LEBANESE SOCIETY OF GASTROENTEROLOGY
الجمعية اللبنانية لأمراض الجهاز الهضمي

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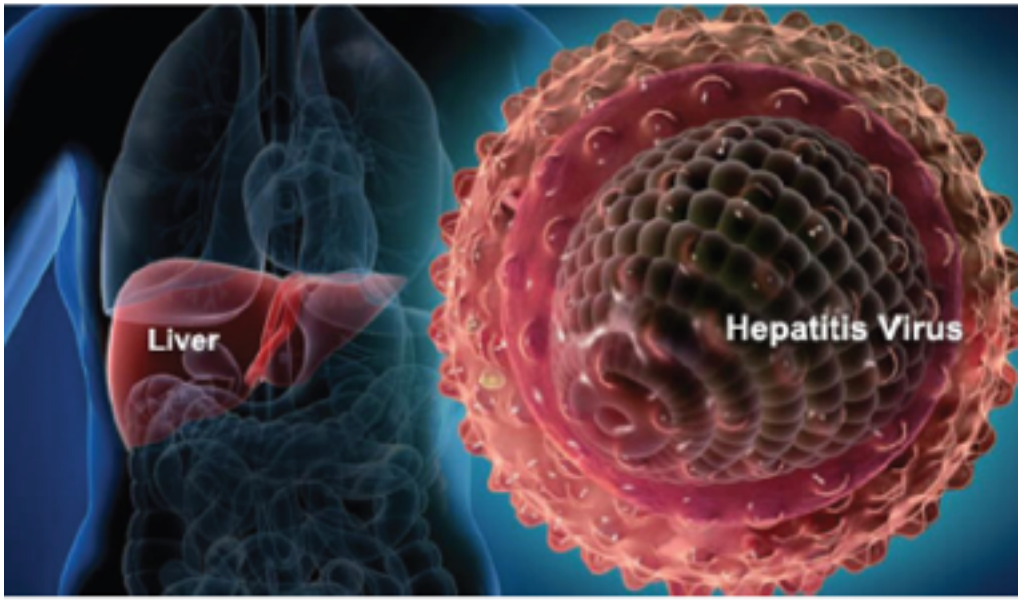

Lebanese Guidelines for the

Treatment of HBV Infection

Joint Taskforce from

the Lebanese Society of Gastroenterology
& the Lebanese Society of Infectious Diseases

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Questions ?

- Laboratory testing in the investigation of hepatitis B
  - Normal ALT, AST level
  - Quantitative HBsAg

Questions ?

- Review the algorithm concerning the management of hepatitis B (eAg+, eAg-)
  - Normal ALT ?
  - When liver biopsy is mandatory ?
  - Specify criteria for treatment
  - Specify criteria to stop treatment:
    - Each type of treatment
    - When to measure

Questions ?

- Treatment in specific situations:
  - Acute hepatitis B
  - Hemodialysis patients
  - HIV patients
  - Patients receiving immunosuppressive or immunomodulator treatment.

- I –Introduction and natural history
- II- Who should be screened for hepatitis B?
- III- Diagnosis and staging
- IV- Evaluation of Patients with Chronic HBV Infection
- V- Treatment
- VI- Monitoring During and After Treatment and Deciding When to Stop Treatment
- VII- Prevention of viral hepatitis, vaccination indications and vaccination protocols

I - Who should be screened for hepatitis B?

- Donors of blood, plasma, tissues, organs or semen
- Persons who are at risk of blood or body fluid exposures that might warrant post exposure prophylaxis
- Household and sexual contacts of persons with CHB
- HIV or HCV infected persons
- Persons who inject drugs (PWID)
- Men who have sex with men (MSM)
- Multiple sexual partners (>2/year or more than 20/life)
- History of sexually transmitted disease
- Sex workers
- Persons who are incarcerated
- Persons of transgender.
- Pregnant women
- Patients on hemodialysis
- Infants born to positive HBs Ag mother.
- Persons born in geographic regions with HBsAg prevalence > 2%
- Persons with elevated ALT/AST of unknown etiology
- Persons with selected conditions who require immunosuppressive therapy:
  - Chemotherapy
  - Immunosuppression for rheumatologic or gastroenterologic disorders
  - Immunosuppression related to organ transplantation

II- Diagnosis and staging

- Serologic and other laboratory tests for viral Hepatitis B
- Noninvasive assessment of liver damage
- Invasive assessment

II- Diagnosis and staging

Serologic and other laboratory tests for viral Hepatitis B

- HBsAg
- Anti – HBs
- HBeAg
- Anti – HBe
- Anti – HBc Total
- Anti – HBcIgM
- **qHBsAg**
- PCR HBV DNA
- Other Laboratory Tests
  - CBCD, BUN, creatinine
  - ALT, AST, gamma GT, Alkaline phosphatase, bilirubin, Albumin, globulin.(**normal ALT<30 IU/ml, AST<30 IU/ml**)
  - PT

