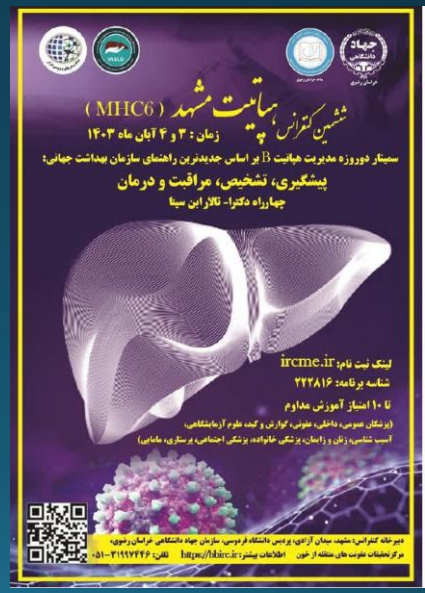
شبکه تحقیقات بیماری های
ایران

مرکز تحقیقات ویروس شناسی بالینی
دانشگاه علوم پزشکی تهران

تشخیص سرولوژیک و مولکولی هپاتیت دلتا

دکتر سید محمد جزایری
شبکه تحقیقات بیماریهای ویروسی ایران
مرکز تحقیقات ویروس شناسی بالینی
دانشگاه علوم پزشکی تهران

