

### HEPATITIS INDUCTION PROGRAM FOR DOCTORS

# IDENTIFICATION AND TREATMENT OF COMPLICATIONS OF VIRAL HEPATITIS

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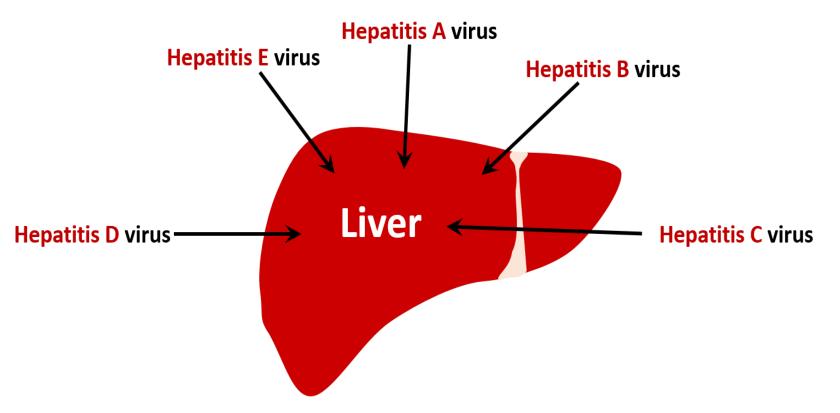




**INSTITUTE OF LIVER & BILIARY SCIENCES, NEW DELHI** 



## Hepatitis

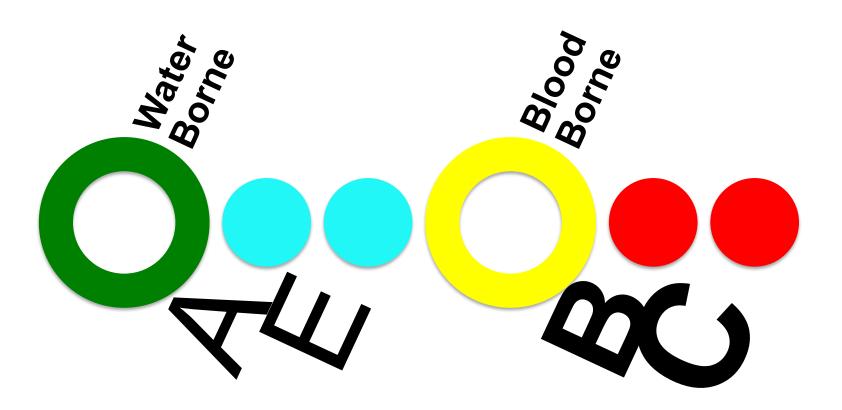


Of an estimated 1.4 million deaths per year caused by hepatitis virus:

- ~47% are attributable to hepatitis B
- 48% to hepatitis C
- ~5% to hepatises A and E, (World Health Organization)



## Hepatitis





Treatments

usually tackle

the symptoms



## Viral Hepatitis -types

VPg (5)

Treatments

usually tackle

the symptoms.

	RNA capsid	2014	E protein	RNA	Of me
Name of Virus	Hepatitis A Virus (HAV)	Hepatitis B Virus (HBV)	Hepatitis C Virus (HCV)	Hepatitis D Virus (HDV)	Hepatitis E Virus (HEV)
Classification	Picornavirus	Hepadnavirus	Flavivirus	Deltavirus	Hepevirus
Viral genome	ssRNA	dsDNA	ssRNA	-ssRNA (-ve)	ssRNA
Transmission	Enteric	Parental	Parental	Parental	Enteric
Incubation period	15-45 days	45-160 days	15-150 days	30-60 days	15-60 days
Chronic Hepatitis	No.	Yes. 10% chance	Yes. >50% chance	Yes. <5% of coinfectious >80% of superinfectious	No.
Cure?	No cure.	No cure.	No cure.	No cure.	No cure.

Treatments

usually tackle

the symptoms.

Treatment: Alpha

interferon for 12

months.