II- Diagnosis and staging

Noninvasive assessment of liver damage

Test	Components	Fibrosis stages assessed	Requirements
APRI	AST, platelets	≥F2,F4 (cirrhosis)	Basic haematology and clinical chemistry
FIB-4	Age, AST, ALT, platelets	≥F3	Basic haematology and clinical chemistry
fibrotest	Gamma GT, haptoglobin, bilirubin, A1 apolipoprotein, alpha2 macroglobulin	≥F2, ≥F3, F4 (cirrhosis)	Specialized tests. Requires testing at designated laboratories. Commercial assay
Fibroscan	Transient elastography	≥F2, ≥F3, F4 (cirrhosis)	Dedicated equipment

II- Diagnosis and staging
Invasive assessment

– Liver biopsy is considered

- The gold standard method to stage liver disease and assess for the degree of fibrosis.

- The scoring system recommended is **METAVIR.**

III- Evaluation of Patients with Chronic HBV Infection

- Initial evaluation should include
  - History and physical examination
  - Family History of liver disease, HCC
  - Laboratory tests to assess liver disease
    - Complete blood counts with platelets,
    - Hepatic panel
    - Prothrombin time
  - Tests for HBV replication
    - HBeAg/anti-HBe
    - HBV DNA

III- Evaluation of Patients with Chronic HBV Infection

- Tests to rule out
  - viral coinfections
    - anti-HCV,
    - anti-HDV
    - anti-HIV

- Tests to screen for HCC
  - Alpha Foeto Protein
  - ultrasound

- Consider liver biopsy and /or fibroscan to grade and stage liver disease for patients who meet criteria for chronic hepatitis

IV- Treatment

- Who should be treated
- Who should not to be treated but monitored
- Monitoring for disease in persons who do not meet the criteria for antiviral therapy

IV- Treatment

Who should be treated:

- The group that has priority for treatment includes:
  - All adults, adolescents and children with **chronic hepatitis B and clinical evidence of compensated or decompensated cirrhosis**
  - Adults who do not have clinical evidence of cirrhosis but are **more than 30 years** old and have **persistently abnormal ALT (>2ULN)** levels and evidence of **high level HBV replication** regardless of HBeAg status

IV- Treatment

Who should not to be treated but monitored

- Antiviral therapy is not recommended and can be deferred in persons:
  - without clinical evidence of cirrhosis
  - with persistently normal ALT levels
  - low level of HBV replication regardless of HBeAg status or age

- Continued monitoring is necessary in all persons with chronic hepatitis B These include:
  - Persons without cirrhosis aged 30 years or less with HBVDNA levels>20000IU/ml but persistently normal ALT
  - HBeAg-negative persons without cirrhosis and are 30 years old or less, with HBV DNA levels that fluctuate between 2000 and 20000 IU/ml, or who have intermittently abnormal ALT levels

IV- Treatment

Monitoring for disease in persons who do not meet the criteria for antiviral therapy

- Persons with normal ALT: annual monitoring
- Persons who have intermittently abnormal ALT levels or HBV DNA levels that fluctuate between 2000 IU/ml and 20000 IU/ml: more frequent monitoring every 3-6 months

Monitoring tests:

- ALT levels, HBsAg, HBeAg and HBVDNA levels
- Non-invasive tests (APRI score or fibrotest or fibroscan annually) to assess for the presence of cirrhosis, in those without cirrhosis at baseline.

IV- Treatment

Drugs used for the treatment of chronic hepatitis B

Medication	form	dose	indications
Pegylated interferon alpha 2b	Injection 180 µg	180 µg once per week	Adult with chronic hepatitis or compensated cirrhosis
Tenofovir	Tablets 300mg	1 tablet qd	Children > 12years and weighing >35 kg adult with chronic hepatitis or compensated decompensated cirrhosis
Entecavir	Tablets 0.5mg	0.5mg qd	adult with chronic hepatitis or compensated cirrhosis and lamivudine naïve
	Tablet 1mg	1mg	adult with decompensated liver disease and lamivudine experienced
	Solution 10ml: 0.5mg	10 Kg to 11kg; 3ml >11Kg to 14Kg: 4ml >14Kg to 17Kg: 5ml >17kg to 20Kg: 6ml >20Kg to 23Kg: 7ml >23Kg to 26Kg: 8ml >26Kg to 30Kg: 9ml > 30Kg: 10ml	children 2 years of age or older and weighing at least 10 kg.
Lamivudine	Tablet 100mg	100 qd	adult with chronic hepatitis or compensated decompensated cirrhosis