آبان ۱۴۰۳
مشهد



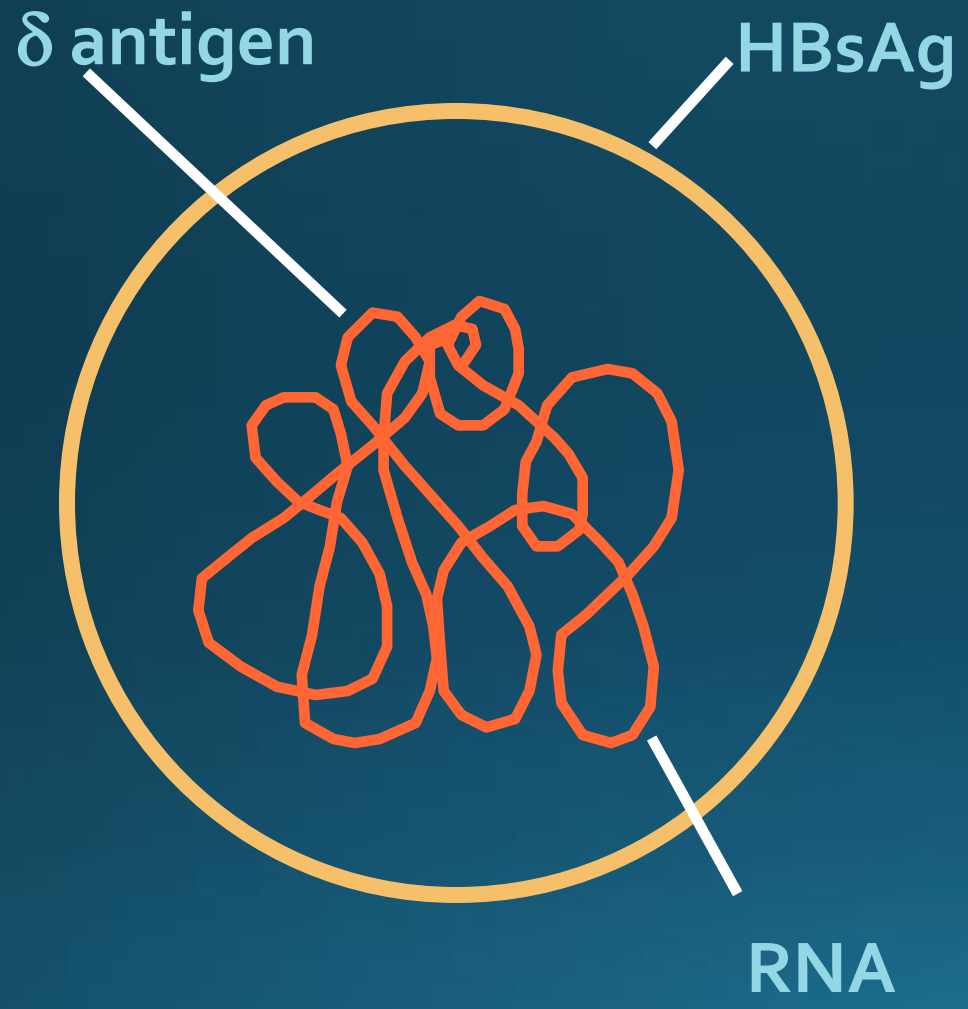
HDV, AN OVERVIEW

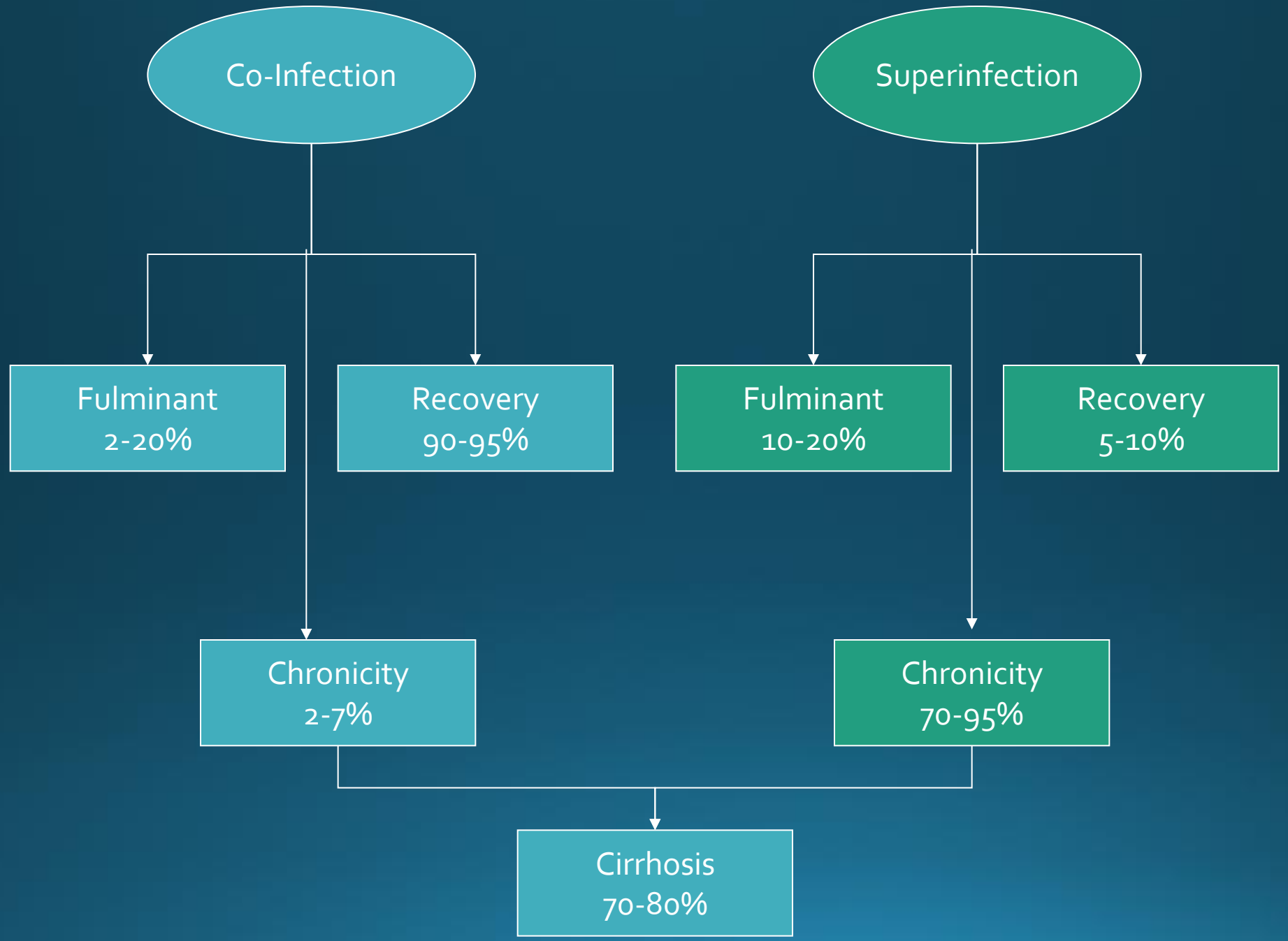
- Virus: Incomplete RNA virus, dependent on HBV envelope proteins.
- Disease:

1. Co-infection: acute infection simultaneously with hepatitis B virus.
2. Superinfection: acute HDV infection on chronic HBV.