Treatments

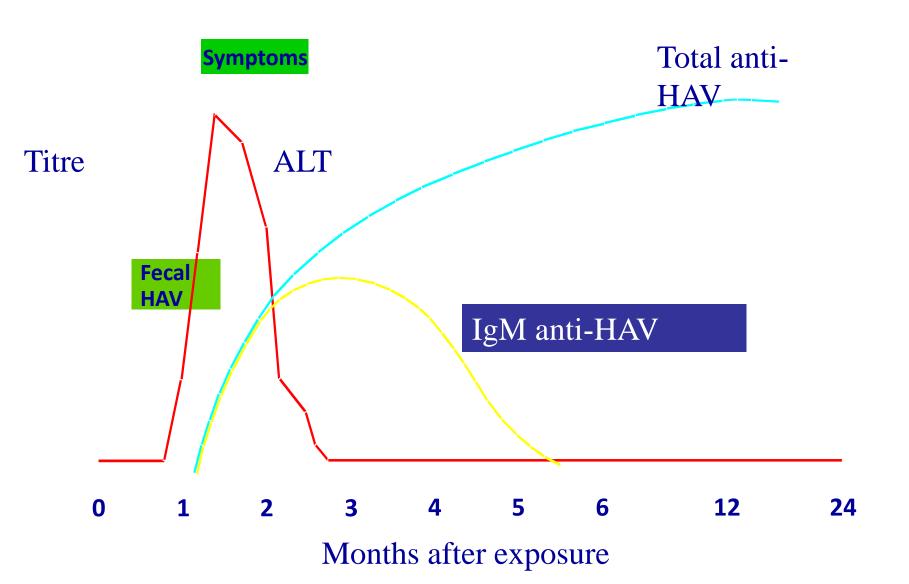
usually tackle

the symptoms.





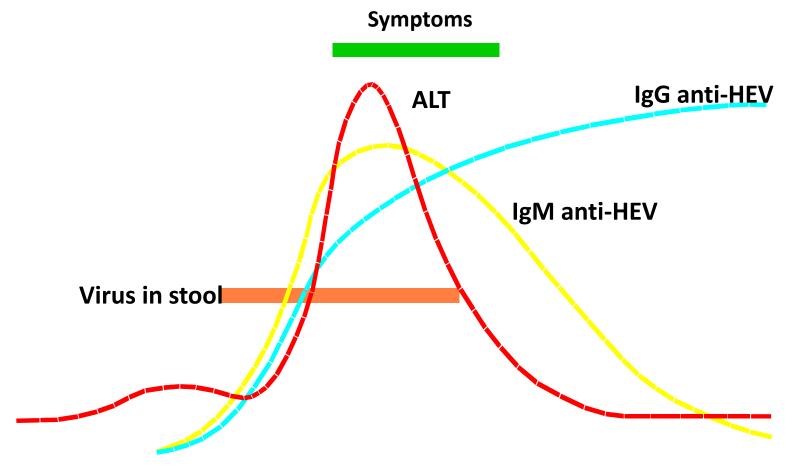
## Hepatitis A Infection Typical Serological Course





**Titer** 

## Hepatitis E Virus Infection Typical Serologic Course



Weeks after Exposure



#### Acute Viral hepatitis-Phases

#### <u>Phases</u>

Incubation period

A: 4 weeks

B: 10 weeks

C: 7 weeks

D: 6 weeks

E: 2-8 weeks

- 2. Pre-icteric phase: anorexia, nausea, vomiting, malaise, fatigue, headache, fever
- 3. Icteric phase (1-4 weeks): jaundice, dark color urine, enlarged liver Liver function test positive
- 4. Post-icteric phases (2-12 weeks):

Recovery
Chronic phase
Fulminating hepatitis





#### Acute Viral hepatitis-HAV

- Incubation period:
- Jaundice by age group:
- Complications:

Chronic sequelae:

Range 15-50 days

Average 30 days

<6 yrs, <10%

6-14 yrs, 40%-50%

>14 yrs, 70%-80%

Fulminant hepatitis Cholestatic hepatitis Relapsing hepatitis

None



# Acute Viral Hepatitis – HEV related

■ Incubation period: Average 40 days

Range 15-60 days

■ Case-fatality rate: Overall, 1%-3%

Pregnant women,

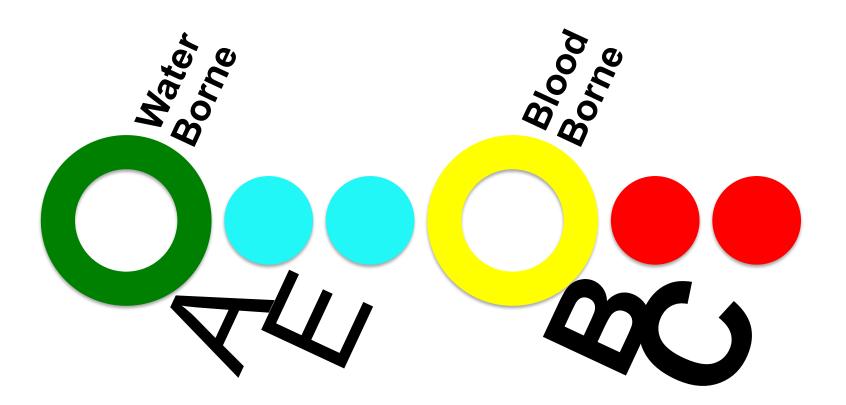
15%-25%

■ Illness severity: Increased with age

Chronic sequelae: None identified



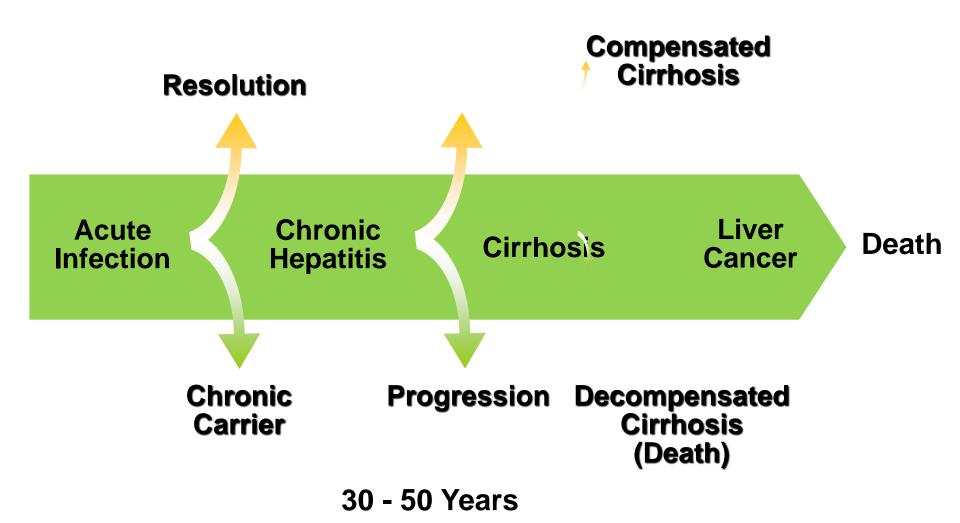
## Hepatitis





# Natural history of chronic HBV infection

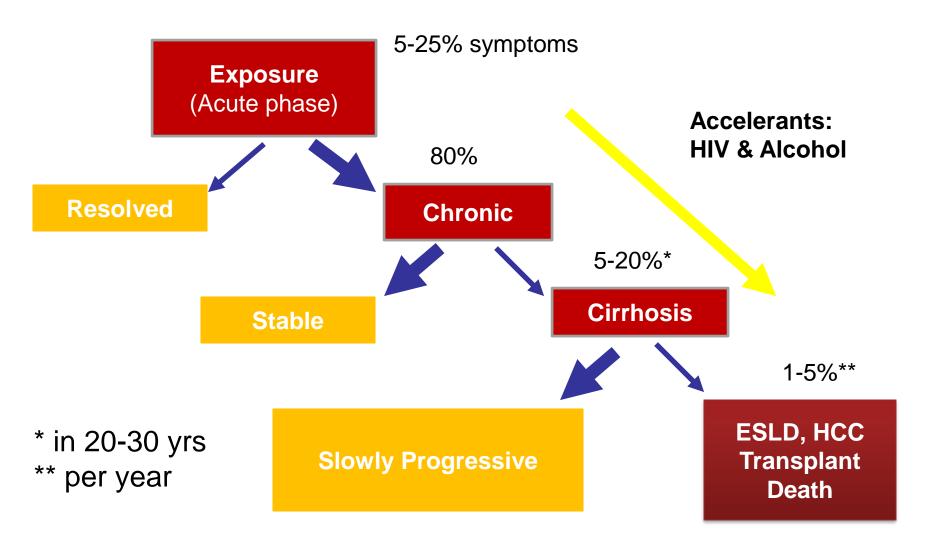








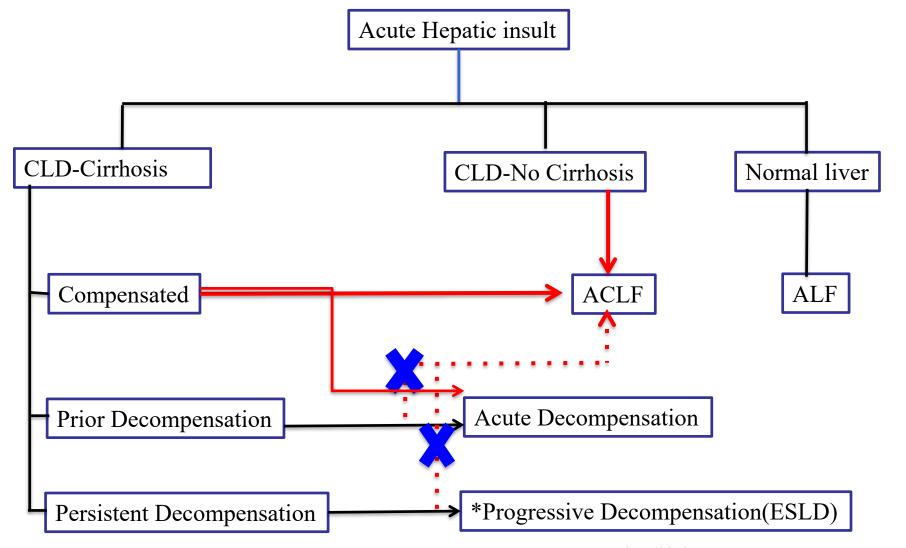






## Decompensation events in CLD





X = Needs validation

The dotted line indicates the controversy in ACLF





# Complications of Viral Hepatitis

#### Acute

- Severe hepatitis
- ALF
- FCH
- LOHF
- Extra hepatic
- Multi-organ involvement

#### **Chronic**

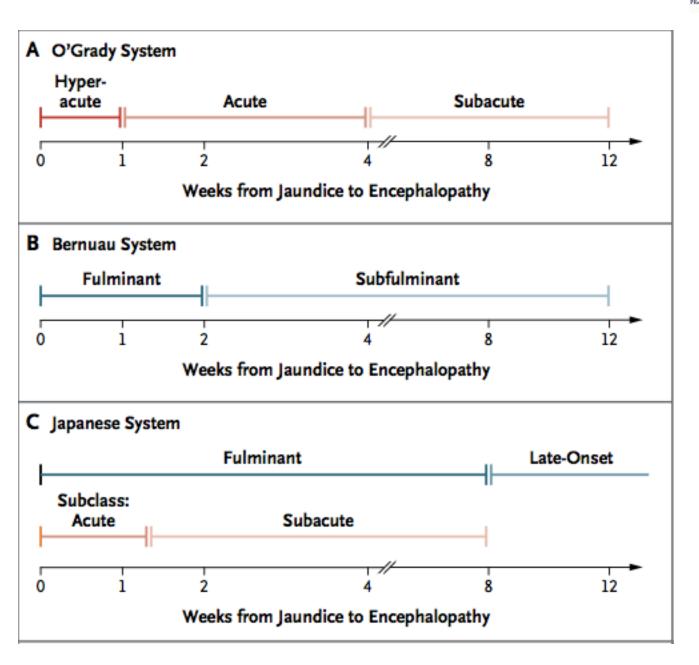
- Cirrhosis
- Decompensation
- Cancer –HCC
- Extra Hepatic