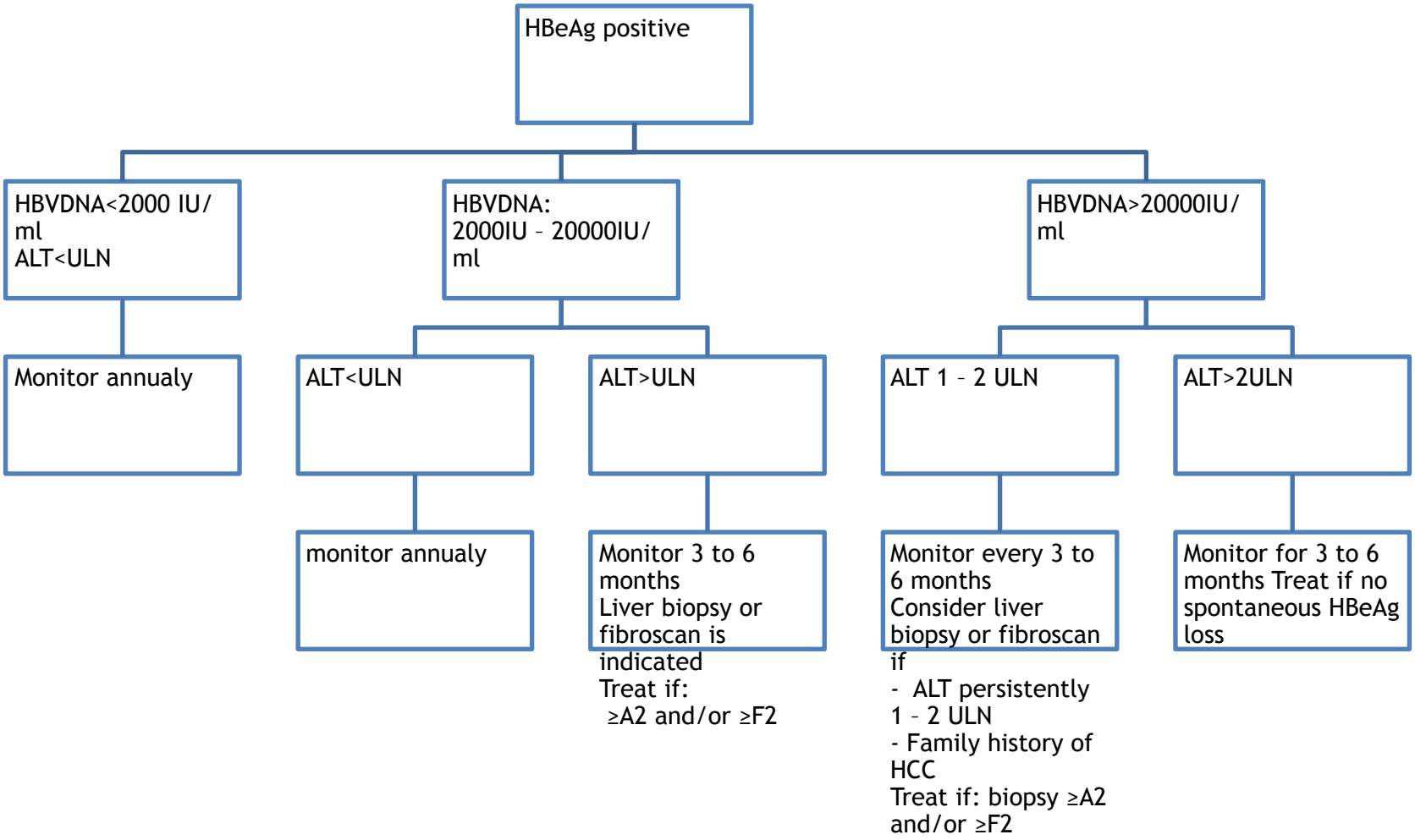
IV- Treatment

Recommended dosage in adults with renal impairment

Drug	Creatinine Clearance (mL/min)			
	>50	30 - 49	10 - 29	<10, Hemodialysis or CAPD
Tenofovir	300mg every 24 hours	300mg every 48 hours	300mg every 72 – 96 hours	300 mg every 7 days or 300mg following completion of approximately 12 hours of dialysis
Entecavir	0.5mg every 24 hours	0.25mg every 24 hours or 0.5mg every 48 hours	0.15 mg every 24 hours or 0.5 mg every 72 hours	0.05 mg every 24 hours or 0.5mg every 7 days
Entecavir (decompensated liver disease)	1 mg every 24 hours	0.5 mg every 24 hours or 1 mg every 48 hours	0.3 mg every 24 hours or 1 mg every 72 hours	0.1mg every 24hours or 1mg every 7 days

