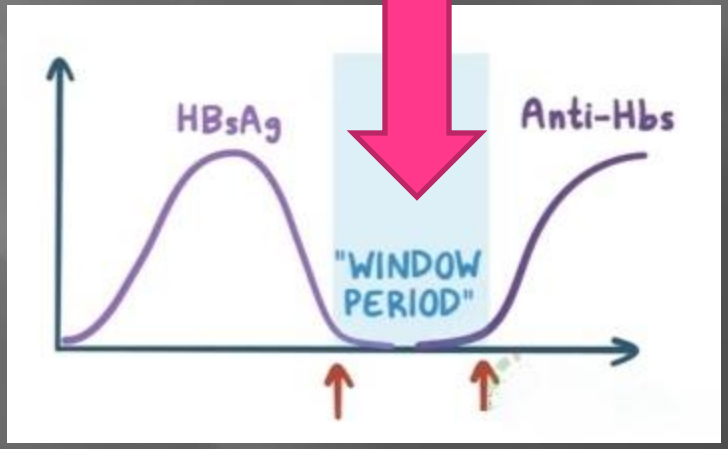
Hepatitis B

- **ACUTE** and **CHRONC** HEPATITIS
- CONTACT with
  - BLOOD ► needle or syringes
  - BODY FLUIDS ► unprotected sex , pregnant mother to newborn
- **Dx ► SEROLOGY**
  - **HBsAg**
  - **Anti-Hbs**

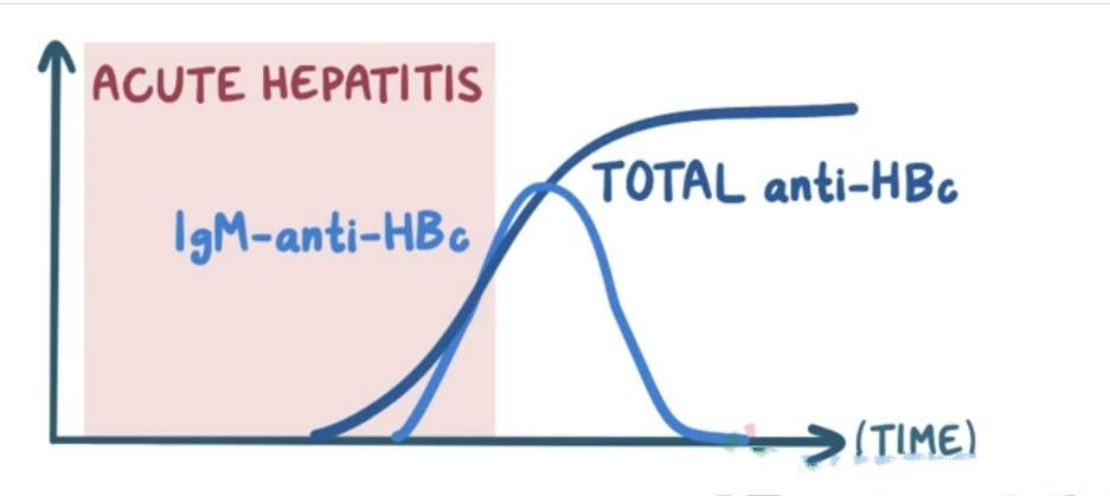
Usually if one is + the other is –

- **ANTIBODIES AGAINST HBcAg**
- **HBeAg**
- **HBV DNA PCR**

	NEVER EXPOSED	CLEARED INFECTION	ACUTE or CHRONC	IMMUNIZED or RECOVERED From naturnal inf (PROTECTED from Hepatitis B
HBsAg	–	–	+	–
Anti-Hbs	–	– NOT DETECTED	–	+

