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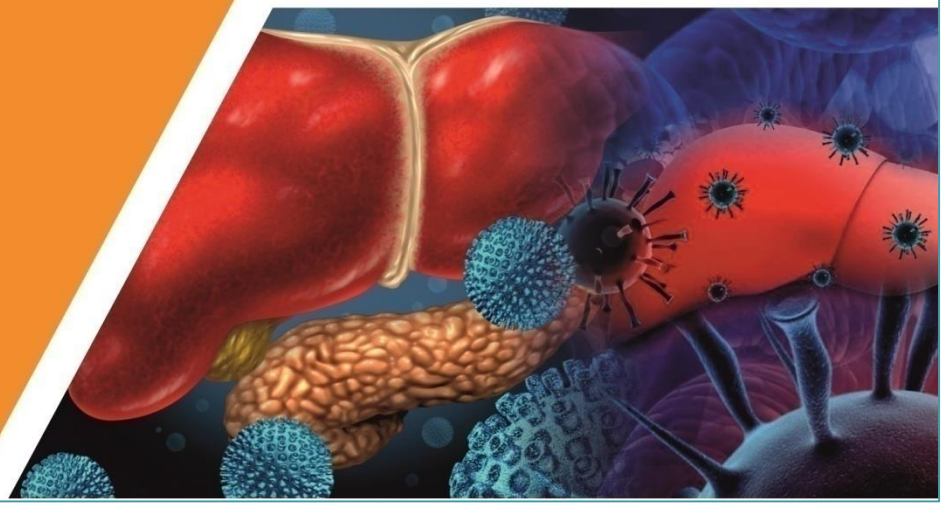
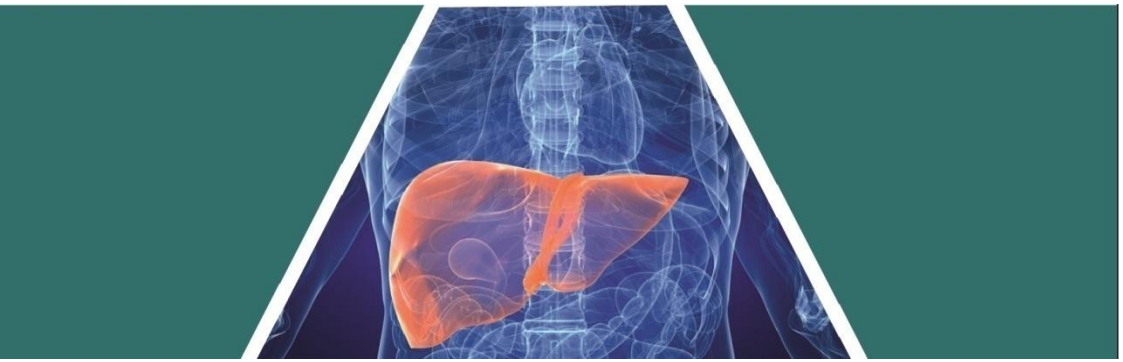
PROJECT PRAKASH

Pogrammed Approach to Knowledge and Sensitization on Hepatitis





HEPATITIS INDUCTION PROGRAM

FOR NURSES

CLINICAL FEATURES & DIAGNOSIS OF VIRAL HEPATITIS

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Introduction

Viral hepatitis often presents as subclinical infection.

- Hepatitis A and E present as acute hepatitis.
- Hepatitis B, C and D predispose to a chronic hepatitis and is related to liver cirrhosis and hepatic cancer
- Subclinical conditions are common.