### **Defining Acute Liver Failure**

- INR > 1.5
- Altered mental status
- Illness of < 26 weeks duration</li>
- Hyperacute < 7 days</li>
- Acute 7-21 days
- Subacute > 21 days and < 26 weeks</li>
- Fulminant (2 wks) vs subfulminant (2-12 wks)









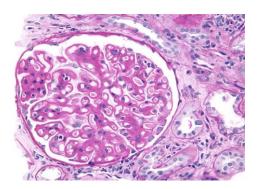
#### **Clinical Manifestations**

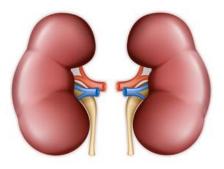




Acrodermatitis lesions











## Complications of Acute Liver Failure

- CNS disturbances
  - Hepatic encephalopathy
  - Cerebral edema
- Hemodynamic Collapse
- Infections
- Coagulopathy and bleeding
- Renal failure
- Metabolic derangements



### King's College Criteria

#### Acetaminophen-Induced ALF:

- Strongly consider OLT listing if:
- arterial lactate >3.5 mmol/L after early fluid resuscitation
- List for OLT if: pH<7.3 Or</li>
- arterial lactate >3.0 mmol/L after adequate fluid resuscitation
- List for OLT if all 3 occur within a 24-hour period:
- 1- presence of grade 3 or 4 hepatic encephalopathy
- 2- INR >6.5
- 3- Creatinine >3.4 mg/dL



