UNDERSTANDING VIRAL HEPATITIS

Dr George Patrick Akabwai

Specialist Physician

5th July,2024

Ministry of Health and Busoga Health Forum webinar

PRESENTATION OUTLINE

- Burden of Viral Hepatitis
- Viral hepatitis infection,transmission, natural history and clinical presentation
- MOH hepatitis program implementation
- Testing for viral hepatitis
- PMTCT
- Treatment guidelines
- New WHO guidelines on Hepatitis B 2024-Highlights
- Take home points

BURDEN OF HEPATITIS B

- In 2022, WHO estimated that 254 million people were living with chronic hepatitis B, of whom 65% were in the African and Western Pacific regions.

- Chronic HBV is a major public health problem and cause of chronic liver disease and led to an estimated 1·1 million deaths in 2022, mainly due to cirrhosis and hepatocellular carcinoma.

- However, hepatitis B birth-dose coverage is only 45% globally, with less than 20% coverage in the WHO African Region.

BURDEN OF HEPATITIS B

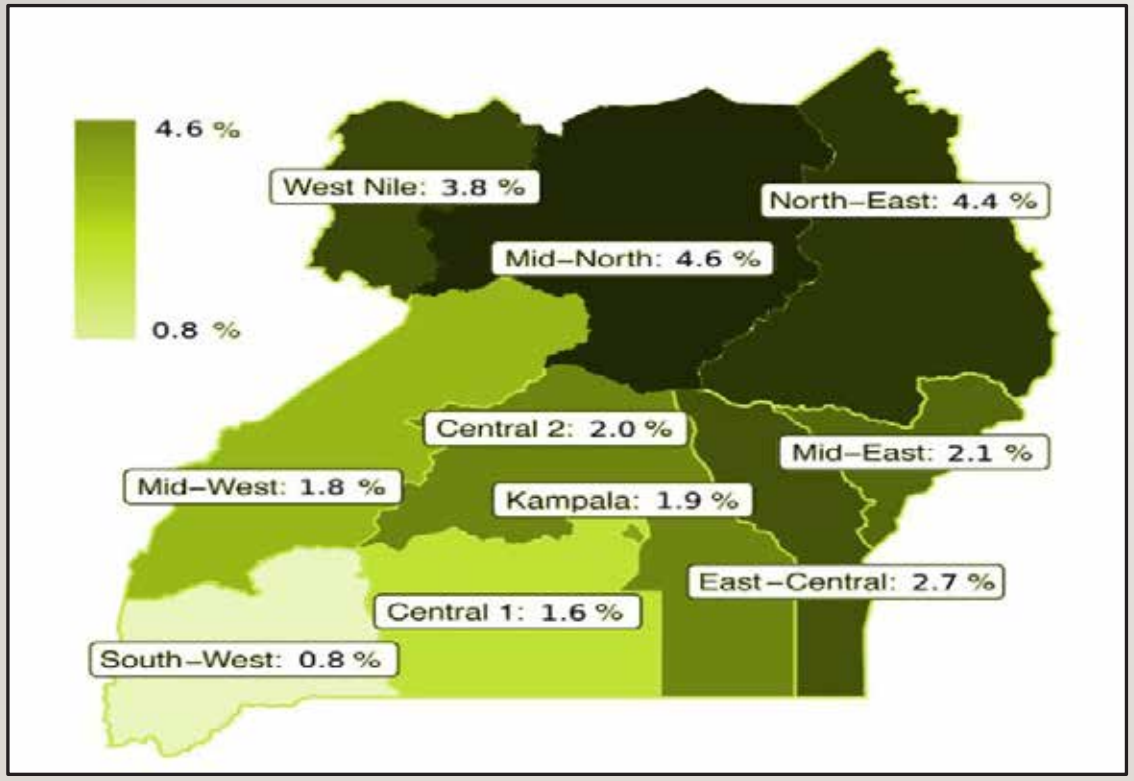
- WHO’s global hepatitis strategy, endorsed by all WHO Member States, aims to reduce new hepatitis infections by 90% and deaths by 65% between 2016 and 2030.

- Viral Hepatitis infection is of public health concern in Uganda.

- In 2022, an estimated 1250 Ugandans died of complications arising from HBV and approximately 6% of Uganda's population remains chronically infected.

VIRAL HEPATITIS SITUATION ANALYSIS

- **Disease prevalence:**
  - Regional variation in prevalence of Hepatitis B (UPHIA 2016)-North-South gradient.



- **Hepatitis C prevalence also shows regional variations using data from Blood Banks. Gulu and Mbale regional prevalence go up to 6% in Gulu and 5% in Mbale. In Fort Portal, there was an increase in prevalence from 1% in 2015/16 to 4% in 2019/20.**

VIRAL HEPATITIS INFECTION

- Viral hepatitis is a viral infection that causes inflammation of the liver.

- In humans its caused by only five different hepato-trophic viruses; Hepatitis A virus(HAV), Hepatitis B virus(HBV), Hepatitis C virus(HAC), Hepatitis D(HDV) and Hepatitis E virus(HEV).

- All Hepatitis viruses cause acute infection however HBV, HCV and HDV frequently cause chronic infections.

- Chronic hepatitis may progress to cause liver cirrhosis and hepatocellular carcinoma thus accounting to most of the burden of disease.

KEY DEFINITIONS

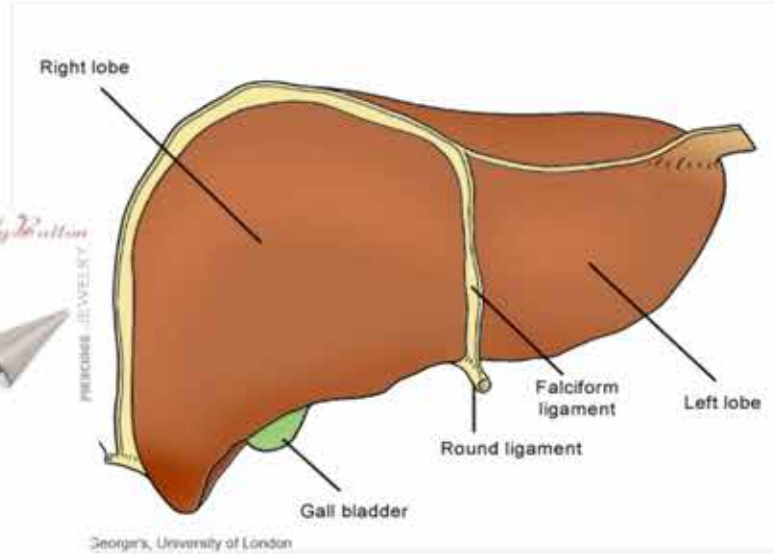
- **Acute hepatitis B:** New-onset hepatitis B infection that may or may not be symptomatic and is usually within 6 months. It is usually self limiting

- **Chronic hepatitis B:** Persistence of hepatitis B surface antigen (HBsAg) for six months or more after acute infection.

