REPUBLIC OF GHANA

NATIONAL GUIDELINES FOR PREVENTION, CARE AND TREATMENT FOR VIRAL HEPATITIS

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Forward

Viral hepatitis is inflammation of the liver caused by viruses. The causes of viral hepatitis include the five unrelated hepatotropic viruses, namely Hepatitis A, Hepatitis B, Hepatitis C, Hepatitis D, and Hepatitis E. Hepatitis A and E viruses typically cause acute and self-limiting infections. Hepatitis B and C (HBV and HCV) infections may progress into chronicity. HBV and HCV are currently the most important viral hepatitides in Ghana because they cause chronic infections. Infection is associated with increased risk of chronic liver disease, cirrhosis, and hepatocellular carcinoma (HCC). The latter is one of the commonest cancers in the country and has a high mortality. Suppression of HBV and HCV leads to reduction or delay in the development of cirrhosis and hepatocellular carcinoma (HCC).

The purpose of these guidelines is to provide evidence based step by step instructions for health staff required in the prevention, care and treatment of viral hepatitis.

I will therefore entreat all health workers to study and use these guidelines in-order to reduce the impact of Viral hepatitis on the populace of Ghana

Hon. Minister of Health

Preface

These treatment guidelines have been revised in collaboration with Hepatitis Society of Ghana (HepSoG) in line with current information. Several newer drugs since the last edition, have expanded the scope of treatment; however some of these are not yet available in Ghana.

Ghana is also yet to embark on any organized therapy countrywide. Hopefully this situation will change with time. Co-infection is recognized as a growing problem with important implications on management. These guidelines will assist clinicians in managing patients with chronic hepatitis B and C.

Dr Kofi N. Nkrumah.

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Abbreviations and Acronyms

CHPS	Community-Based Health Planning System
CMV	Cytomegalovirus
CHB	Chronic hepatitis B
HAV	Hepatitis A Infection
HBV	Hepatitis B Infection
HBV	Chronic Hepatitis B
HCV	Hepatitis C Infection
HDV	Hepatitis D
HCC	Hepatocellular carcinoma
HEV	Hepatitis E Infection
WHO	World Health Organization
CIF	Case-based Investigation Form
RNA	Ribonucleic acid
HBsAg	Hepatitis B Surface Antigen
IgM	Immunoglobulin M
IgG	Immunoglobulin G

HELLP Syndrome

ULN

APRI Score	Aminotransferase/platelet ratio index
DAA	Direct-acting antiviral (drugs)
PWID	Persons who inject drugs
ALT	Alamine aminotransferase
AST	aspartate aminotransferase
gGT	gamma glutamine transpeptidase

1. Introduction

1.1 Background

Hepatitis (plural:hepatitides) is inflammation of the liver characterized by the presence of inflammatory cells in the liver. Hepatitis can be caused by infectious or non-infectious agents/substances such as viruses, bacteria, toxins, drugs, and alcohol use. Viral hepatitis is inflammation of the liver caused by viruses. Viral Hepatitis is commonly caused by one of several viruses[2, 3, 4]. The causes of viral hepatitis include the five unrelated hepatotropic viruses, namely; Hepatitis A, Hepatitis B, Hepatitis C, Hepatitis D and Hepatitis E. In addition to the nominal hepatitis viruses, other viruses that can also cause liver inflammation include Herpes simplex, Cytomegalovirus (CMV), Epstein-Barr virus, Yellow fever virus, coxsackie viruses and adenovirus among others[2, 3, 4]. Hepatitis A and E viruses typically cause acute and self-limiting infections. Hepatitis B and C (HBV and HCV) infections may progress into chronicity. HBV and HCV are currently the most important viral hepatitides in Ghana because they cause chronic infections. Both may be acquired in childhood and any time thereafter. Infection is associated with increased risk of chronic liver disease, cirrhosis, and hepatocellular carcinoma (HCC). The latter is one of the commonest cancers in the country and has a high mortality. Suppression of HBV and HCV leads to reduction or delay in the development of cirrhosis and hepatocellular carcinoma (HCC). The introduction of standard interferon (alpha -2a & 2b) monotherapy marked the beginning of drug therapy in 1992 (insert reference) although the overall response was low. Subsequently several other molecules have been developed all in attempt to improve response.

1.2 Scope and Objectives

The general objectives of these guidelines is to provide evidence based step by step instructions for health staff required in the prevention, care and treatment of viral hepatitis. These guidelines covers the management of all the five different types of viral hepatitis namely; acute viral hepatitis A, B, C, D and E and chronic hepatitis B and C.