### King's College Criteria

### Non-acetaminophen:

- INR > 6.5 OR
- Any 3 of the following 5:
  - Age < 10 or > 40
  - Serum bilirubin > 18
  - Jaundice to encephalopathy interval > 7 days
  - -INR > 3.5
  - Unfavorable Etiology
    - Non-A, non-B hepatitis, halothane, idiosyncratic drug reaction, Wilson's



#### **HBV Markers in ALF**

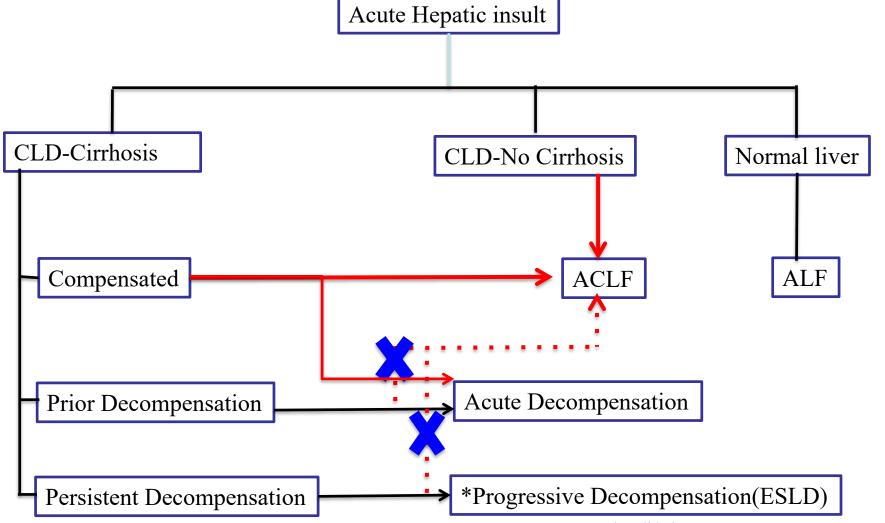
```
IgM Anti HBc 100%
HBsAg 90%
HBV DNA (Abbott) 10%
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\*Absence of HBsAg favors better prognosis (47% v 17%).
Higher frequency ALF with mutant HBV form



## Decompensation events in CLD





X = Needs validation

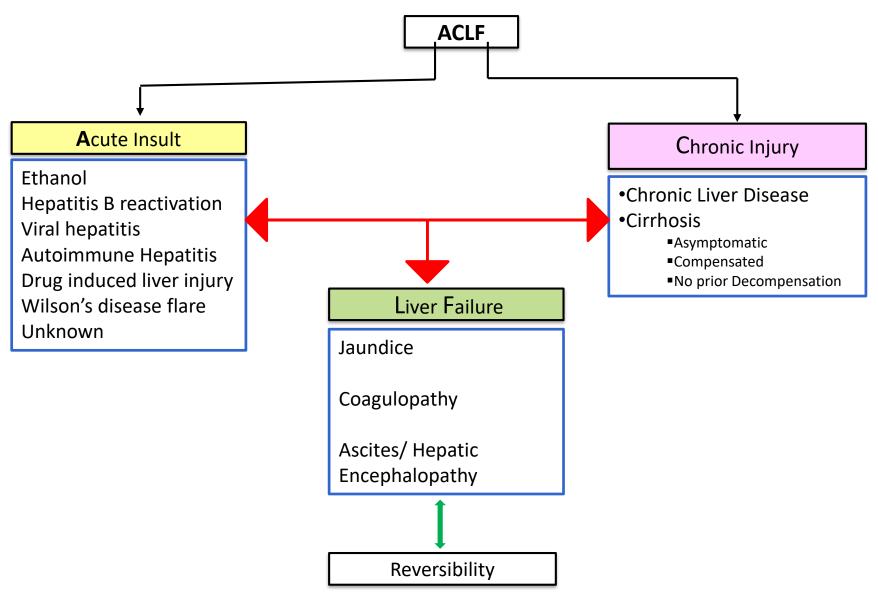
The dotted line indicates the controversy in ACLF

Sarin SK & Choudhury A. Curr Gastroenterol Rep. 2016 Dec;18(12):61.



### **ACLF: Concept**





Sarin SK & Choudhury A. Nat Rev Gastroenterol Hepatol. 2016

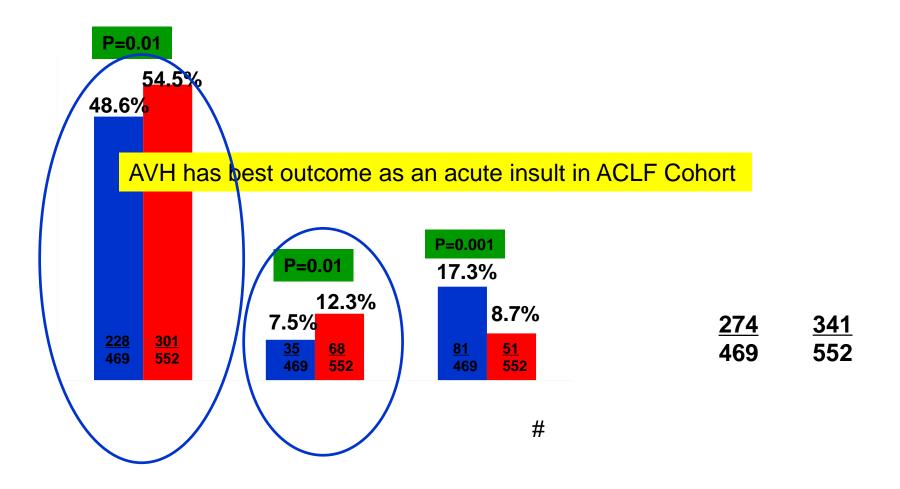


#### **AVH and ACLF**

- AVH as an acute insult in 9.4% (132/1402)-AARC Data(Choudhury et.al Hep Int 2017)
- HEV is common
- HAV
- Non hepatotropic viruses
  - CMV
  - EBV
  - HSV
  - Dengue



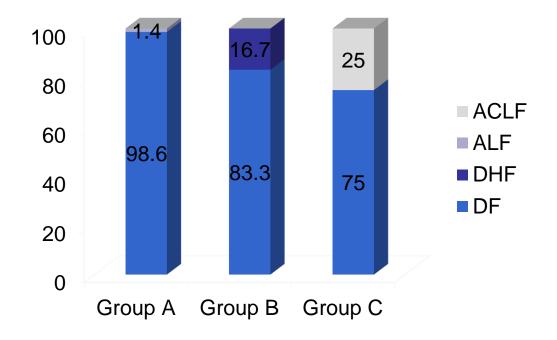