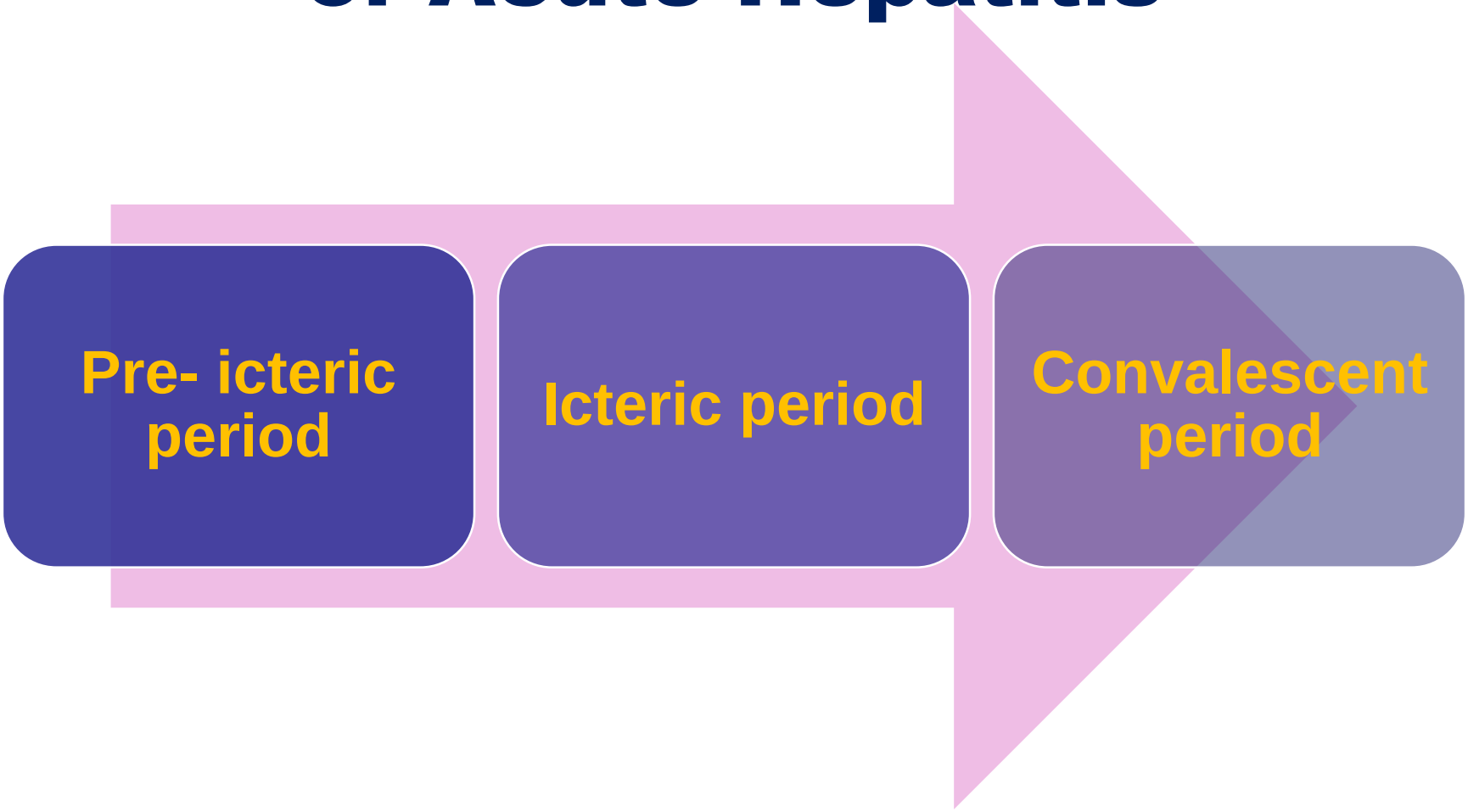
Classification

Acute hepatitis – lasts for less than 6 months

Chronic hepatitis – lasts longer than 6 months

Fulminant hepatitis – severe impairment or necrosis of liver cells and potential liver failure within 8 weeks of onset of hepatitis.

Clinical Features of Acute Hepatitis



Pre Icteric Period

Hep A, Hep E — Onset is abrupt with fever

Hep B, Hep C — onset is insidious.

Initial symptoms:

Loss of appetite, Nausea/vomiting, Lassitude, Abdominal pain, Diarrhea.

Pre Icteric Period

Fever, headache, upper respiratory tract symptoms are main manifestations

The Pre icteric period ends when the urine turns dark.

Duration of Pre Icteric period: 1 - 21 days with an average of 5-7 days

Icteric Period

- The urine colour darkens
- Jaundice appears on the skin and sclera within 2 weeks
- Pruritus may appear in about 1 week
- Liver palpable in 7%
- Spleen palpable in 20%
- The period lasts 2-6 weeks

Convalescence Period

- The jaundice disappears gradually, symptoms disappear.
- Liver and spleen retract
- Liver function returns to normal
- The period lasts 2 weeks to 4 months, average 1 month
- About 10% of Hep- B and 50% of Hep-C will become chronic hepatitis