NOTE; Highest risk of chronic Infection occurs in childhood.

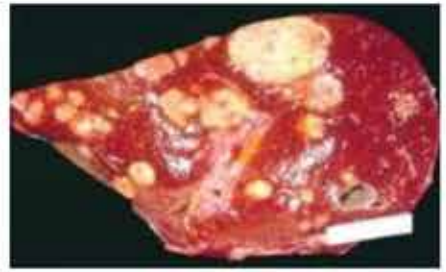
Consequences of Hepatitis

- HepA
- **HepB**
- **HepC**
- HepD
- HepE

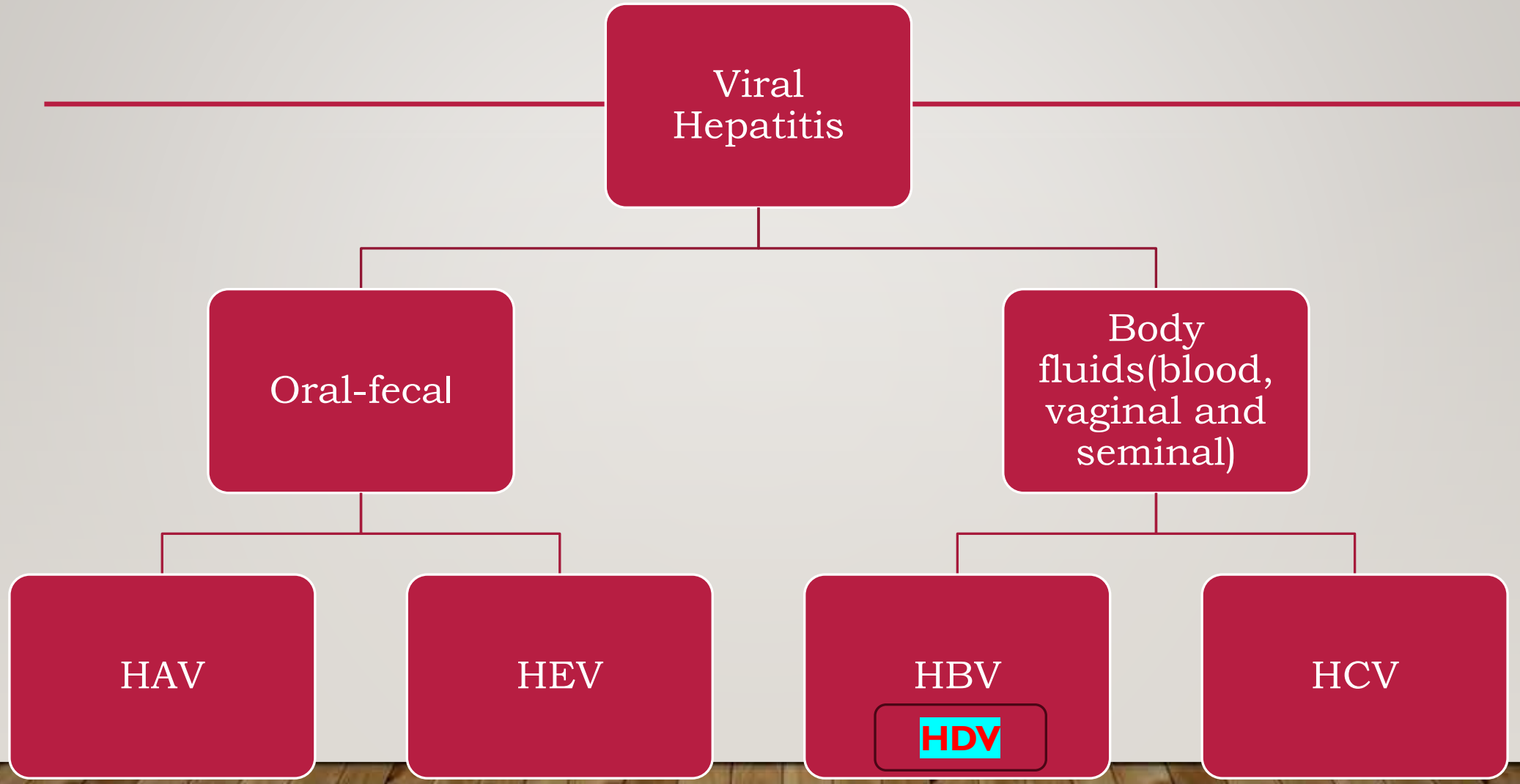


HepB
HepC

Liver with Cirrhosis



TRANSMISSION OF VIRAL HEPATITIS



Transmission of HBV/HCV

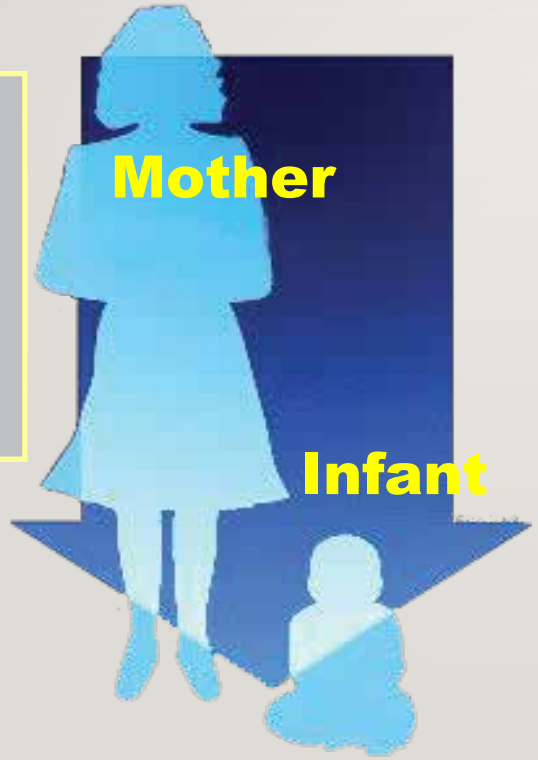
Transmission via percutaneous exposure to blood:

- Contaminated therapeutic injections, or medical or dental surgical equipment
- Blood transfusion from infectious donor
- Transplantation from infectious donor
- Occupational blood exposure (needle sticks)
- Birth to an infected mother
- Sex with infected partners

TRANSMISSION OF HBV

Vertical Transmission

- 90-95% of infected infants become chronically infected



Horizontal Transmission

- 3-5% of people infected over the age of 5 become chronically infected

Recipient

Child-to-Child

Contaminated Needles

Sexual Contacts

Healthcare Worker

Blood Transfusion

CDC Viral hepatitis B fact sheet.

HBV DOES NOT SPREAD THROUGH

- Sweat
- Greeting
- Sharing clothes
- Sharing toilets
- Sharing beddings
- Sharing food, drinks

NATURAL HISTORY OF HBV

- Some people are able to get rid of the infection after exposure to the virus.

- In this case the body becomes immune to the infection and such a person will not be infected again.

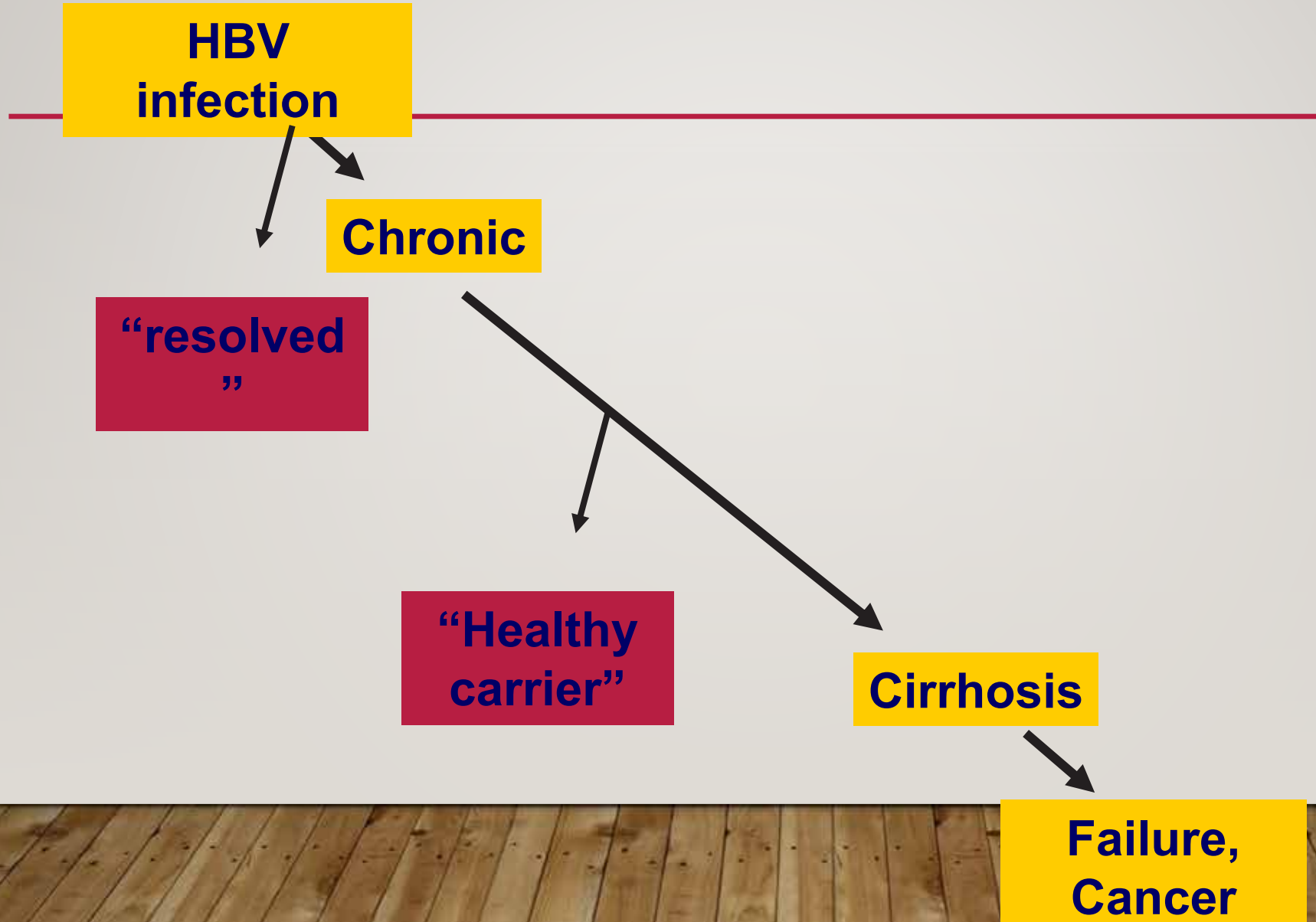
- This clearance of the virus depends on age of exposure. In those who are exposed perinatally, 90%-95% will not be able to clear the infection and will lead to chronic infection.

NATURAL HISTORY OF HBV

- HBV infection often goes undetected in childhood, as those infected are typically asymptomatic until they present with liver complications later in life(>25-30years).