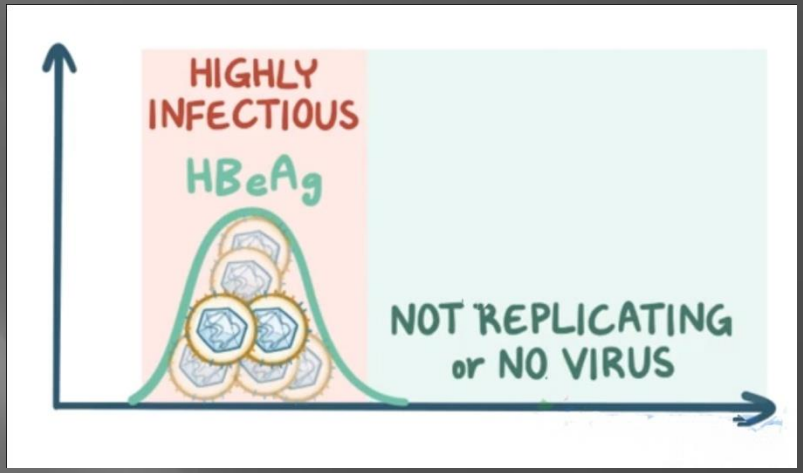


- **ANTIBODIES AGAINST HBcAg**
  - IgM-anti-HBcAg
  - TOTAL anti-HBcAg (Mostly are **IgG**)
- DON'T ↑ WHIT VACCINE



- **HBeAg**

Show REPILCATION OF VIRUS



- **HBV DNA PCR** **More info than HBeAg**
  - **↑↑↑ ► VIRUS REPLICATING**
  - **↓↓↓ ► VIRUS NOT REPLICATING**
  - **NOT DETECTED ► NO VIRUS**

	SUSEPTIBLE NOT IMMUNIZED	MMUNIZED	ACUTE HEPATITIS	WEEKS LATER	INFECTION UNDER CONTROL
HBsAg	–	–	+		
Anti-Hbs	–	+	–		
IgM-anti-HBcAg	–	–	+	–	
TOTAL anti-HBcAg	–	–	+	+ For Life	
HBeAg	–	–	+		–
HBV DNA PCR	–	–	+		↓↓↓

Anti-HBeAg APPEAR

CHRONC HEPATITIS	IMMUNE-TOLERANT	IMMUNE-ACTIVE HBeAg+	IMMUNE-ACTIVE HBeAg–	INACTIVE-CHRONIC HBV	CLEARED INFECTION
ALT & AST	NORMAL or ↑	↑↑	↑↑	NORMAL	
HBsAg	+	+	+	+ ⇢	–
Anti-Hbs	–	–	–	– ⇢	+
IgM-anti-HBcAg	–	–	–	–	–
TOTAL anti-HBcAg	+	+	+	+	+
HBeAg	+	+ ⇢	–	–	–
HBV DNA PCR	+ ⇢	↓ ⇢	↓↓ ⇢	↓↓↓	–

CIRRHOSIS

- Complication of **CHRONC HEPATITIS B**
- Can lead to **HEPATOCELLULAR CARCINOMA**
  - ↑ HBV DNA
  - ↑ HBsAg

  } ↑ **CIRRHOSIS**

- **Every 6 months**
  - **US**
  - **ALPHA FETOPRTEIN**

TREATMENT
for ACUTE HEPATITIS

- **MAINLY SUPPORTIVE**
  - FLUIDS
  - ANTIEMETIC MEDICATION (METOCLOPRAMIDE)

TREATMENT
for CHRONIC HEPATITIS

- In individual without **CIRRHOSIS**

HBV DNA (IU/ml)	> 20.000	> 20.000	2.000 – 20.000	< 2.000
ALT	> 2x UPPER LIMIT	≤ < 2x UPPER LIMIT	< 2x UPPER LIMIT	< 2x UPPER LIMIT
		MONITOR 3-6 months	MONITOR 1- 3 months	MONITOR 3-6 months

(6 months)

TREATMENT

TREATMENT for CHRONIC HEPATITIS

- **PEGYLATED INTERFERON** (pegIFN)
  - SC **Inj** 1/wk for 48 wk
- **NUCLEOSIDE or NUCLEOTIDE ANALOGUES**
  - **ENTACAVIR** or **TENOFOVIR**
  - **ORALLY** UNTIL HBeAg BECOMES NEGATIVE
  - **+** 1 YEAR AFTER