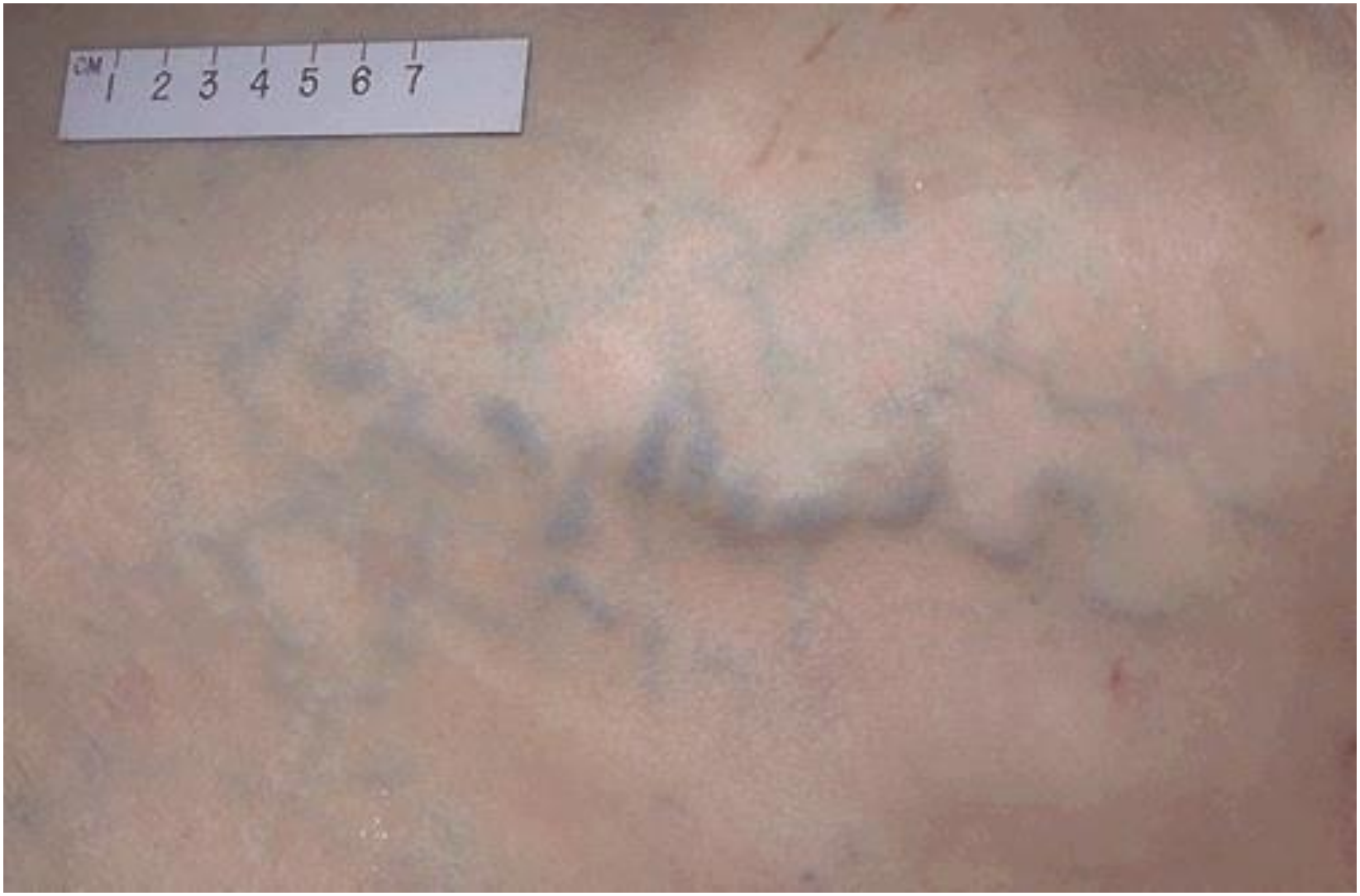
Clinical Features of Chronic Hepatitis

- Course is variable:
- Jaundice
- Hepatomegaly
- Tenderness right upper quadrant
- Liver edge firm and nodular on palpation
- Depression

Clinical Features of Chronic Hepatitis

In advanced stage

- Liver size reduced and not palpable
- Spleenomegaly
- Muscle wasting
- Ascites
- Peripheral edema
- Shortness of breath
- Decreased BP
- Bleeding tendencies – ecchymosis, hematemesis, malena



Collateral Veins in Abdomen In Portal Hypertension

Clinical Features in advanced disease

- Hepatic encephalopathy
- Hemorrhage–due to Deficiency of blood coagulating factors, DIC, thrombocytopenia
- Hepatorenal syndrome
- Hepato - pulmonary syndrome
- Ascites

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Fulminant Hepatitis

- Jaundice deepens rapidly
- Frequent Vomiting
- Obvious anorexia
- Hemorrhage
- Liver size shrunken
- Prothrombin time prolonged
- Ascites
- Acute renal failure
- Hepatic encephalopathy

Hepatitis A

Clinical Features of Hepatitis A

- Fever
- Fatigue
- Abdominal pain, diarrhoea
- Nausea
- Loss of appetite
- Jaundice and dark-coloured urine.