#### **Acute Insult and Outcome**







## Dengue and presentation with Decompensation/liver failure





#### AARC ACLF Score and Grade: Early proritization

#### **AARC ACLF Score**\$

Points	Bilirubin	HE Grade	INR	Lactate	Creatinine
	(mg/dl)			(mmol/lit)	(mg/dl)

1

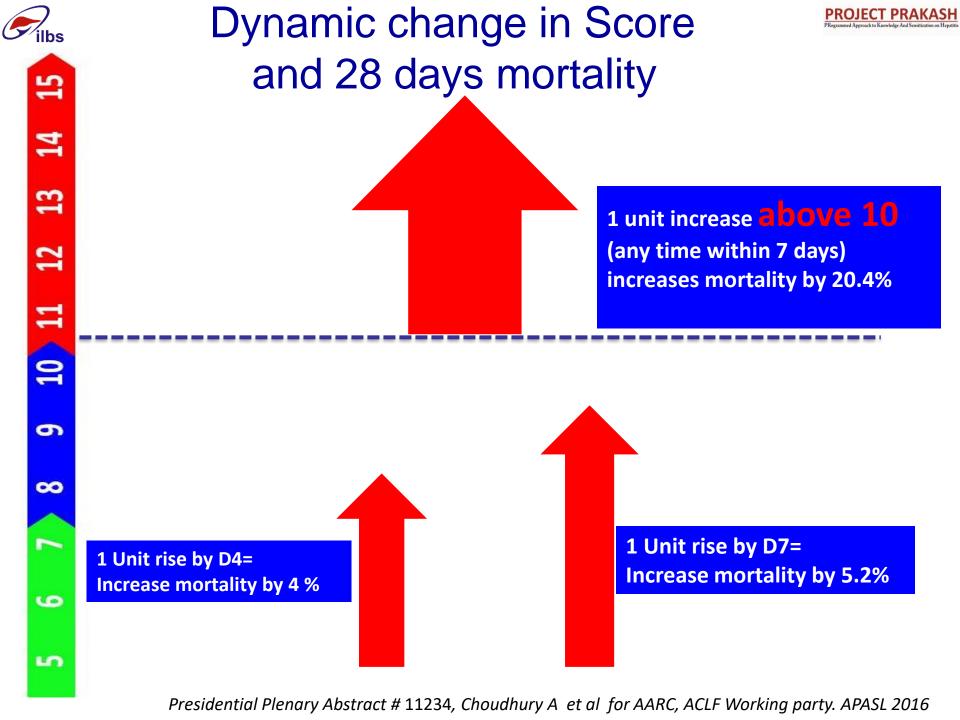
2 APASL-ACLF definition for ACLF and LT is better

3

- Infection excluded as an acute insult
- Organ failure-extra hepatic are not at the beginning
- Provision for LT early

C

11-15







# Complications of Viral Hepatitis

#### Acute

- Severe hepatitis
- ALF
- FCH
- LOHF
- Extra hepatic
- Multi-organ involvement

#### **Chronic**

- Cirrhosis
- Decompensation
- Cancer –HCC
- Extra Hepatic





### Chronic HCV Infection Affects Many Sites Beyond the Liver

Neurological (e.g. cognitive impairment)

Pulmonary fibrosis

Renal (e.g. glomerulonephritis)



Cardiovascular Diseases (CAD)

Metabolic (e.g. diabetes)

Lymphoproliferative (e.g. B cell lymphoma)

Dermatological (e.g. porphyria cutanea tarda)

Immune Complex (e.g. cryoglobulinemic)



### Progression to Cirrhosis

- Longer duration of infection
- HBV genotype C
- High levels of HBV DNA