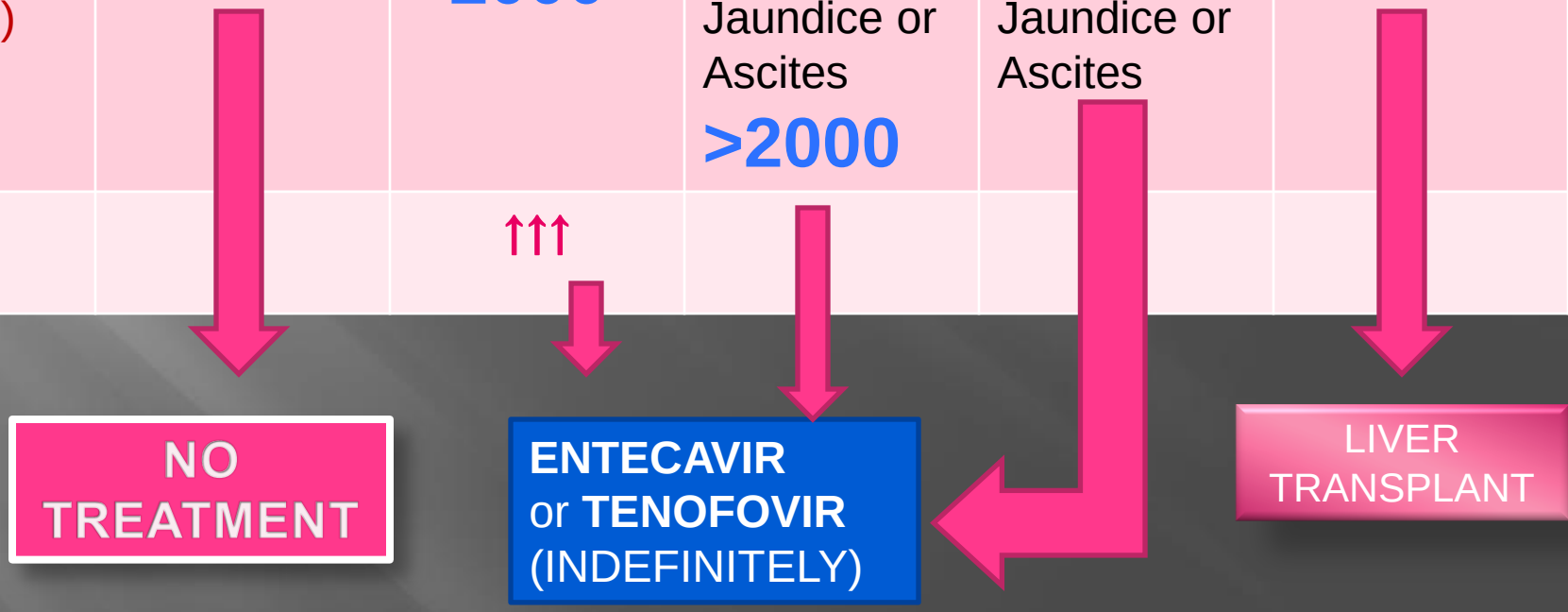
- IF …..
  - **HBeAg** **–**
  - **HBV DNA > 2000 (IU/ml)**
  - **ALT > 2x UPPER LIMIT**

} **TREATMEN RESTARTED**
pegIFN ….1 YEAR
NUC ANA …. SEVERAL YEARS

TREATMENT
for CHRONIC HEPATITIS

- with **CIRRHOSIS**

	COMPENSATED			DECOMPENSATED	
HBV DNA (IU/ml)	UNDETECTED	<2000	NO Jaundice or Ascites >2000	WITH Jaundice or Ascites	UNDETECTED
ALT		↑↑↑			



PREVENTION

- **VACCINATION**

- **NEWBORN**
  - After Birth
  - 1 mo
  - 6 mo
- **ADULT**
  - 2 doses , 1 month apart
- **HIGH RISKS**
  - Health care personel
  - Drug users
  - immunocompromised

Table 3.19. Recommendations for Hepatitis B Virus (HBV) Prophylaxis After Occupational Percutaneous or Mucosal Exposure to Blood or Body Fluidsa