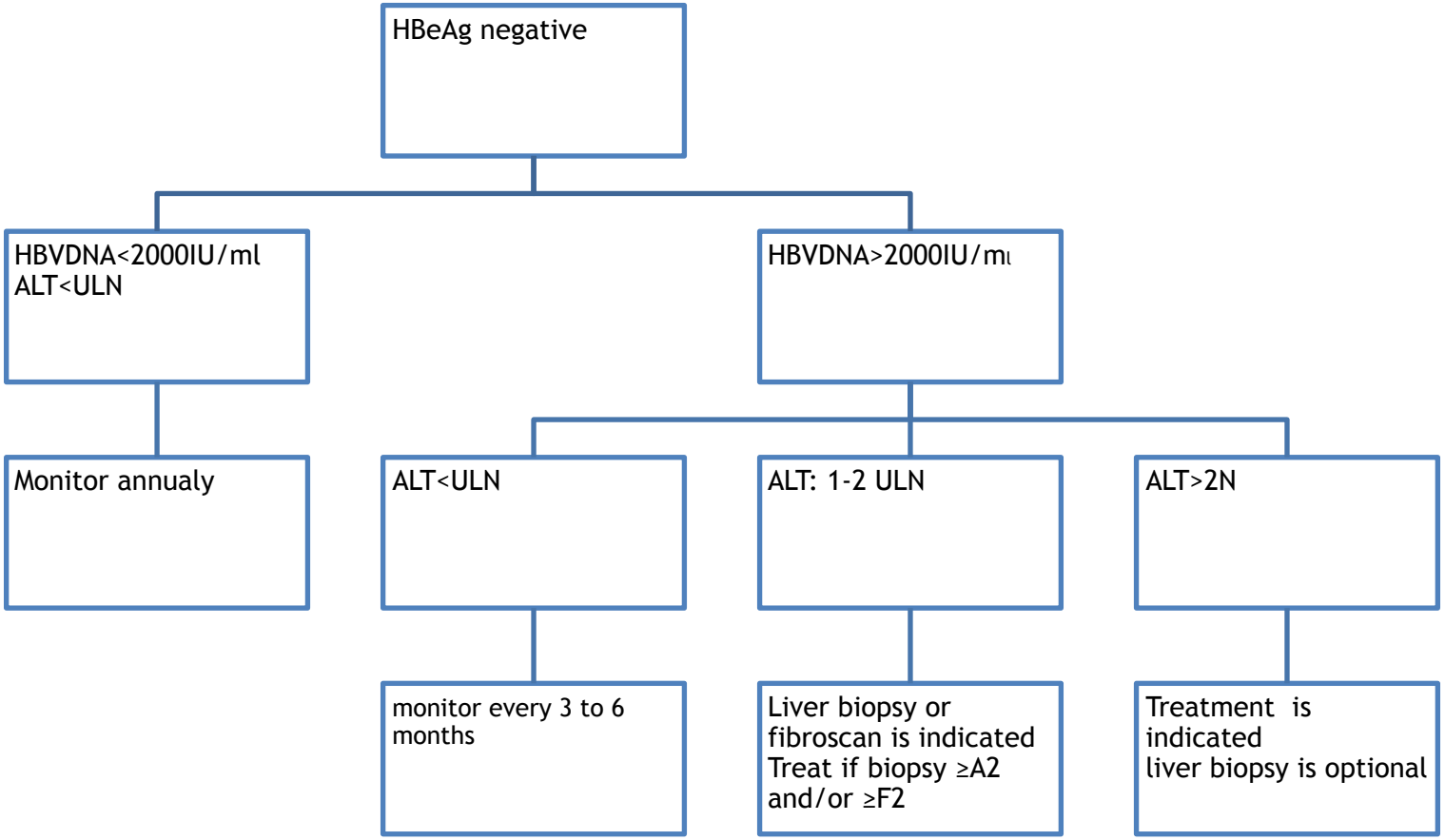
IV- Treatment algorithms

patients with HBeAg-positive



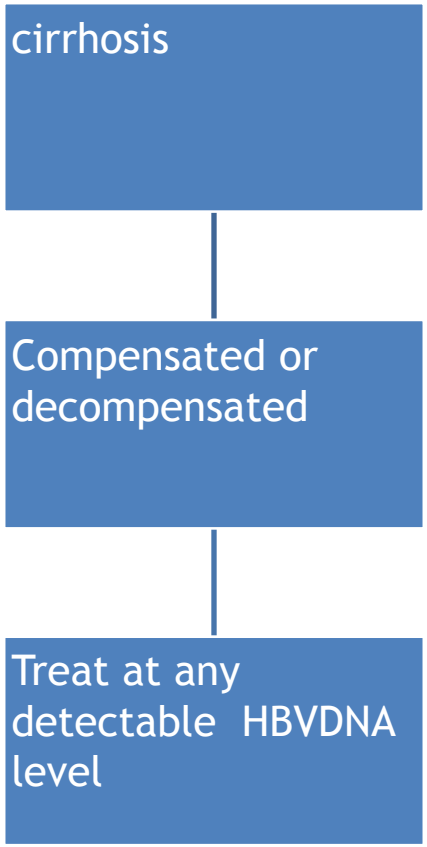
IV- Treatment Algorithms

patients with HBeAg-negative



IV- Treatment Algorithms

patients with cirrhosis



IV- treatment
Management of Specific situations

- Acute hepatitis
- Fulminant hepatitis
- Health care workers
- Pregnant women
- Treatment of patients on Chemo/ Immunosuppressive therapy