- Outcome: May cause persistent infection (80% as superinfection, <10% with coinfection). Long-term sequels as with HBV, but more severe/accelerated.
- Epidemiology: Transmission: blood borne and sexual. Risk groups: as with HBV.

Hepatitis D (Delta) Virus




Co-Infection
Superinfection
Fulminant
2-20%
Recovery
90-95%
Fulminant
10-20%
Recovery
5-10%
Chronicity
2-7%
Chronicity
70-95%
Cirrhosis
70-80%

HDV Pathogenesis

- There is no distinguishing features of the liver histology that differentiate HDV from other types of viral hepatitis, except that the former is more severe.
- HDV RNA replication is not acutely cytopathic, supporting the notion that damage to hepatocytes is immunologically mediated.
- Ab response to HDV is relatively slow.

Reasons for HDV Diagnosis

1. Chronically infected HDV infection is more likely to progress to cirrhosis and liver failure,

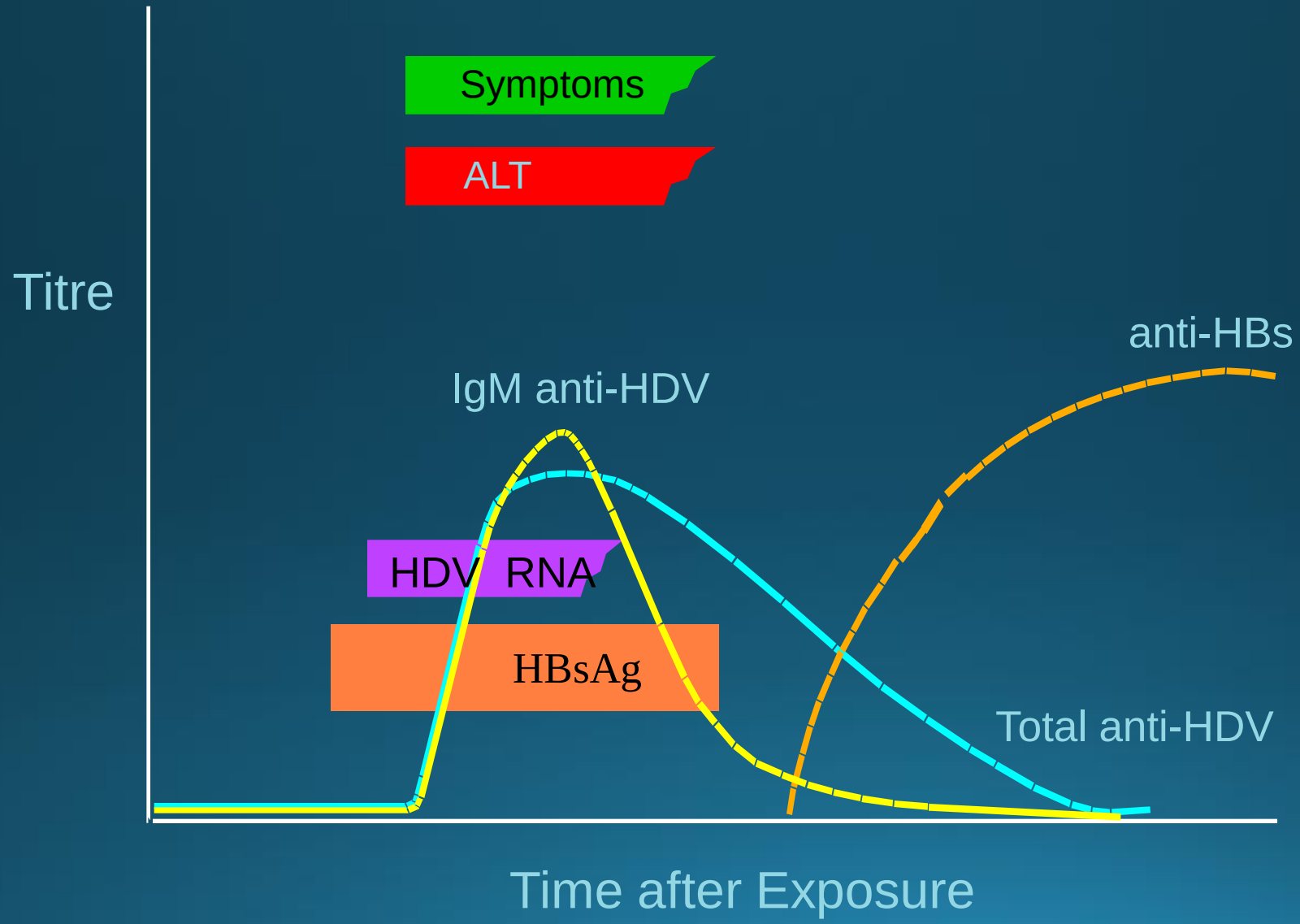
2. Response of patients with chronic HDV to antiviral therapy differs from that of patients with chronic HBV,