Diagnosis for Hepatitis A

- Liver Function Test
  - Aminotransferases (ALT and AST)- Raised
  - Total Bilirubin- Raised.

- Specific Diagnosis:
  - Anti HAV IgM-Raised in acute & recent course.
  - Anti HAV IgG - Raised in past infection.
  - Bile examination in stool and urine
  - Reverse Transcriptase Polymerase Chain Reaction
    (to detect Hepatitis A virus RNA)

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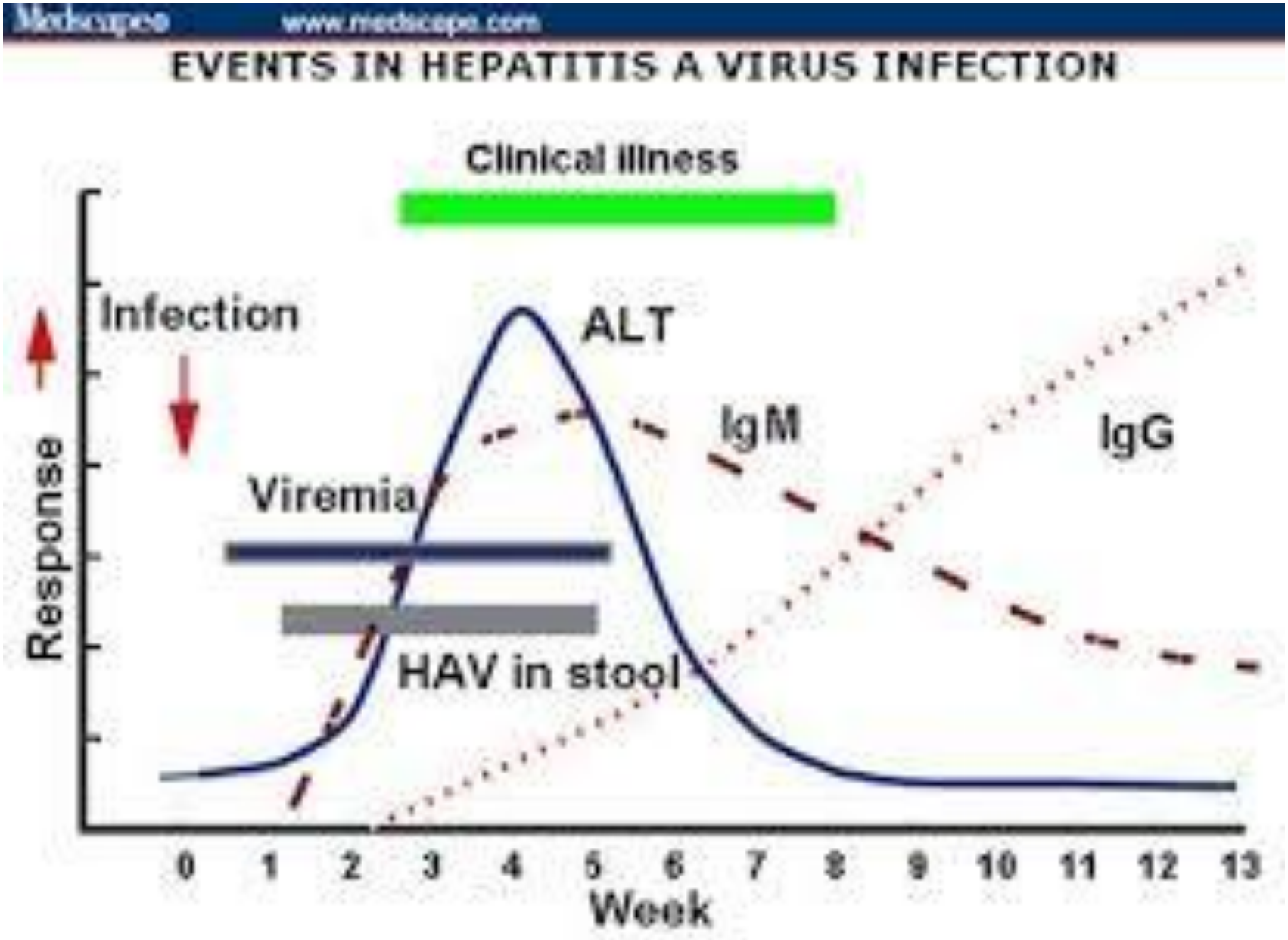
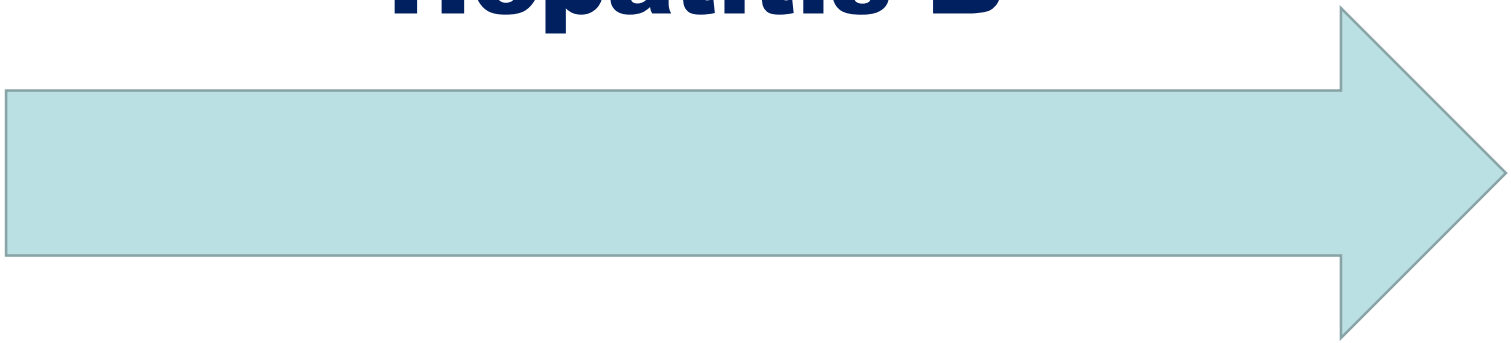
Liver test reference ranges