Exposed Person	Treatment When Source Is HBsAg Positive	HBsAg Negative	Unknown or Not Tested
Unimmunized	Administer HBIGb (1 dose) and initiate HBV series	Initiate HBV series	Initiate HBV vaccine series
Previously immunized			
Known responder	No treatment	No treatment	No treatment
Known nonresponder		No treatment	If known high-risk source, treat as if source were HBsAg positive
After 3 doses:	HBIG: 1 dose and initiate reimmunization`		
After 6 doses	HBIG: 2 doses separated by 1 month		
Response unknown	Test exposed person for anti-HBs[d] If adequate, no treatment If inadequate, HBIG x 1 and vaccine booster	No treatment	Test exposed person for anti-HBsd • If adequate, no treatment • If inadequate, vaccine booster dosee

Table 3.20. Guidelines for Postexposure Prophylaxisa of People With Nonoccupational Exposuresb to Blood or Body Fluids That Contain Blood, by Exposure Type and Vaccination Status

Exposure	Treatment	
	Unvaccinated Person°	Previously Vaccinated Persona
HBsAg-positive source		
Percutaneous (eg, bite or needlestick) or mucosal exposure to HBsAg-positive blood or body fluids	Administer hepatitis B vaccine series and hepatitis B immune globulin (HBIG)	Administer hepatitis B vaccine booster dose
Sexual or needle-sharing contact of an HBsAg-positive person	Administer hepatitis B vaccine series and HBIG	Administer hepatitis B vaccine booster dose
Victim of sexual assault/abuse by a perpetrator who is HBsAg positive	Administer hepatitis B vaccine series and HBIG	Administer hepatitis B vaccine booster dose
Source with unknown HBsAg status		
Victim of sexual assault/abuse by a perpetrator with unknown HBsAg status	Administer hepatitis B vaccine series	No treatment
Percutaneous (eg, bite or needlestick) or mucosal exposure to potentially infectious blood or body fluids from a source with unknown HBsAg status	Administer hepatitis B vaccine series	No treatment
Sex or needle-sharing contact of person with unknown HBsAg status	Administer hepatitis B vaccine series	No treatment

HEPATITIS D

- **ACUTE** and **CHRONIC** HEPATITIS
- TRANSMITTED through **BLOOD** and **BODY FLUIDS**

- **ACUTE** HEPATITIS D ➔ **CHRONIC** HEPATIT
  - COINFECTION → SAME TIME
  - SUPERINFECTION → AFTER HEPATITIS B

CONFIRMATION of HEPATITIS D

TESTING for	ACUTE	CHRONIC
HDV IgM	↑↑↑	–
TOTAL HDV Ab	–	+
HDV RNA	+	+
HDAg	+ or –	–

TREATMENT
HEPATITIS D

- INITIATED if :
  - ↑↑↑ **HDV RNA**
  - ↑↑↑ **AST & ALT**

} **PEG-INF alfa-2 a**
PEG-INF alfa-2 b

- **PREVENTION**
  - **HBV VACCINATION**

HEPATITIS C

- **ACUTE** and **CHRONIC** HEPATITIS
- CONTACT with **BLOOD** and **BODY FLUIDS**

- **EXTRAHEPATIC MANIFESTATIONS**
  - **CRYOGLOBULINEMIA**
  - **MPGN**
  - **PORPHYRIA CUTANEA TARDA**

HEADACHES
CONFUSION

EROSIONS
BLISTERS

DIAGNOSIS

- **ANTI-HCV IgG**

- **HCV RNA**

- **HEPATITIS C Infection**
  - **ACUTE**
  - ↑↑↑ > 6 MONTHS ➔ **CHRONIC**

- **INFECTION CLEARED**

TREATMENT

- **- /+ COMPENSATED CIRRHOSIS**
  - **SOFOSBUVIR + VELPATASVIR or DACLATASVIR**
  - **GELECAPRAVIR + PIBRENTASVIR**

- **DECOMPENSATED CIRRHOSIS**
  - **SOFOSBUVIR + VELPATASVIR or DACLATASVIR**

Cytomegalovirus

- Gastroenteritis
- Pneumonitis
- mononucleosis-like syndrome
  - fever
  - Lymphadenopathy
  - lymphocytosis.