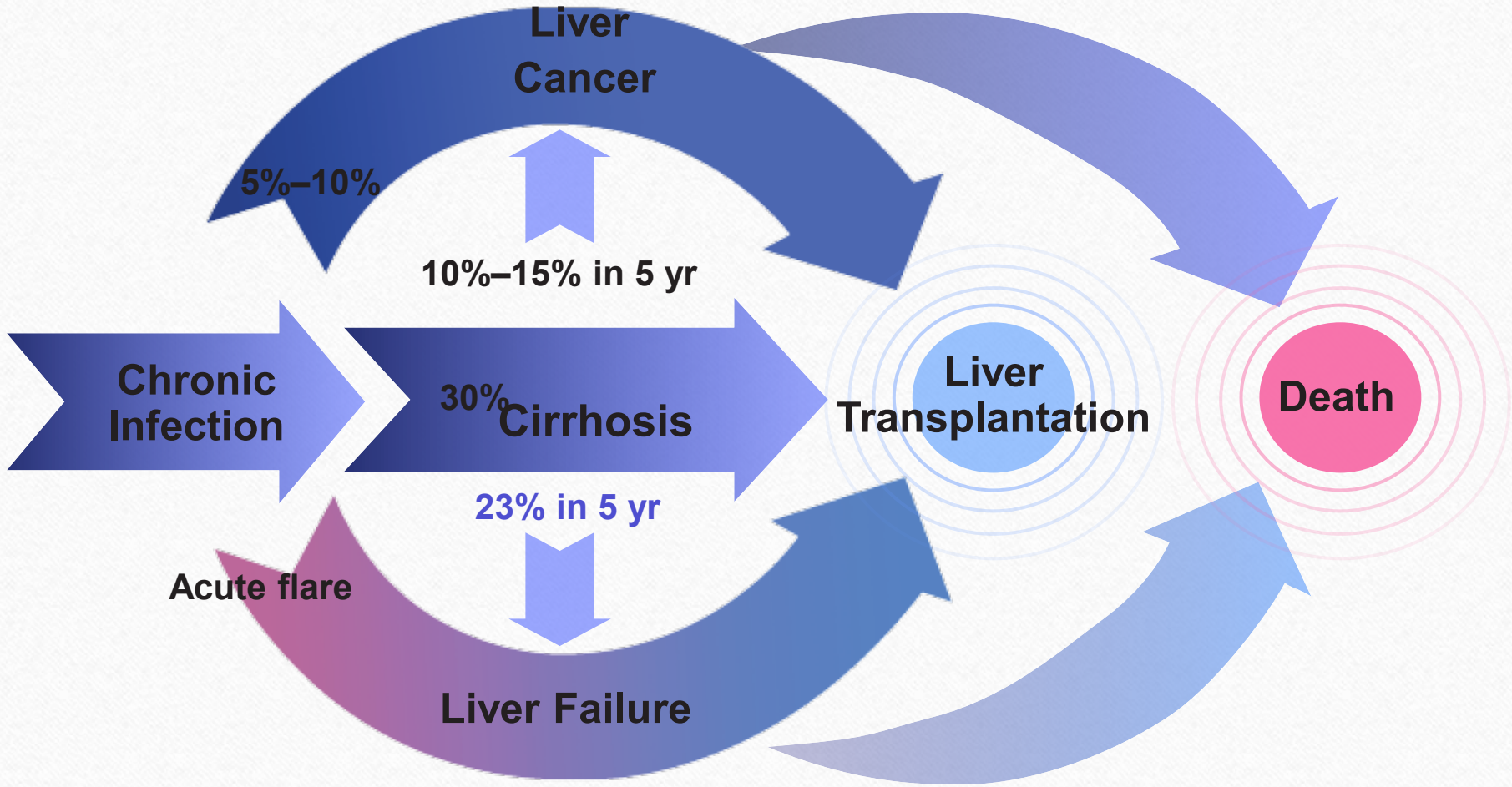
- In persons with depressed immune function chronicity may be more common even if they are older than 5 years.

NATURAL HISTORY OF HEPATITIS B



NATURAL PROGRESSION AND CONSEQUENCES OF CHB

15%–40% of CHB patients may experience disease progression



Adapted from: Fattovich, et al. *Gastroenterology*. 2004;127:S35-S50. Torresi, et al. *Gastroenterology*. 2000;118:S83-S103. Fattovich, et al. *Hepatology*. 1995;21:77-82. Perrillo, et al. *Hepatology*. 2001;33:424-432.

CLINICAL PRESENTATION- ACUTE HEPATITIS B

Acute infection may cause nonspecific symptoms and clinical signs, such as:

- Jaundice
- Weakness
- Fatigue
- Malaise
- Anorexia
- Nausea
- Vomiting
- Myalgia
- Arthralgia
- Abdominal pain
- Hepatomegaly
- Splenomegaly
- Dark urine
- Low-grade fever

Approximately 5 percent of adults acutely infected with HBV progress to chronic infection and stay in preclinical phase for decades

CLINICAL PRESENTATION-CHRONIC HEPATITIS B

Compensated cirrhosis

- No ascites, no varices

Decompensated cirrhosis

- Portal hypertension
- Ascites
- Esophageal /gastric varices
- Spontaneous bacterial peritonitis
- Hepatic encephalopathy
- Hepato-renal syndrome
- Hepatocellular carcinoma

GOVERNMENT RESPONSE

- Early childhood vaccination against Hepatitis B(UNEPI, 2002) at 6, 10 and 14 weeks,including the introduction of the timely Hepatitis B infant birth dose into the Universal Immunisation Program-Closing the tap on MTCT.
- Promotion of safe injection practices esp. among health workers(non-reusable injections).
- Screening for Hepatitis B, C and other transfusable- transmissible infections(TTIs) among blood donors.
- Government commitment politically-disease of public health concern in 2014.
- Budget allocation to support control activities