- Albumin: 3.3 to 5.0 g/dL (33 to 50 g/L)
- Alkaline phosphatase • Male: 45 to 115 international unit/L; • Female: 30 to 100 international unit/L
- Alanine aminotransferase (ALT): Male: 10 to 55 international unit/L; Female: 7 to 30 international unit/L
- Aspartate aminotransferase (AST): Male: 10 to 40 international unit/L; Female: 9 to 32 international unit/L
- Bilirubin, total: 0.0 to 1.0 mg/dL (0 to 17 micromol/L)
- Bilirubin, direct: 0.0 to 0.4 mg/dL (0 to 7 micromol/L)
- Gamma-glutamyl transpeptidase (GGT) • Male: 8 to 61 international unit/L; • Female: 5 to 36 international unit/L
- Prothrombin time (PT): 11.0 to 13.7 seconds

Liver test reference ranges will vary from laboratory to laboratory


Medscape
www.medscape.com
EVENTS IN HEPATITIS A VIRUS INFECTION
Clinical illness
Infection
ALT
IgM
IgG
Viremia
HAV in stool
Response
0 1 2 3 4 5 6 7 8 9 10 11 12 13
Week

Hepatitis B



Hepatitis B

- Hepatitis B Virus is a DNA virus.
- Infection causes both acute and chronic hepatitis
- Incubation period is 30 to 180 days

Hepatitis B

- More than 90% of healthy adults who are infected with the hepatitis B virus will recover.

- The likelihood that infection with the hepatitis B virus becomes chronic depends upon the age at which a person becomes infected.

Hepatitis B

- Children less than 6 years of age who become infected with the hepatitis B virus are the most likely to develop chronic infections

- 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.