- ***CMV infection usually is asymptomatic***
- **Hepatitis** occurs
  - as part of these syndromes
  - but often is **silent** or **mild**
  - rarely is accompanied by **jaundice**

- **Granulomatous hepatitis** also may be associated with CMV.

- congenitally CMV infection
  - hepatosplenomegaly,
  - elevated aminotransferase levels,
  - conjugated hyperbilirubinemia.

- The **hepatitis** that neonates and infants experience with **postnatal** infection is **selflimited** and generally **resolves** within the first few months

- If hepatitis with **cholestasis** persists, other diseases such as extrahepatic biliary atresia should be considered.

- Solid organ and marrow **transplant recipients** and patients with **AIDS** and other **immunodeficiency states** may experience caused by primary or recurrent infection with CMV.
  - persistent fever,
  - malaise,
  - leukopenia, and
  - **Hepatitis**

- **Severe liver disease** can occur in **transplant recipients** and may be associated with GVHD or graft rejection.

- DIAGNOSIS **CMV-associated hepatitis**
  - clinically
  - supported by evidence of **high-level CMV viremia**

  and/or
  - demonstration of involvement of the end organ by **liver biopsy**.

- Treatment in immunocompromised hosts
  - **Ganciclovir**
  - **Valganciclovir**
  - **Foscarnet**
  - **Cidofovir**

- prophylaxis or preemptive therapy may prevent the development of severe CMV disease in transplant recipients
  - **Antiviral Agents**
  - **CMV Hyperimmune Globulin**

Epstein-Barr virus

- ***EBV infection can be***
  - ***asymptomatic but is***
  - ***a frequent*** cause of a **mononucleosis-like syndrome** with **mild hepatitis**.
- in **genetic X-linked predisposition**, a severe, often fatal lymphoproliferative syndrome with **prominent liver involvement** may develop

- Immune Response to EBV in **immunocompromised** hosts may be unusual

- Patients **with tumors** associated with EBV, such as lymphoma, may have hepatic involvement.

- **DIAGNOSIS**
  - Usually is **CLINICAL**
  - **HETEROPHILE** or “Monospot” test
  - **IgM** antibody to viral capsid antigen (**VCA**)
  - **PCR** should not be used IN acute mononucleosis.

- **Transplant recipients** also may be susceptible to **posttransplant lymphoproliferative disease** (**PTLD**), in which the **liver** may be involved.

- **DIAGNOSIS** of PTLD
  A. an **exponential increase in EBV DNA genome copies** in peripheral blood,
  B. generalized **ADENOPATHY**,
  C. visualization by **positron emission tomography**,
  D. the presence of histopathologic features on **BIOPSY**.

- **TREATMENT** options for PTLD
  1. Reducing Immunosuppression
  2. Rituximab (Anti-cd20 Monoclonal Antibody)
  3. Adoptive Immunotherapy
  4. Interferon-α
  5. Anti–interleukin-6 antibody

- Antiviral agents such as **acyclovir** or **foscarnet** should be used only as an adjunct therapy because they are less effective in the latent phase of PTLD.

Herpes Simplex Virus

- **TRANSIENT, SUBCLINICAL HEPATITIS**

may occur during acute mucocutaneous HSV disease,

- **FULMINANT HEPATITIS** **RARE** in a normal host
  - Except **PREGNANT WOMEN**
    - High mortality rates in both the mother and infant

NEONATES Term and Preterm

- At Risk For The Development Of Neonatal HSV Hepatitis
- As part of a **disseminated HSV disease**
  - viral sepsis–like syndrome,
  - coagulopathy,
  - abdominal distention with hepatomegaly and ascites,
  - pneumonitis with respiratory distress,
  - meningoencephalitis.