IV – treatment
Acute hepatitis

- Oral antiviral therapy may be given for patients with severe acute hepatitis B.
- Drugs should be stopped when HBsAg becomes negative
- HIV status should be tested before starting treatment

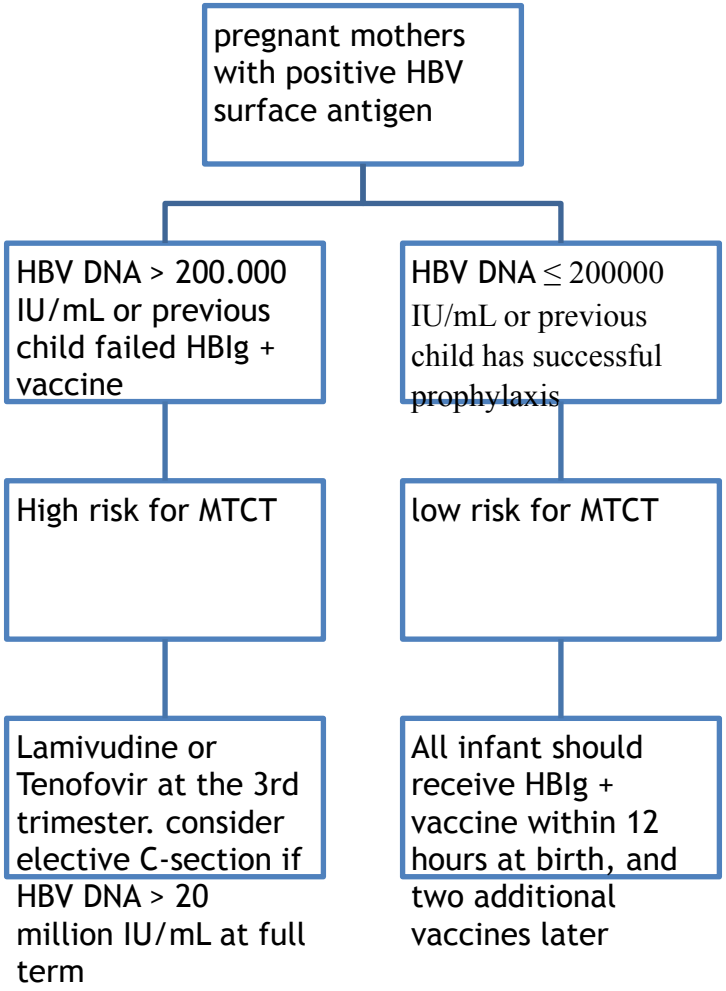
IV- Treatment
Fulminant hepatitis

- NUC should be given as soon as possible
- Start therapy before the prothrombin time goes below
  - 40% in patients with severe acute hepatitis B
  - 60% in patients with acute exacerbation of the carrier state.
- IFN may be administered in combination with NAs