- HBeAg positive
- Habitual Alcohol
- Concurrent infections with HIV, HCV, HDV
- Carcinogens aflatoxin, smoking



### Progression to HCC

- Longer duration of infection
- Male gender; family history of HCC
- HBV genotype C
- Cirrhosis
- High levels of HBV DNA
- HBeAg positive; history of reversion to HBeAg
- Habitual Alcohol
- Concurrent infection with HCV
- Carcinogens aflatoxin, smoking



### Screening for HCC

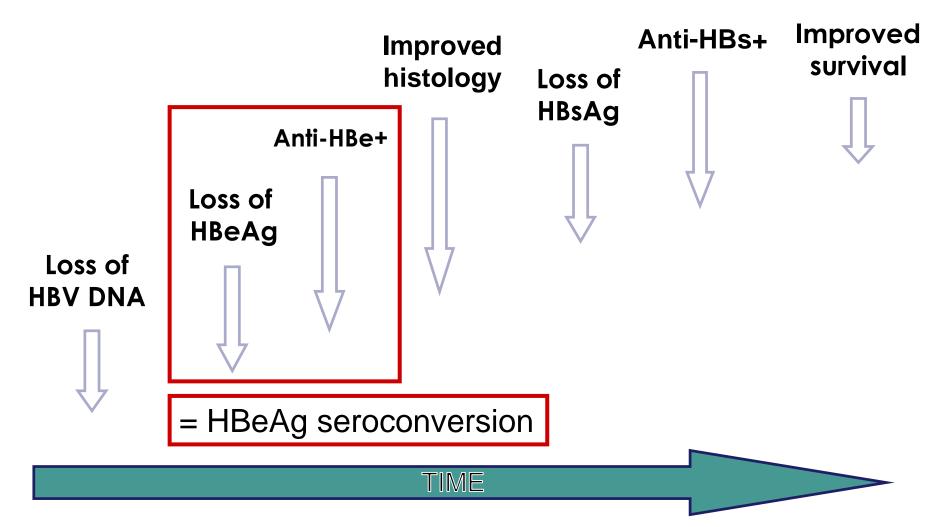
AFP every 6 – 12 months

Ultrasound every 6-12 months

 Frequency depends on assessment of risk



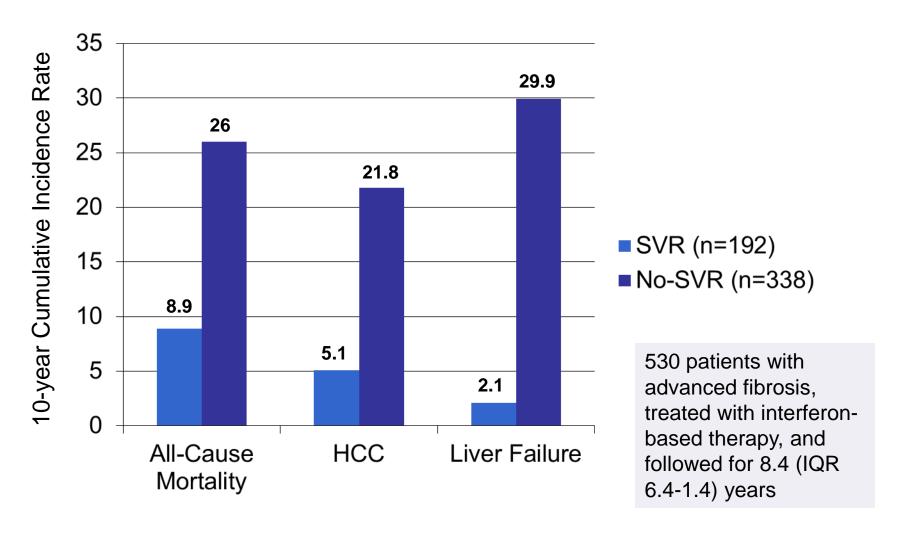
#### **Therapeutic Endpoints**



With current drugs available cure is not possible



## SVR (Cure) Associated with Decreased All-Cause Mortality

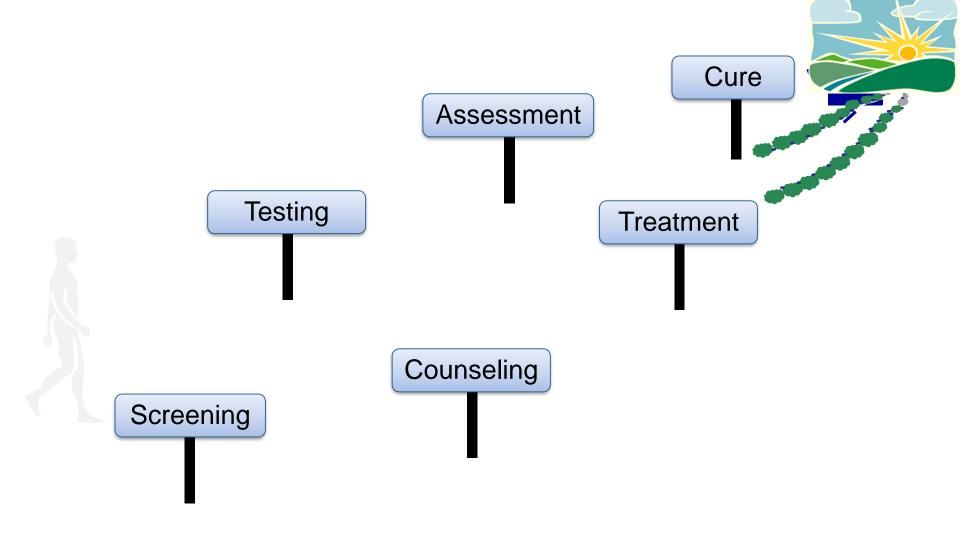


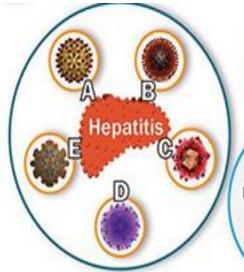


#### Therapy complications

- DAA
  - Kidney failure
- Nucs
  - Bone
  - kidney
- Interferon
  - Cytopenia
  - Constitutional symptoms









One in 12 people worldwide is living . witheither chronic hepatitis B or C.

'Am I Number 12?'

### **††††††**††

#### 500 million

people in the world are currently infected with HBV & HCV

3 out of 4 people with Hepatitis C infection are not aware of it

#### 4 Crore

**HBV** carriers in India Equal to ~66% Of Karnataka's population

#### **HBV** and HCV

are the major causes of liver cancer.

#### 50X

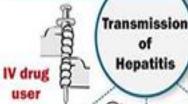
HBV is 50 to 100 times more infectious than HIV

A/E: Contaminated food or water

B: Blood or body fluids, unprotected sex

C: Direct blood to blood contact

B/C: Both infections does not usually spread through everyday contact, e.g. shaking hands





transfusion

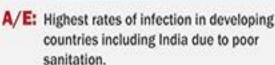




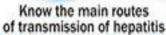
Unprotected Sex

Contaminated food/water





E: A previus outbreak of HEV in UP had affected ~79,000 people











**Blood transfusions** 



Sharing needles



Mother to child



Using the toilet

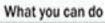




Sharing utensils









See a doctor



Get vaccinated



 The risk of transmission of hepatitis C during unprotected sex is considered very low, especially if you are in a long-term. stable relationship. This risk may be higher among men. who have sex with men or if blood is involved.



## Thank You!