3. Unlike HBV, patients with HDV often do quite well after liver transplantation.

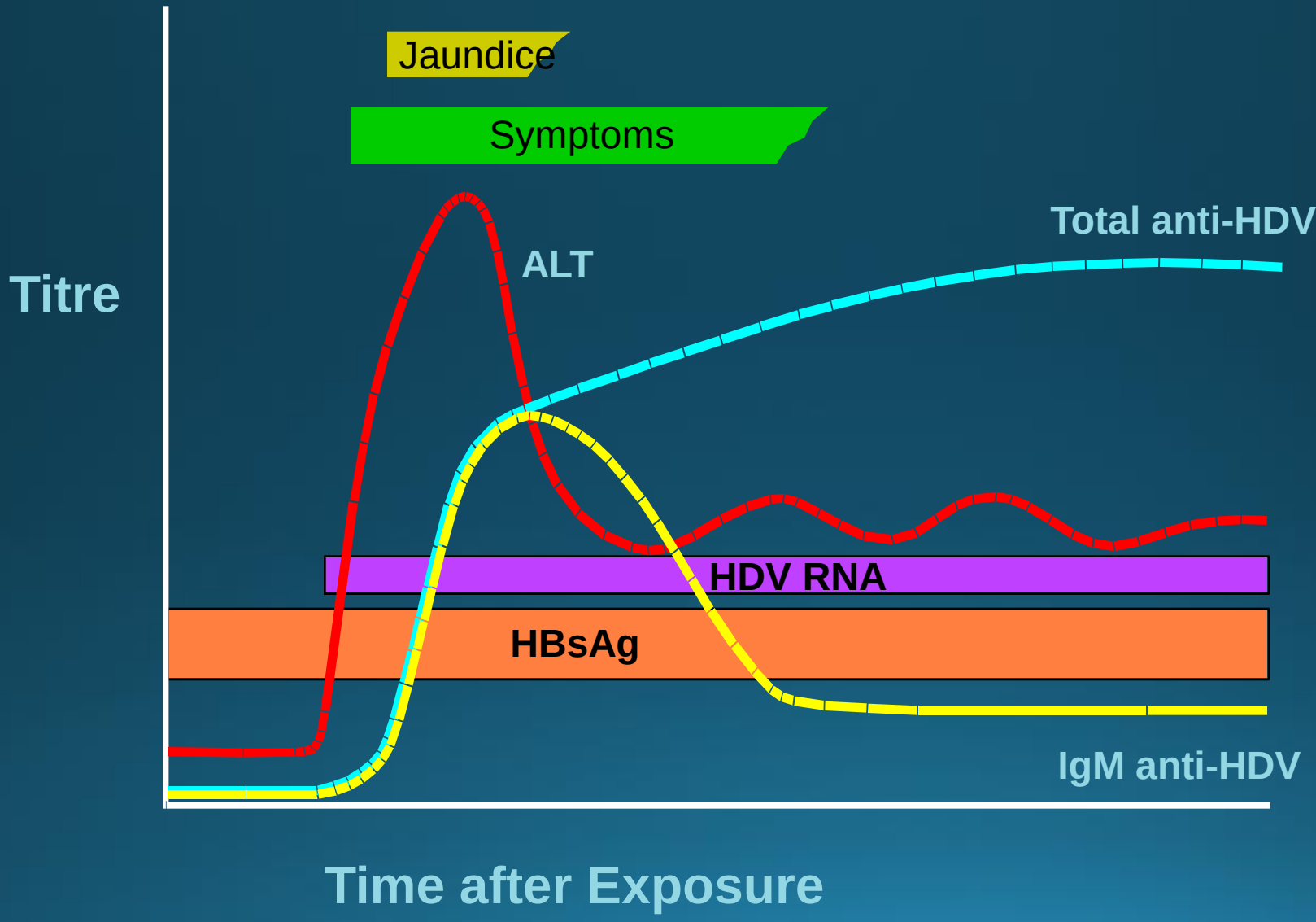
Laboratory Diagnosis

1. Serologic markers of HBV infection (virtually, all patients with HDV infection have HBsAg in serum).
2. Serologic markers of HDV infection: Anti-HDAg (Ig/M and/or IgG)
3. HDV RNA PCR

HBV - HDV Coinfection



HBV - HDV Superinfection



HDV Molecular Diagnosis

- PCR (either standard or quantitative, real time format) has overcome the limitation of serologic detection of HDAg caused by Ag sequestration in immune complex.
- Quantitative PCR may be particularly useful for monitoring the efficacy of antiviral therapy.

WHO guidelines Recommendations for HDV Testing