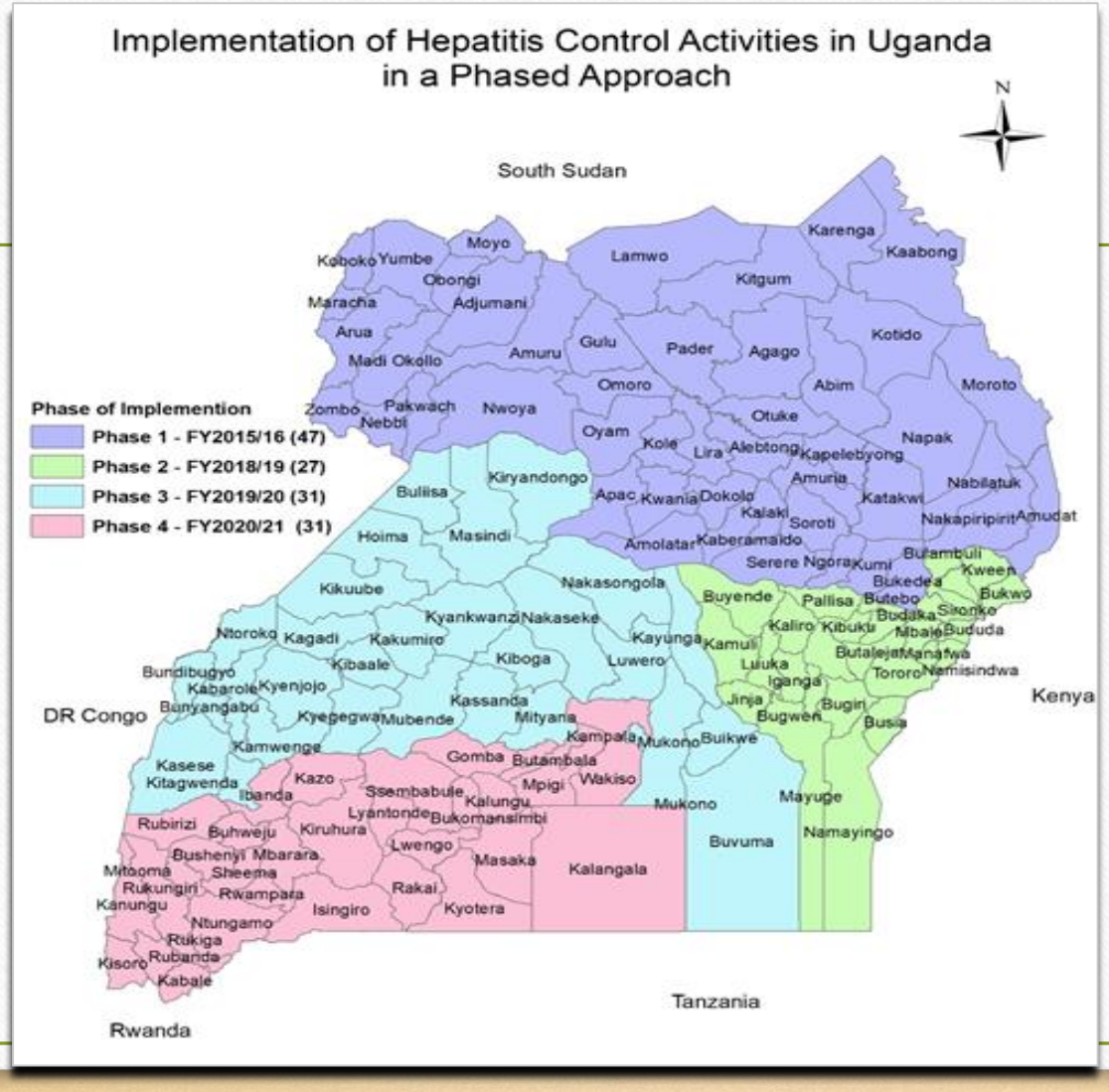
GOVERNMENT RESPONSE

- MOH started screening and vaccination of adolescents and adults against hepatitis B virus disease in 2015.
- Hepatitis B control activities implemented in a phased manner based on the prevalence of the disease.

Activities include:

- Testing all adolescents and adults who were born before the year 2002
- Vaccination of those not infected with hepatitis B(3 doses) given at 0,1 and 6 months)
- Linking those who test positive into care and treatment.
- Ratification of the timely infant HepB Birth dose into the Universal Immunisation Program
- A costed National Viral Hepatitis Strategic plan 2024-2028 developed and approved.

PROGRESS AND SUCCESSES



IMPLEMENTATION CONSIDERATIONS

- **Integration**
- **Multi - Sectoral approach**(Collaboration and strong advocacy efforts are very critical),academia, CSOs, Ministries and MDAs, Research institutions..etc
- **Client focus**
- **Community involvement**

WHO TO TEST

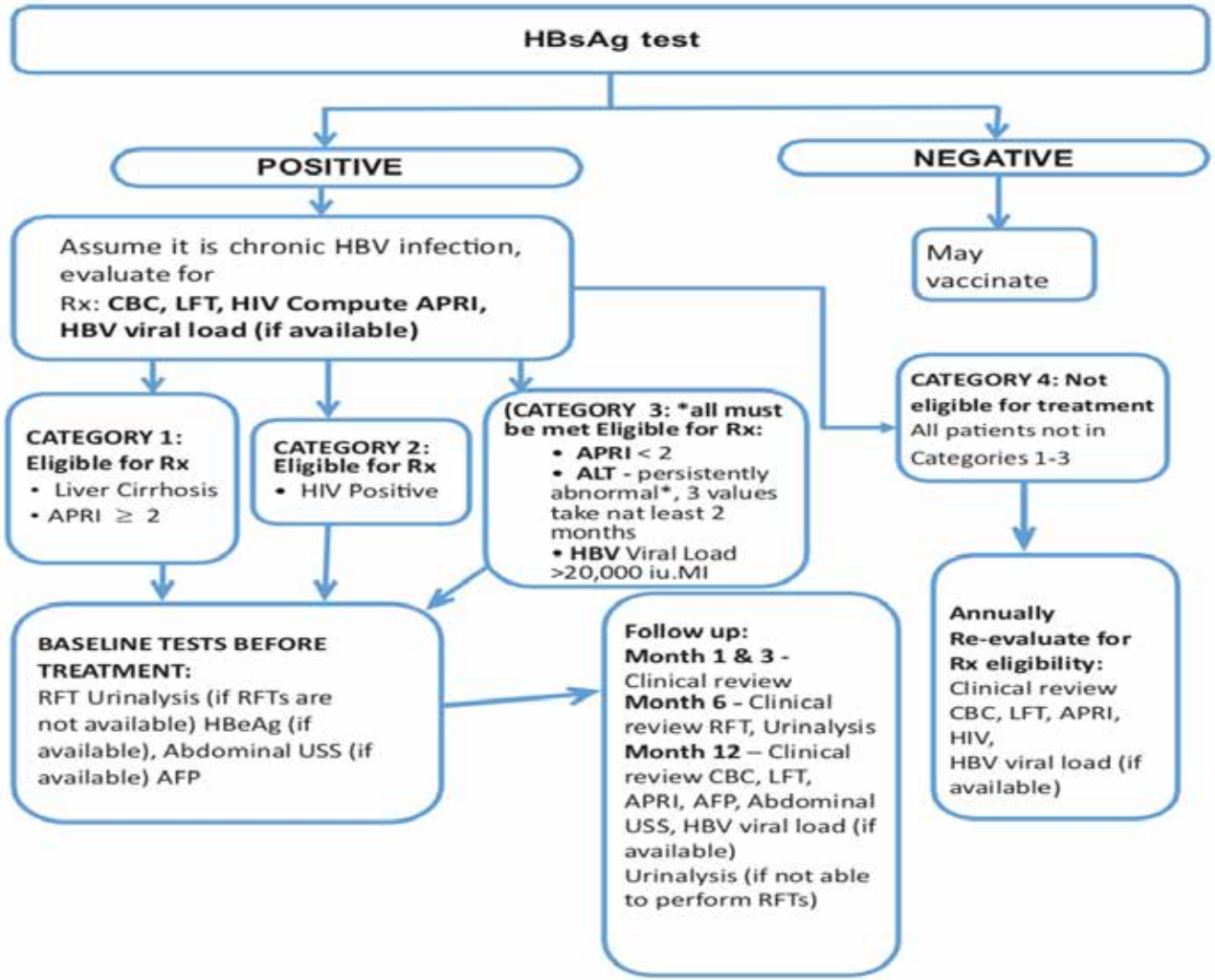
All persons in Uganda should be screened, however the following categories are at a higher risk and should be given priority.