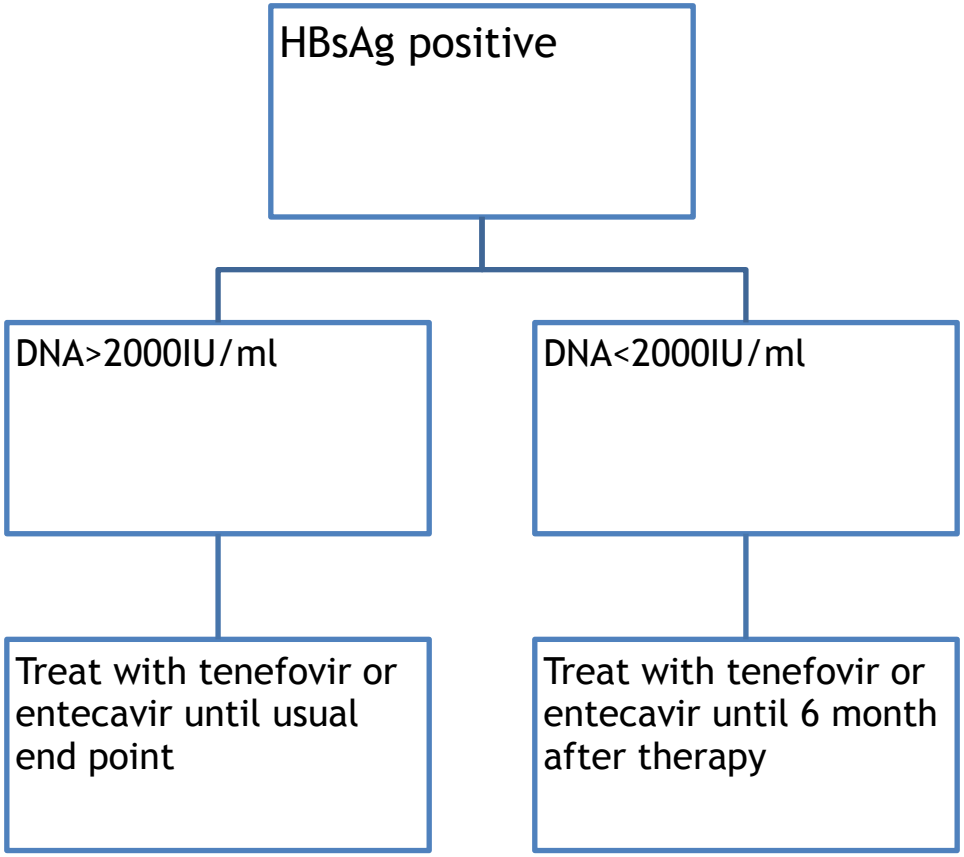
IV- Treatment
Health care workers

- Health care workers who are **HBsAg-positive with HBV DNA >2000 IU/ml** should be treated with a potent antiviral agent with a high barrier to resistance , to reduce levels of HBV DNA ideally to undetectable or at least to <2000 IU/ml before resuming exposure-prone procedures.

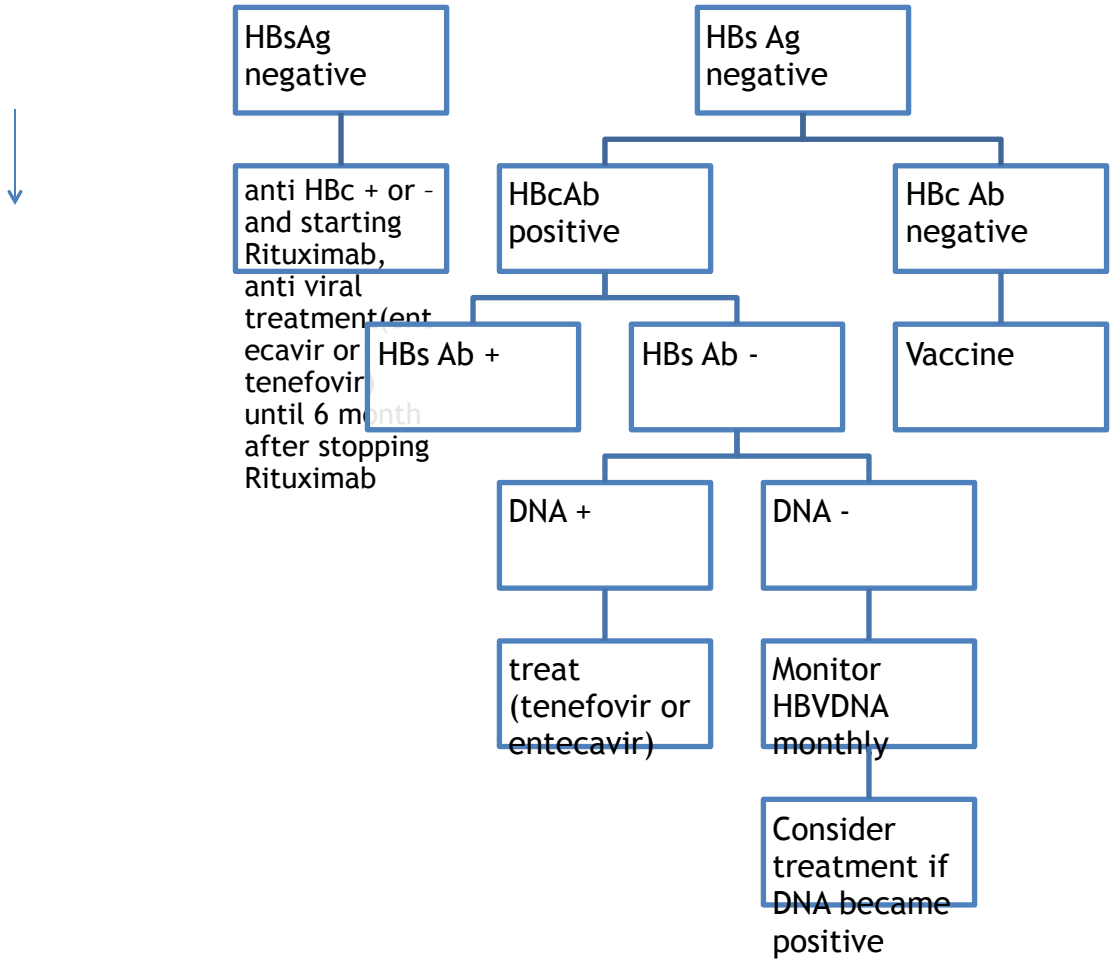
Pregnant women



Treatment of patients on Chemo/ Immunosuppressive therapy



Treatment of patients on Chemo/ Immunosuppressive therapy



V- Monitoring Patients receiving PEG-IFN During Treatment

- The following follow-up blood tests should be performed:
  - Blood count and liver panel at 4 weeks and then every 4 to 12 weeks as required according to previous CBC.
  - TSH every 12 weeks
  - HBV-DNA at week 24 and 48 (optional at week 12)
  - Quantitative HBsAg at week 24 (optional at week 12)
  - HBeAg and Ab every 24 week in initially HBeAg positive patients