- WHO guidelines promote two main approaches:

1. Universal HDV antibody testing:

- This approach performs routine HDV antibody testing of everyone with CHB (HBsAg positive), regardless of place of birth, risk behaviour or clinical characteristics.
- All HBsAg-positive individuals are systematically offered HDV testing services.

WHO guidelines Recommendations for HDV Testing

2. Focused (risk-based) HDV antibody testing.

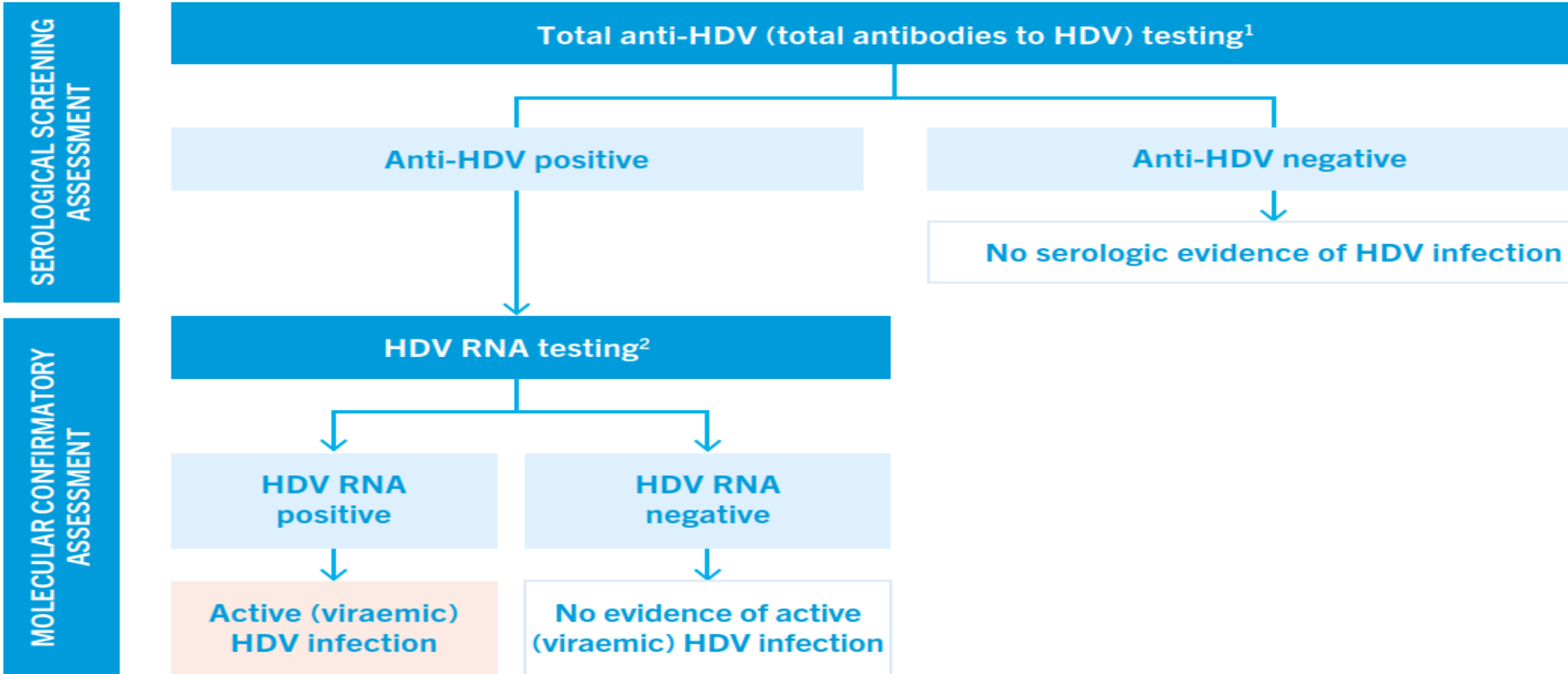
- This approach tests specific populations of HBsAg-positive individuals considered at increased risk of HDV infection based on current knowledge of epidemiology, risk factors and clinical characteristics of CHD.