- Health workers/students undertaking health-related course
- Pregnant women
- People living with HIV or other sexually transmitted infections
- Household contacts of an infected person
- Sexual contacts of people with CHB
- Armed forces: police and army
- Prisoners
- Sicklers or other patients who frequently receive blood/blood products
- Blood and organ donors or recipients
- Multiple sexual partners
- Sex workers
- People who inject drugs
- Men who have Sex with Men (MSM)
- All persons deemed at risk

HEPATITIS B TESTS AVAILABLE AT DIFFERENT FACILITY LEVELS

No	TYPE OF TEST	FACILITY LEVEL	PURPOSE
1	HBsAg	Health facility (HCII, III, IV, GH and RRH or community outreach	Initial testing
2	CBC, LFTs, HIV HBV viral load	Local lab facility (HCIV, GH and RRH) to UNHLS Hub facility to UNHLS	Evaluating HBsAg positives patients before deciding to treat
3	RFT, urinalysis, abdominal Ultrasound scan HBeAg, AFP	Local lab facility (HCIV, GH and RRH) Hub facility to UNHLS Hub facility to UNHLS	Baseline tests before antivirals Monitoring renal function during treatment Screening for liver cancer

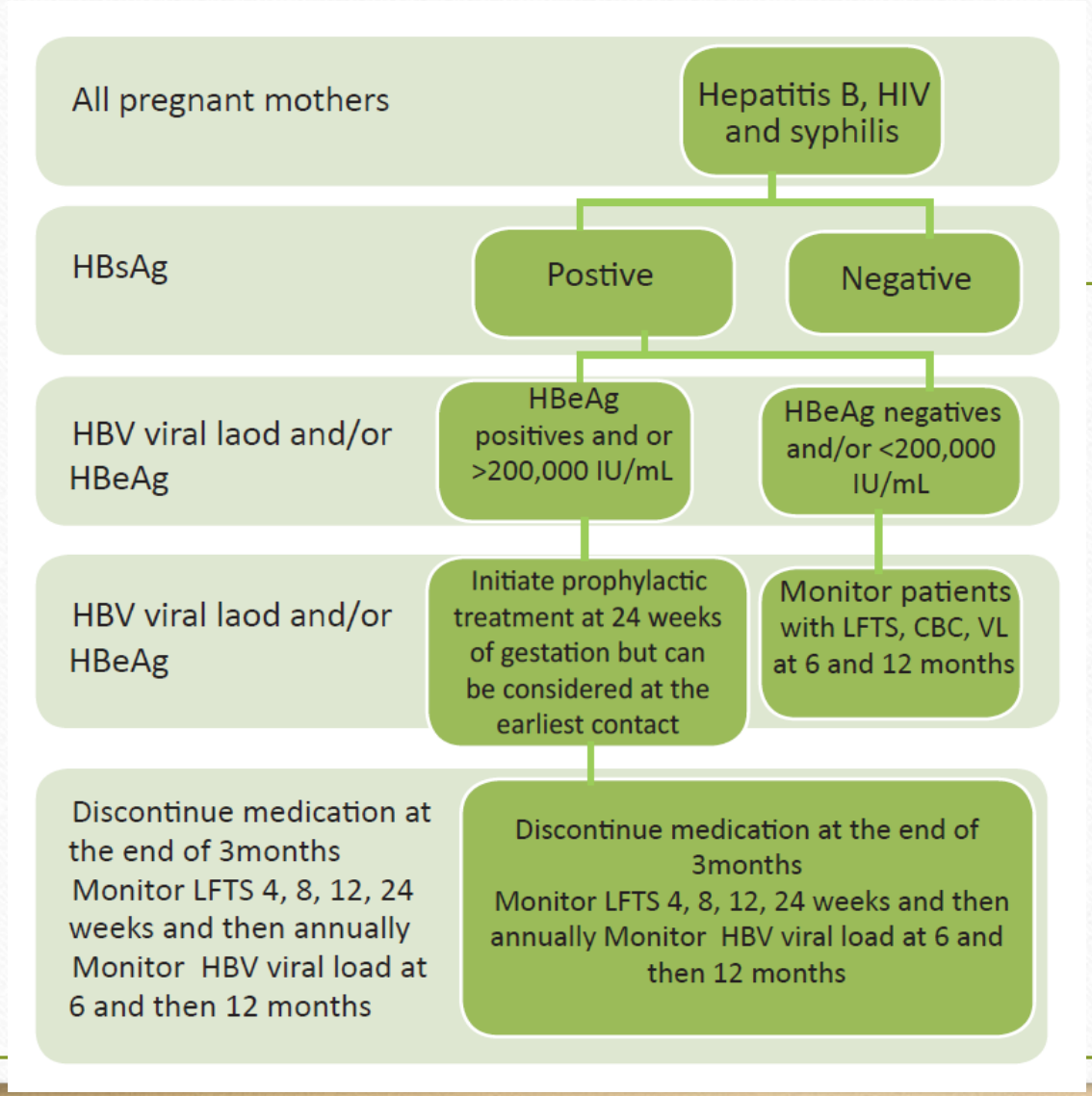
HEPATITIS B TESTING/TREATMENT ALGORITHM



*Abnormal ALT refers to ALT values that are atleast 2 times the upper limit of normal

UGANDA PMTCT-HBV IN PREGNANCY GUIDELINES

MINISTRY OF HEALTH



Recommendations:

- Pregnant women testing positive for HBV infection with an **HBV DNA ≥200 000 IU/mL** receive **tenofovir** prophylaxis from the **24th week of pregnancy** until at least birth, to prevent mother-to-child transmission of HBV.