V- Monitoring Patients receiving PEG-IFN When to Stop Treatment

- On treatment stopping rules:
  - Treatment should be stopped:
    - In HBeAg positive patients:
      - At Week 12: there is no decline in qHBsAg from baseline (any decline?) and/or HBsAg> 20000IU/ml
      - At Week 24: qHBsAg>20000 IU/ml
    - In HBeAg negative patients:
      - At week 12: there is no decline in qHBsAg and there is <2 log decline in HBV DNA
      - At week 24: the qHBsAg is >7500 IU/mL and/or there is ≤10% decline in HBsAg

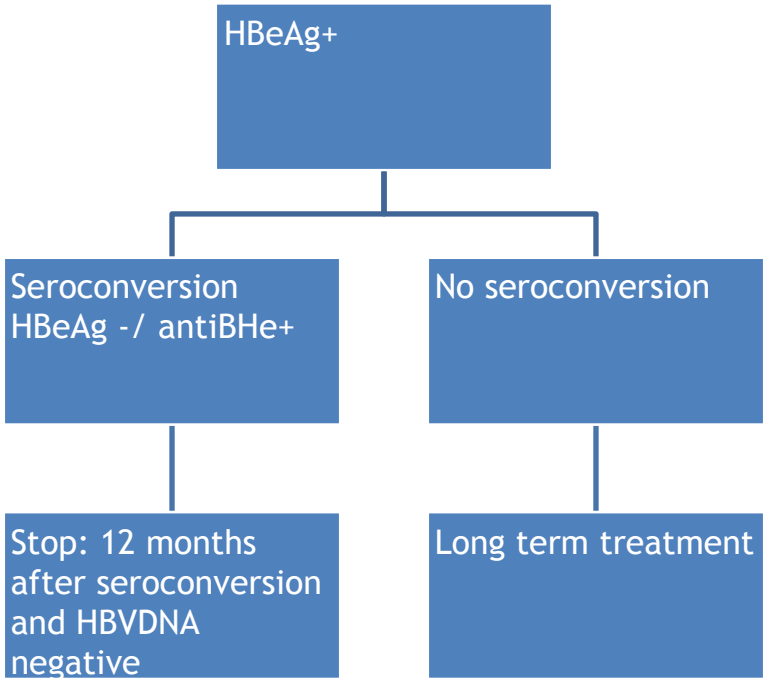
V- Monitoring Patients receiving PEG-IFN After Treatment discontinuation

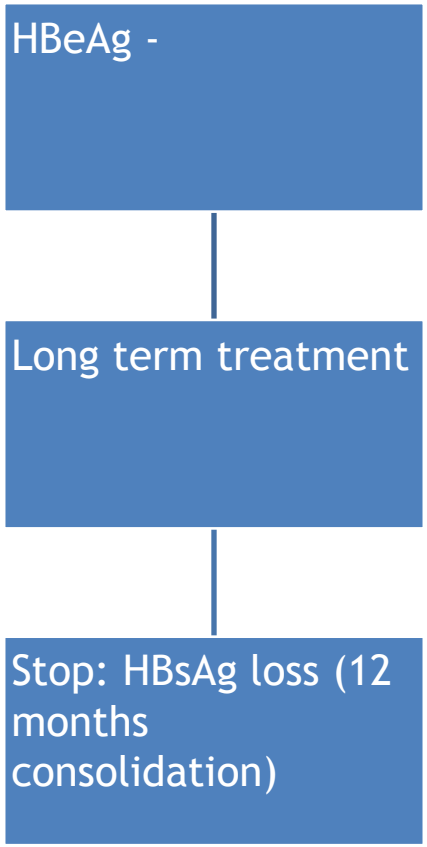
- After completion of treatment, the following blood tests should be performed:
  - Complete blood count, liver panel, HBe-Ag and anti-HBe (if initially HBe-Ag positive) at weeks 12 and 24 post- treatment
  - If HBe-Ag seroconversion occurs, test for HBsAb every 12 months
  - HBV-DNA every 3 months for the first year

V- Monitoring Patients receiving NUC During Treatment

- following blood tests should be performed:
  - Measurement of baseline renal function, monitoring annually
  - Growth should be monitored carefully in children.
  - Annual monitoring of ALT
  - HBV DNA every 6 months until it becomes undetectable, then every 12 months
  - HBe-Ag and Ab every 12 months
  - HBs-Ag every 12 months in patients HBeAg negative or patient who seroconvert from HBe-Ag positive
  - In compensated or decompensated cirrhosis, monitoring is recommended every 6 months.