- **Skin lesions often are absent in this form of HSV disease.**
- Neonatal HSV hepatitis most often in **first 2 weeks of life**
- **AMINOTRANSFERASE** levels may initially be slightly elevated and then rise to be more than a thousand times higher than normal as disease progresses

TRANSPLANTS

Solid Organ
Bone Marrow
Stem Cell

- HSV infection
  - **DISSEMINATION** include **HEPATITIS**
  - within the first 3 weeks after Tx
  - Most are **REACTIVATION**
  - **ACYCLOVIR** therapy is recommended

Varicella-zoster virus

- **ONE-FOURTH** of healthy children experiencing varicella will have **SILENT HEPATITIS** with aminotransferase levels at least twice normal

- **Fulminant hepatitis** with varicella is **rare**
  - generally is seen in **immunocompromised hosts**

Human herpesviruses 6, 7, and 8

- May Involve The **LIVER**
- ESPECIALLY in **immunocompromised**
  - Reactivation
- Normal hosts **SILENT HEPATITIS**
  - mild elevation of aminotransferase levels.
- Rarely severe disseminated disease with FULMINANT HEPATITIS

Herpes B virus

herpesvirus simiae

- **MONKEYS**
- severe disease in humans
  - skin vesicles at the portal of entry
  - regional lymphadenitis
  - hemorrhagic encephalitis
- disseminate to the **LIVER** and lungs
  - **HEMORRHAGIC NECROSIS**, with a high mortality rate

Adenoviruses

- Disseminated disease with **HEPATITIS**
- **HEPATIC NECROSIS**
  - Immunocompetent
  - Immunocompromised Hosts
  - **NEONATES**
- **SEROTYPE 5** → severe hepatitis,
- **Hepatitis** is marked by **HEPATOMEGALY**
  - ↑↑↑ aminotransferases and bilirubin

Erythroviruses

Human Parvovirus B19

- **ERYTHEMA INFECTIOSUM** → fifth disease
- Liver involvement, often severe, may be seen in intrauterine infection with hydrops fetalis
- in patients with **APLASTIC ANEMIA**
  - Fulminant liver failure with massive hepatic necrosis
- Coinfection in Fulminant Liver Failure from the **Hepatotropic Viruses** have more
  - severe disease and high mortality
- in **Immunocompromised** hosts
  - Persistent infection

Enteroviruses

- **ECHOVIRUS 11**
  - in **NEONATES** with disseminated dx
  - Significant hepatic necrosis can occur

- **hepatomegaly**
- **thrombocytopenia**
- **viral sepsis syndrome**
- **aseptic meningoencephalitis**
- **myocarditis**
- **elevated aminotransfera**
- **serum bilirubin levels**

- COXSACKIEVIRUS B and ECHOVIRUSES 9 and 30
  - associated with fatal disease

Measles Virus

- Of all the paramyxoviruses, measles virus is associated most often with hepatitis
- **10 to 20 percent** of children
  - **SUBCLINICAL HEPATITIS**
- **Severe Disease** of the liver, lungs, and brain may occur in immunocompromised
- Rare reports of severe giant-cell hepatitis
  - Leading to liver failure

Rubella Virus

- **10%** of children with rubella may have subclinical hepatitis
  - transient elevation of aminotransferase levels

- **Congenital rubella syndrome**
  - Significant Liver Involvement,
  - Hepatomegaly
  - Jaundice is noted at birth

- **intrauterine growth re**
- **cataracts**
- **congenital**
- **heart disease**
- **thrombocytopenia**
- **purpura**
- **hearing loss**

Hemorrhagic Fever Viruses

- Diverse group of **RNA viruses**
  - ARENAVIRUSES →Lassa fever virus,
  - BUNYAVIRUSES → hantavirus,
  - FILOVIRUSES → Marburg and Ebola,
  - FLAVIVIRUSES → yellow fever virus and dengue

- **Liver involvement** with these viruses is a very common event
- Elevation of Aminotransferase levels to 500 IU/ mL occurs in almost every patient
- **Jaundice** is a significant component of yellow fever

fever
malaise
lethargy
headache
retroorbital pain
myalgia
conjunctivitis
rash
Intravascular coagulation
hemorrhage

THANKS FOR YOUR ATTENTION