- All infants should receive their dose of hepatitis B vaccine as soon as possible after birth; The birth dose should be followed by two or three doses to complete the primary series.

WHAT A SUCCESSFUL NATIONAL HEP B PMTCT ELIMINATION EFFORT NEEDS

- High ANC and neonatal care coverage
  - Intervention In Mother
    - Screening for Hepatitis B
    - Linkage to Management & Anti viral
  - Intervention in Infant
    - Vaccine : Birth Dose and three doses as per UIP
    - HBIG
    - Testing: Follow up; PVST*

Programmatic considerations:

Financing

Stigma, discrimination

Interventions

Health workforce

Testing

Data

*PVST: post vaccination serologic testing.

WHO TO TREAT

Category 1

- All children, adolescents and adults with CHB (HBsAg positive) with
  - Clinical evidence of cirrhosis and or
  - Adult patients with APRI score > 2
- ***Treat regardless of the Hepatitis B viral load level, HBsAg , ALT or HBeAg***

WHO TO TREAT
Category 2

- Patients who are co-infected with HBV and HIV
  - ***Treat irrespective of CD4, WHO stage, Liver enzymes, HBeAg***
  - ***Follow HIV treatment guidelines***

Signs and symptoms	**Acute Phase:** Non specific signs and symptoms : abdominal pain, fever, nausea, vomiting, +/-jaundice. **Chronic Phase:** Chronic fatigue, ascites, bleeding under the skin, jaundice, and mental derangement.
Screening for HBV	All PLHIV initiating or failing on ART should be routinely screened for HBV infection using Hep B surface Antigen (HBsAg).
Tests in persons diagnosed with HBV infection	**These tests should be done at baseline and at six months** ✓ A complete blood count. ✓ Liver function tests (ALT,AST, albumin and bilirubin levels, and PTT). ✓ Abdominal ultrasound scan ✓ AFP and HBeAg if available.
Treatment of HBV/HIV co-infected person	Initiate ART with TDF-containing regimen. <u>If ART cannot be given or if the patient refuses ART use:</u> Peg-IFN-alfa 2a 180 mcg subcutaneously once weekly for 48 weeks *or* Peg-IFN-alfa 2b 1.5 mcg/kg subcutaneously once weekly for 48 weeks.
Follow-up after six months	Evaluate the patient for HBV treatment failure: ✓ If jaundice, malaise and abdominal right upper quadrant pain are present **or** if LFTs are abnormal→ **do a viral load test.** ○ If HB VL unavailable or HB VL >200,000 IU/ml at 24 weeks of Rx: refer for further evaluation and management while continuing ART.
HBV prevention	✓ Risk reduction: Safe sex practices, avoid needle sharing and minimize risk from household contacts. ✓ Screen all household members and sexual partners/contacts ✓ HBV vaccination to all people regardless of HIV status in endemic areas.

WHO TO TREAT
Category 3

1. All patients **without** clinical evidence of cirrhosis with APRI score <2 but with

2. Persistent elevation of ALT- **ALT at least two times above the upper limit of normal, on 3 occasions at least every 3 months over a period of 6-12 months**

Exclude other causes of ALT elevation (Alcohol, drugs or herbs. If present, manage first

3. Hepatitis B viral load more than 20,000 IU/mL

Note: Both conditions MUST be fulfilled for treatment decision

PRE-TREATMENT ASSESSMENT

- **Complete medical history** must be completed, including identifying risk factors, co-morbidities, co-infections and pregnancy.

- **Complete physical exam** must be performed to look for the following symptoms: leukonychia, wasting, gynecomastia, jaundice, distended abdominal veins and palmar erythema.

- APRI scoring is a non-invasive measure of liver fibrosis/cirrhosis and is the recommended method for liver staging in Uganda.

WHAT TO TREAT WITH

- TDF and Entecavir are the recommended drug options
  - ~~Entecavir in children aged 2-11 years (who weigh at least 10 Kg) should be~~ given entecavirat 0.02mg/Kg (the medication is available in 0.5 and 1mg strength)
  - TDF for adolescents > 12 years and adults weighing at least 30 kg
- In renal disease, patients should be on Entecavir

In case of elevated creatinine, all those initially on TDF should be switched to Entecavir; if seen at a lower facility patients requiring this switching should be referred to a general hospital for further evaluation of their renal disease

WHEN TO STOP TREATMENT

- HBV has no CURE at the moment(Studies ongoing in the “CURE” agenda)

- Treatment if indicated is largely **LIFE-LONG!**

In very specific scenarios, treatment may be discontinued under stringent monitoring-*Functional cure,a very rare phenomenon.*

HBV TREATMENT DISCONTINUATION

- Hepatitis B treatment could be discontinued in patients with;
  - No cirrhosis (baseline APRI score <2)
  - Sero-conversion (loss of HBeAg and its replacement with anti-HBeAb),
  - Undetectable HBV viral loads
  - Persistently normal ALT
- When this seroconversion occurs, treatment should be continued for another 12 months after which it can be stopped
- These individuals should also be monitored since recurrence can occur
- Regardless of prior HBeAg status, treatment can be stopped one year after HBsAg becomes negative (functional cure)
  - This seroconversion is a rare occurrence!