V- Monitoring Patients receiving NUC
When to Stop Treatment





V- Monitoring Patients receiving When to Stop Treatment

- When can we stop NUC treatment
  - Persons with cirrhosis should never discontinue NUC therapy
  - HBV/HIV-coinfected persons initiated on therapy should also remain on long-term HBV suppressive therapy
  - Discontinuation of therapy can be considered in:
    - Sustained HBsAg loss.
    - HBeAg-positive persons
      - who seroconvert to anti- HBe after at least 1 year of treatment consolidation and
      - have undetectable HBV DNA levels and normal ALT levels.

    These persons should be closely monitored with serum ALT and preferably HBV DNA levels immediately after and for 1 year after stopping therapy because of the high early risk of relapse.

V- Monitoring Patients receiving NUC Monitoring after treatment discontinuation

- Long-term monitoring is required.
  - ALT and HBV DNA can be measured monthly for the first 3 months
  - Then every 3 months during the first year to detect severe exacerbations.

- Retreatment is recommended if there are consistent signs of reactivation
  - HBsAg or HBeAg becomes positive
  - ALT levels increase
  - HBV DNA becomes detectable again.

V- Monitoring for hepatocellular carcinoma (HCC)

- The risk of HCC is reduced but not eliminated with treatment.

- Routine surveillance for HCC with abdominal ultrasound and alpha-fetoprotein testing is recommended

  - Every year for HBs Ag positive without cirrhosis

  - Every six month for:
    - Persons with cirrhosis, regardless of age or other risk factors
    - Persons with a family history of HCC
    - Persons aged over 40 years, without clinical evidence of cirrhosis, and with HBV DNA level >2000 IU/mL

VI- Prevention of viral hepatitis, vaccination indications and vaccination protocols

- Prevention of viral hepatitis:
  - General measures to reduce HBV transmission include
    - HBV vaccination of household and sexual contacts
    - Alcohol reduction to reduce disease progression
    - Individuals who are HBsAg positive should also
      - Adopt correct and consistent condom use during sexual intercourse
      - Not share razors, toothbrushes, or other personal care items
      - Not donate blood, organs or sperm
      - Follow standard universal precautions with open cuts or bleeding.

VI- Prevention of viral hepatitis, vaccination indications and vaccination protocols

- Who should be vaccinated?
  - All neonates
  - Healthcare workers
  - Sexually active individuals with multiple sexual partners and homosexual or bisexual males
  - Household contacts of patients with hepatitis B
  - Intravenous drug users
  - Patients on chronic hemodialysis and patients requiring repeated blood or blood products transfusion
  - Patients with chronic liver disease
  - Immunocompromised patients
  - HIV infected patients
  - Prisoners

VI- Prevention of viral hepatitis, vaccination indications and vaccination protocols

- Vaccination protocols
  - At birth:
    - Administer monovalent Hepatitis B vaccine to all newborns before hospital discharge.
    - If mother is HBsAg-positive, administer Hepatitis B vaccine and 0.5 mL of hepatitis B immune globulin (HBIG) within 12 hours of birth.
    - If mother's HBsAg status is unknown, administer Hepatitis B vaccine within 12 hours of birth. Determine mother's HBsAg status as soon as possible and, if HBsAg-positive, administer HBIG (not later than age 1 week).
    - After the birth dose, the second dose should be administered at age 1 or 2 months and the final dose should be administered no earlier than age 24 weeks.
    - Administration of 4 doses of Hep B vaccine to infants is permissible when combination vaccines containing Hep B vaccine are administered after the birth dose.
  - In adults
    - Regimen consists of 3 doses: at times 0, 1 month and 6months
    - Booster in 10 years (in high risk groups)

VI- Prevention of viral hepatitis, vaccination indications and vaccination protocols

- Post vaccination testing for Serologic Response
  - Serologic testing for immunity (anti-HBs) is not necessary after routine vaccination of adults.
  - Testing after vaccination is recommended only for the following persons
    - Health-care workers and public safety workers at high risk for continued percutaneous or mucosal exposure to blood or body fluids
    - Chronic hemodialysis patients, HIV-infected patients, and other immunocompromised patients
    - Sexual partners of HBsAg-positive persons
    - Infants born to HBsAg-positive mothers should be tested for HBsAg and antibody to HBsAg (anti-HBs) after completion of 3 doses of the HepB vaccine, at age 9 through 18 months.
  - Testing should be performed 1-2 months after administration of the last dose of the vaccine (concentration of anti-HBs >10 mIU/mL).