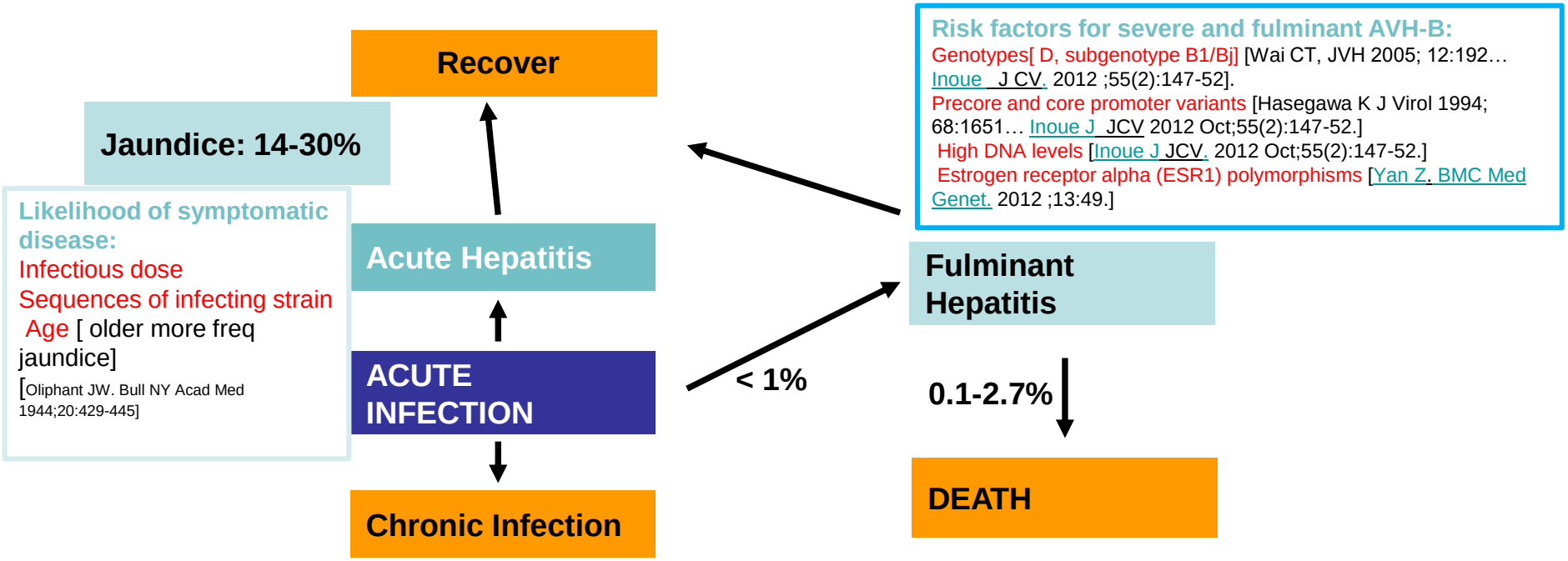
Hepatitis B

In adults:

- <5% of otherwise healthy adults who are infected will develop chronic infection

- 15–25% of adults who become chronically infected during childhood die from hepatitis B related liver cancer or cirrhosis.

Outcomes of Acute HBV Infection



Risk of chronic infection is Related to Age at Infection			
Outcome	**Neonates, %**	**Children, %**	**Adults, %**
Chronic carrier	90	20	< 5
Recover	10	80	> 95

Juszczyk J. Vaccine. 2000;18(suppl 1):S23-S25.

Progression to CHBV:
Genotype [A] [Ito K. Hepatology 2014;59(1):89-97]

High levels of HBsAg at 12 wk &
HBV DNA at 8 weeks [Yotsuyanagi H. Clinic Infect Dis. 2013;57(7):935-42].

Clinical features of hepatitis B

- Acute viral hepatitis B/ Acute liver failure
- Reactivation of CHBV infection including ACLF
- Chronic phase of HBV infection

Clinical features of hepatitis B

Symptoms of hepatitis B may not appear for up to 6 months.

Early symptoms include:

- Appetite loss
- Fatigue
- Low fever
- Muscle and joint aches
- Nausea and vomiting
- Jaundice

Clinical features of Hepatitis B

Acute HBV with Severe Presentation:

- Fatigue
- Jaundice
- Altered mental status- encephalopathy
- Ascites
- Bleeding tendencies

- **In patients with chronic HBV infection,** spontaneous flares of disease can result in fulminant hepatitis.

Diagnosis in Hepatitis B

Three types of antigens are seen in serum:

- HBsAg Surface antigen
- HBcAg Core antigen
- HBeAg antigen

Hepatitis B
Antigen – Antibody System

- HBsAg-- anti-HBs system:
  - HBsAg appears 1-2 weeks (late to 11-12 weeks) after exposure, persists for 1-6 weeks (even 5 months) in acute hepatitis B.
  - It persists for many years in chronic patients.
  - It is the marker of infectivity.
  - Anti-HBs appear after HBsAg disappear several weeks (or months)

Hepatitis B
Antigen – antibody system

HBcAg—anti-HBc system

- HBcAg can be found in the nuclei of liver cells, no free HBcAg in serum
- HBcAg is the marker of replication of HBV.
- Anti-HBc IgM is a marker of acute infection and acute attack of chronic infection of HBV.
- Anti-HBc IgG is the marker of past infection, high titer means low level replication of HBV

Hepatitis B
Antigen – antibody system

HBeAg—anti-HBe system

- HBeAg is a reliable indicator of active replication of HBV
- Anti-HBe is a marker of reduced infectivity.

Diagnosis in Hepatitis B

- Acute HBV infection is characterized by the presence of HBsAg and immunoglobulin M (IgM) antibody to the core antigen, HBcAg.

- During the initial phase of infection, patients are also seropositive for HBeAg.

Diagnosis in Hepatitis B

- Chronic infection is characterized by the persistence (>6 months) of HBsAg (with or without concurrent HBeAg).

- Persistence of HBsAg is the principal marker of risk for developing chronic liver disease and hepatocellullar carcinoma (HCC) later in life.