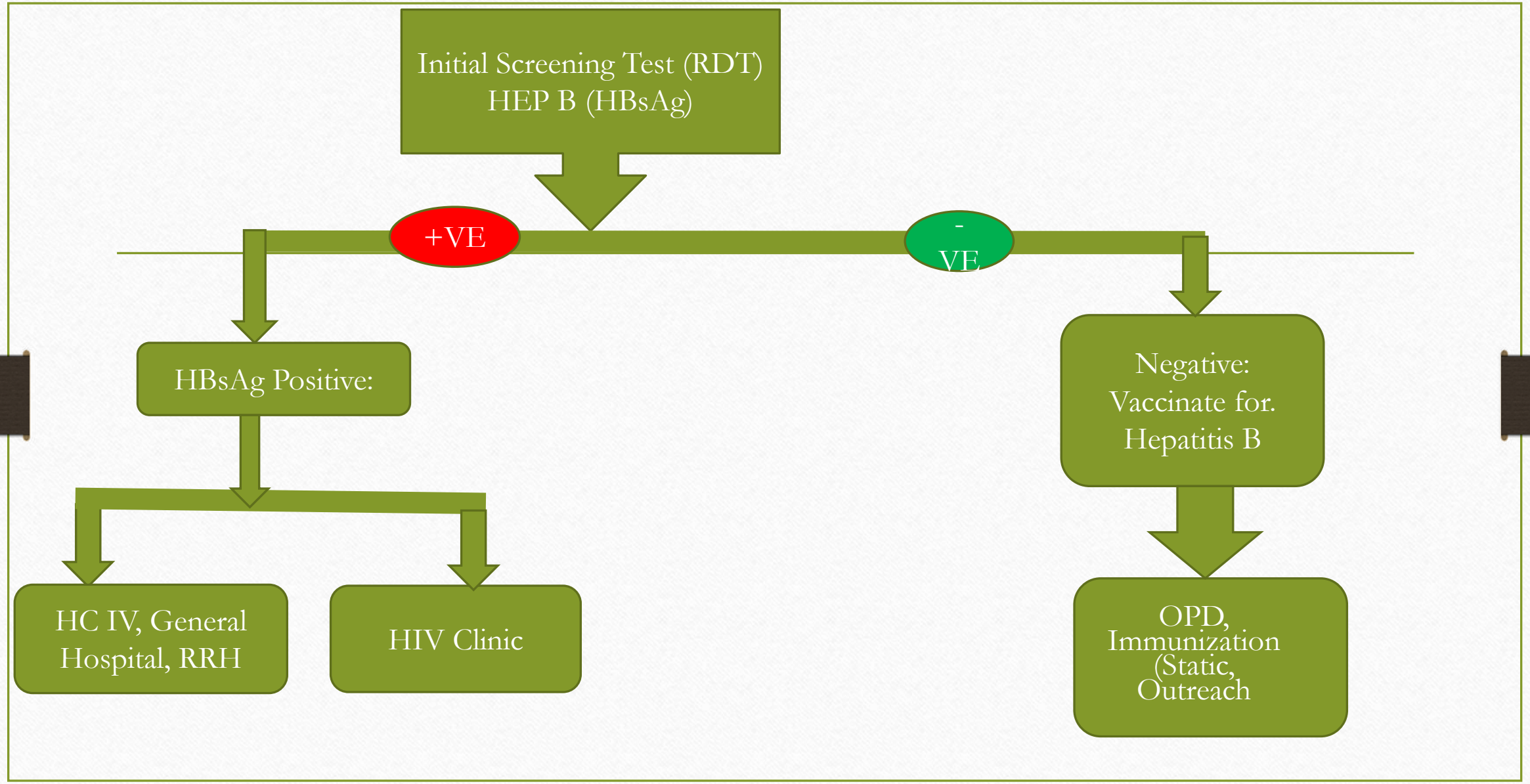
NEW WHO GUIDELINES FOR VIRAL HEPATITIS,2024(Highlights)

- Expanded treatment eligibility, and inclusion of adolescents;
- Alternative antiviral therapy regimens;
- Expanded eligibility for antiviral prophylaxis among pregnant women to prevent mother-to-child transmission;
- HBV diagnostics – use of point-of-care (POC) DNA assays and reflex HBV DNA testing;

NEW WHO GUIDELINES FOR VIRAL HEPATITIS,2024(Highlights)

- Testing for hepatitis delta(HDV) coinfection(accelerates progression to cirrhosis and Liver cancer; and
- Approaches to promote delivery of high-quality HBV services, including strategies to promote adherence to long-term antiviral therapy and retention in care.
- Note; Please wait for official guidance from MOH on implementing the revised guidelines.(The current National Hepatitis guidelines,2019 still apply until otherwise communicated).

REFERRAL AND LINKAGE FRAMEWORK



PREVENTION OF TRANSMISSION OF HBV

- Vaccination for Hepatitis B through routine immunization of all infants with the timely Hepatitis B birth dose given within 24 hours of birth or at the earliest opportunity before 7 days postpartum, three dose pentavalent vaccine and supplementary immunization activities-Main stay! Prevents HDV infection as well.

- Vaccination of individuals in all susceptible /high-risk groups(Monovalent vaccine)- health care providers, HIV infected persons, Persons receiving dialysis and others.

- Screening of all Donor blood for HBV

- Adherence to IPC measures in health care setting

- Screening and treatment of HBV pregnant mothers

TAKE HOME MESSAGES

- There is no virologic cure for HBV today.HCV infection is curable using Directly acting Antivirals(DAAs)
- The current goal of treatment is to prevent viral replication and further damage to the liver, as measured by undetectable viral load levels, improved liver histology.
- Pre-treatment assessment is vital to assess eligibility for treatment, complications of CHB and tolerability of the drugs if treatment is indicated.
- Hepatitis A and E mainly occur in outbreaks as transmission is through the oral-faecal route.Symptoms are often acute and self-limiting.
- Strengthening Water, Sanitation,and Hygiene interventions are main stay of prevention of Viral Hepatitis A and E.
- HCV infection is curable using Directly acting Antivirals(DAAs)-Refer to National Guidelines 2019 for details on screening and Management of HCV.

ACKNOWLEDGEMENTS

- Ministry of Health
- WHO
- PEPFAR/GF
- Busoga Health Forum
- CSOs
- Health care workers
- Baylor Foundation Uganda
- Partners

Busoga
HEALTH FORUM
Always caring, Always here, because your life matters

Thank you