WHO Guidelines Recommendations for HDV Testing

- These include:

1. People born in regions with reported high HDV endemicity,
2. People who inject drugs,
3. Men who have sex with men,
4. Sex workers,
5. People living with HCV or HIV,
6. Haemodialysis recipients,
7. People reporting high-risk sexual behaviour
8. People with advanced liver disease (cirrhosis or HCC).

Testing strategy for diagnosing HDV infection among individuals who are HBsAg positive, WHO Recommendations



Rationale For The Recommendations

- The Guidelines Development Group made an overall conditional recommendation for a universal HDV antibody testing approach among people living with CHB based on very- low-quality evidence.
- But also given that implementing this approach may not be feasible because of limited laboratory capacity or other resources, the Guidelines Development Group made a complementary conditional recommendation for testing for anti-HDV to be prioritised in specific HBsAg-positive populations or settings with well-established higher prevalence of HDV infection based on context-specific epidemiological data.

Rationale For The Recommendations

- This includes:

1. People born in HDV-endemic countries and regions;
2. People at higher risk of acquiring HDV (people who inject drugs, men who have sex with men, sex workers, people living with HCV or HIV and haemodialysis recipients);
3. Children and family members of people with HDV infection;
4. People with advanced liver disease;
5. Those already receiving HBV treatment.