The specific objectives are:

- To provide measures required in prevention of viral hepatitis
- To provide steps in early detection and response to viral hepatitis cases
- To provide guidance in the care and treatment for all persons living with chronic viral hepatitis B and C

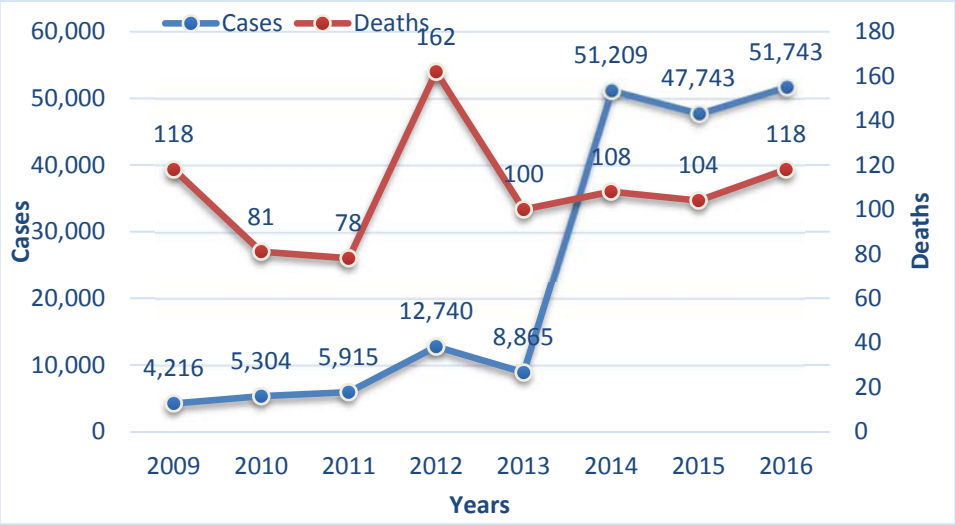
1.3 Target Audience

This guide is primarily intended for all health staff including clinicians, nurses, laboratorians, disease control and surveillance officers, public health experts etc working at all levels of the health system (from Community-Based Health Planning System (CHPS) to Tertiary level).

1.4 Epidemiology

Viral hepatitis has become a major public health concern globally. Over 3 billion people world-wide are exposed to the infection yearly (insert reference). An estimated 1 in 12 persons are currently infected and have to face a life with liver disease like Chronic Hepatitis, Cirrhosis of the Liver and Liver Cancer (Insert reference). Worldwide, over 500 million persons are living with chronic hepatitis B virus or hepatitis C virus infections, and these infections cause over 1 million deaths annually (insert reference); most persons with chronic viral hepatitis are unaware of their infections. Hepatitis B and C are major causes of cirrhosis and liver cancer and the second leading cause of cancer death in the world. Viral Hepatitis has become a major public health problem in Ghana. Surveillance data on clinical viral hepatitis from the Disease Surveillance Department (using the IDSR standard case definition for viral hepatitis) shows an increasing annual trend of reported clinical viral hepatitis cases from all the ten regions of Ghana[1] (Figure 1).

Figure 1: Annual Trend of Reported Acute Viral Hepatitis Cases and Deaths; Ghana, 2009-2016



Source: DHIMS GHS, 2016

Ghana belongs to the areas where the prevalence of chronic HBV infection is high (≥8%) [2] and that of hepatitis C virus is also high (5-10%) [3].

Recent studies have revealed HCV sero-prevalence rates of 2.8% to 5.4% in Ghana [8, 9]. The seroprevalence of HCV is between 1·3 and 8·4% among blood donors in Ghana[9, 12, 13] 5·4% among children in a rural district in Ghana[7] and 2·5% among parturient in Accra, Ghana[16]

The risk of developing cirrhosis increased 8-fold in patients with HBV infections than those without[15]. Hepatitis E (HEV) sero-prevelance was 28.66% (45/157) among pregnant women seen between the months of January and May, 2008 at the Obstetrics and Gynaecology Department,

Korle-Bu Teaching Hospital, Accra, Ghana. 2009 Adjei et al; licensee BioMed Central Ltd.

Acute infection is often insidious and asymptomatic. The virus persists in about 80% of acutely infected patients who become chronic carriers.