Diagnosis in Hepatitis B

- The presence of HBeAg indicates that the blood and body fluids of the infected individual are highly contagious

Initial assessment of persons with HBV prior to therapy-1

- **Assessment of the severity of liver disease:**

  History, physical examination, including for the presence of hepatomegaly and splenomegaly

  Measurement of ALT, AST, ALP and total bilirubin

  Full blood count, including platelet count and white cell count.

  Synthetic function: serum albumin and prothrombin time or INR

  Cross sectional imaging [US], Upper GI Endoscopy as needed

- **Assessment of the level of viral replication:**

  Quantification of serum HBV DNA *and HBeAg and anti-HBe serostatus.*

- **Assessment for the presence of comorbidities:**

  Coinfection with HIV, HCV or HDV

  Impaired glucose tolerance/Diabetes, dyslipidaemia, non-alcoholic fatty liver disease

  Alcoholic liver disease, iron overload and drug/toxin-induced injury

  Review of family history of HCC

Initial assessment of persons with HBV prior to therapy-2

- **Measurement of baseline renal function and assessment of baseline risk for renal dysfunction should be considered in all persons prior to initiation of antiviral**

- **Thyroid Function Tests before initiation of IFN therapy**

Use of noninvasive markers of fibrosis for guiding treatment decisions

Test	Components	Requirements	Cost
APRI	AST, platelets	Basic tests	+
FIB-4	Age, AST, ALT, platelets	Basic tests	+
FibroTest	gGThaptoglobin, bilirubin, A1 apolipopotein, alpha2-macroglobulin	Specialized tests. Commercial assay	+ +
FibroScan	Transient elastography	Dedicated equipment	+++

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HCC screening in chronic HBV infection

- A baseline CECT or CEMRI should be obtained in all cirrhotics at presentation
- Surveillance by USG and AFP should be performed every 6 months (B2), and preferably every 3 months in cirrhotics and those at high risk of HCC .
- Contrast enhanced CT and MRI should be used regularly for confirmation of suspicious lesions on US screening .
- Their use is also recommended in the screening of patients with advanced cirrhosis with high suspicion of development of HCC .
- Alpha Feto protien as specific tumor marker

APASL guidelines 2015 update: Hepatol Int. 2016 Jan;10(1):1-98

Hepatitis C

Hepatitis C

- HCV is RNA Virus
- Blood borne virus resulting in acute and chronic hepatitis
- 85% of patients can have chronic liver disease
- 50% to 70% of infected patients develop cirrhosis
- Liver cancer may be seen in 20% to 30%.