HDV Molecular Diagnosis; Who Guideline

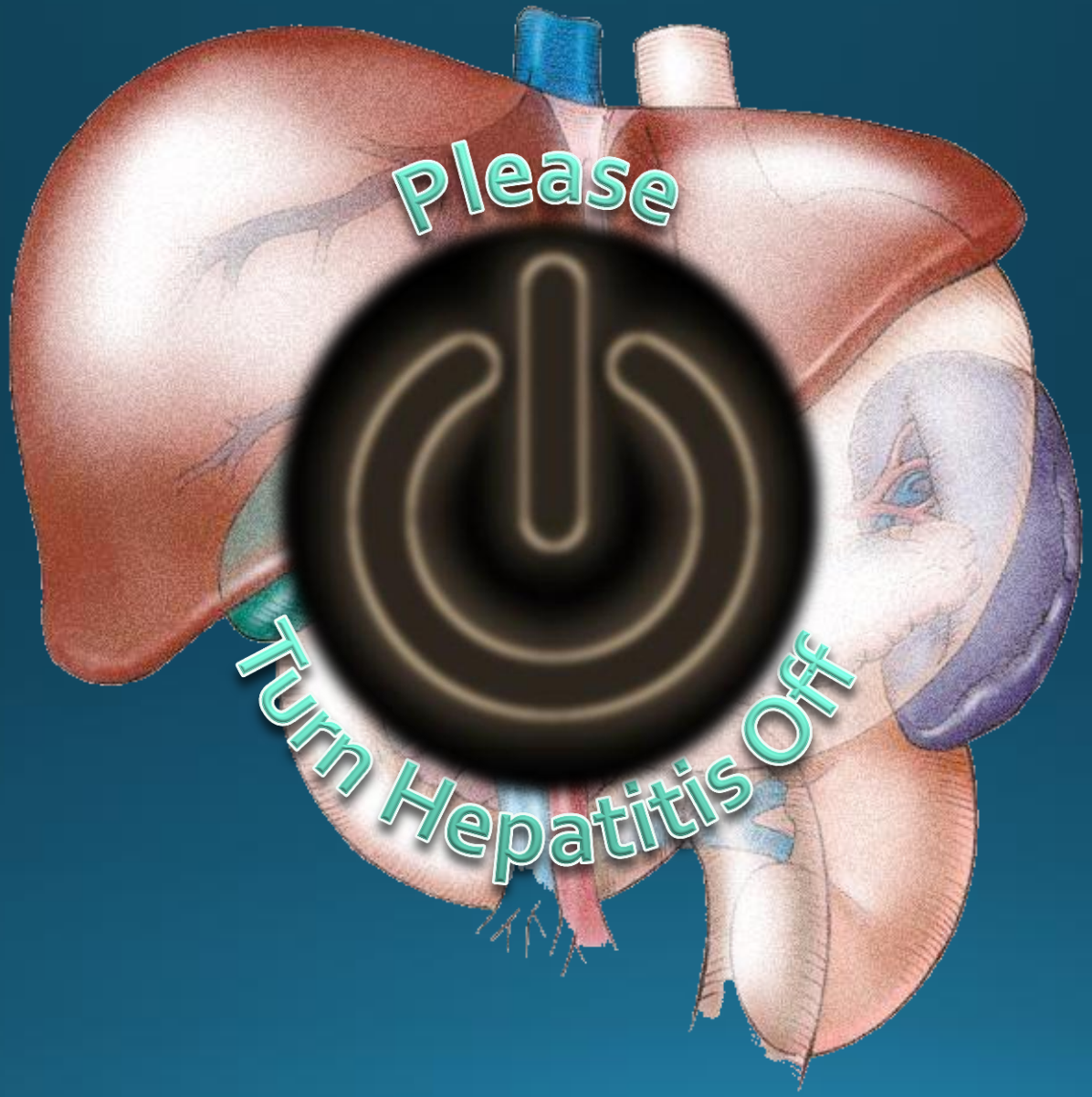
- Most of these are based on assays whose reagents and/or protocols are developed in-house for use in one particular laboratory.
- There are currently no POCT assays for HDV RNA.
- Although HDV RNA assays have been able to consistently quantify HDV genotype 1 in plasma, they underestimate or sometimes fail to detect genotype strains.

Conclusions: WHO Rationale For The Recommendations

- WHO commissioned a review on the diagnostic accuracy of assays for detecting total anti-HDV and HDV RNA.
- It found that the evaluated anti-HDV assays as well as PCR assays appeared to correlate well with one another.
- However, interpreting findings was a challenge because of the lack of a fully recognized or standardized gold standard.
- The certainty of evidence was assessed as being low.

شبکه تحقیقات بیماری های
ویروسی ایران

مرکز تحقیقات ویروس شناسی بالینی
دانشگاه علوم پزشکی تهران



HDV Serology

- Anti-HDV becomes detectable in more than 90% of cases within 1-2 months of acute hepatitis.
- Thereafter, the change in Ab patterns and titres depend on the type of HDV infection:

1. In co-infection, anti-HDV titre may be quite low or even undetectable in some cases.
2. In superinfection, anti-HDV tends to appear sooner and to reach higher titres.

- IgM anti-HDV appears first, correlates with the level of replication, as the hepatitis subsides, the levels may fall.

HDV Serology

- The presence of IgM anti-HDV may persists into the chronic phase of infection and indeed may remain detectable as long as significant levels of viral replication persist.
- Testing for IgM anti-HDV in addition to its diagnostic value, provides also prognostic information: its decrease predicts resolution of chronic HDV either spontaneous or induced by interferon therapy.

Hepatitis D - Clinical Features

1- Coinfection

Severe acute disease.

Low risk of chronic infection.

2- Superinfection

Usually develop chronic HDV infection.

High risk of severe chronic liver disease.

3- Latency

Reverse superinfection by HBV (in the transplant setting)