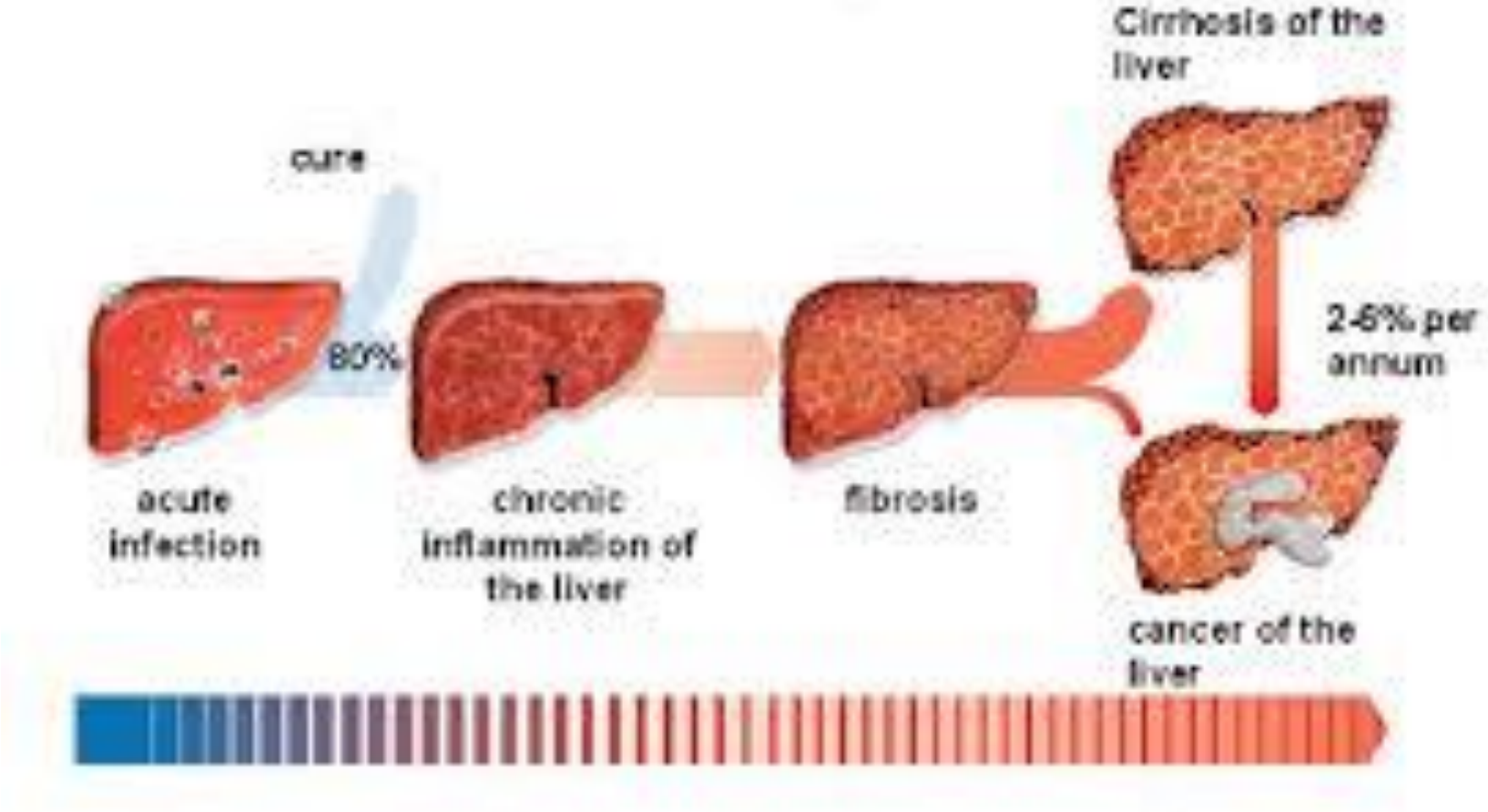
Clinical Features of Hepatitis C

- Many people may be asymptomatic.
- Symptoms occur with acute infection from 2 weeks to 6 months after exposure sometimes decades.
  - Fever
  - Fatigue
  - Loss of appetite
  - Nausea Vomiting
  - Abdominal pain
  - Dark urine
  - Grey-coloured stools
  - Joint pain
  - Jaundice.

Diagnosis of Hepatitis C

- The concentration of HCV in blood is so low that HCVAg can not be detected.
- **Anti-HCV** is the indicator of infection and the marker of infectivity
- HCV- RNA may be detected from blood or liver tissue and is the direct evidence of infectivity

Course of illness with Hepatitis C



Hepatitis D

Clinical Features of Hepatitis D

- Asymptomatic
- Jaundice
- Joint pain
- Abdominal pain
- Vomiting
- Loss of appetite
- dark urine
- Fatigue

Diagnosis for Hepatitis D

- HDV (Delta hepatitis virus) is a kind of defective virus
- HDV is found in the nuclei of infected hepatocytes

Diagnosis for Hepatitis D

- No free HDAg is detected in blood, it's in the nuclei of hepatocytes-
  - Anti-HDV can be detected by RIA or ELISA in serum
- HBV and HDV co-infection or superinfection may make the disease exacerbation and may lead to fulminant hepatitis
- HDV RNA may be detected from liver cells, blood or humor.

Hepatitis E

Hepatitis E

- Hepatitis E Virus replicate within hepatocytes and are discharged via bile tract
- One antigen-antibody system

Clinical Features

- The course of infection has 2 phases, the prodromal phase and the icteric phase.

- The prodromal phase usually is of short duration.

Prodromal Phase

- Myalgia
- Arthralgia
- Mild Fever
- Anorexia (66-100%)
- Nausea/vomiting (30-100%)
- Weight loss (typically 2-4 kg)
- Dehydration
- Right upper quadrant pain that increases with physical activity (in 35-80% of patients)

Icteric Phase

- Jaundice
- Serum bilirubin level is usually higher than 3 mg/dL
- Scleral icterus - usually occurs between the fifth and eighth week after infection
- Dark urine
- Light-coloured stools (20-40%)
- Pruritus (50%)

Other Manifestations

- Malaise (most common), Arthritis, Pancreatitis, Aplastic anemia, Thrombocytopenia.
- Neurologic symptoms: Polyradiculopathy, Guillain–Barré syndrome, Bell palsy, peripheral neuropathy, ataxia, and mental confusion
- Nephrotic symptoms: Membranoproliferative glomerulonephritis

Summary

- The clinical features in Hepatitis A and E are relatively mild.
- Hepatitis B and C may take a chronic course.

Thank You!