1.5 Risk Factors

1.5.1 Risk factors for Viral Hepatitis A and E

- Over-populated communities (slum and refugees camps) characterized by: Poor sanitation, Use of unsafe drinking water
- Poor personal hygiene (low soap utilization, or poor hand washing practices)
- Poor food hygiene
- Floods leading to contamination of domestic water sources
- Broken down water and waste disposal systems
- Open defecation

1.5.2 Risk Factors for Viral Hepatitis B, C and D

- high-risk sexual behaviour
    - Persons with multiple sexual partners

- Commercial sex workers
- Men having sex with men-homosexuals
- Unsafe sex;

- Non-immune partners and household contacts of HBV infected persons
- Intravenous and percutaneous drug use e.g. Injection Drug Users
- Individuals in prisons and persons born in countries with high rates of endemic disease.
- Persons who frequently require blood or blood products e.g regular renal dialysis patient
- Recipients of solid organ transplantation;
- Those at occupational risk of HBV infection, including health care workers; and international travelers to countries with high rates of HBV
- Practices such scarification, blood letting, circumcision with unsterile instruments, tattooing and body piercing.

1.6 Mode of Transmission

Hepatitis A and E virus is transmitted primarily by the faecal-oral route, that is when an uninfected person or ingest ~~i~~ food or water that

has been contaminated with the feaces of an infected person. The virus can also be transmitted through close physical contact of an infected person.

Hepatitis B, C and D viruses are transmitted by exposure to blood and various body fluids through

i. Percutaneous or mucousal exposure to infected blood or various body fluids (vaginal fluids, seminal fluids, menstural fluids and saliva)

   This can happen through

   - un-protected sexual contact with an infected person, either heterosexual or homosexual. This is the most important route of transmission.
   - Re-use of contaminated needles and syringes, eg shared needles in drug abusers
   - Circumcision with unsterilized instruments
   - Tattooing, body piercing, sharing razors

ii. Spread from mother to child at birth (perinatal transmission) An important route of transmission in Ghana.

iii. Horizontal transmission (exposure to infected blood) especially from an infected child to an un infected child during the first 5 years of life

iv. Transfusion with contaminated blood and other blood products (This is less likely now that blood donors are screened)

Modes of transmission are the same for the human immunodeficiency virus (HIV), but HBV is 50 to 100 times more infectious.

Unlike HIV, HBV can survive outside the body for at least 7 days. During that time, the virus can still cause infection if it enters the broken skin or lining of a person who is not infected.

1.6 Clinical Presentation

The presentation of Viral Hepatitis can be in two forms namely Acute and Chronic. Viral Hepatitis is defined as acute when it lasts less than six months and chronic when it persists longer.

The clinical presentation of acute hepatitis is similar for all five viruses. It ranges from the absence of symptoms to mild or moderate features such as jaundice, poor appetite and malaise. In a minority of cases it may result in fulminant hepatitis with a potentially fatal outcome.

Non-specific features are flu-like symptoms, common to almost all acute viral infections and may include malaise, muscle and joint aches, fever, nausea or vomiting, diarrhea, and headache. More specific features include profound loss of appetite, jaundice (yellowing of the skin and eyes), dark urine and abdominal discomfort. Less common features are tender hepatomegaly, lymphadenopathy and splenomegaly. Acute viral hepatitis is more likely to be asymptomatic

in children. Majority become chronic. Only 30% to 50% of adults develop significant symptoms during acute infection.

2. Preventive Measures for Viral Hepatitis

2.1 Hepatitis A and E

The following intervention areas should be implemented to prevent acquiring Viral Hepatitis A and E

- Vaccination
- Regular hand washing with soap under safe running water; before eating, after visiting the wash room, and before cooking
- Practice Good sanitation and personal hygiene practice
- Safe food handling practice; eat food whilst hot, wash plates and cutleries with safe water and soap before use.

2.2 Prevention of Viral Hepatitis B, C and D

The following intervention areas should be implemented to prevent acquiring Viral Hepatitis B, C and D.

1a) Vaccination against Hepatitis B (No Vaccine for Hepatitis C)

Vaccination is recommended for the non-infected (No detectable HBsAg), and non-immune patients (No detectable Anti-HBs) i.e. all

infants.

1b) Hepatitis B Vaccination schedule

- Three doses of hepatitis B vaccine given 0,1 and 6 months interval

1c) Persons eligible for Hepatitis B vaccination

The following categories of persons should be vaccinated with hepatitis B vaccine.

- Infants born to HBsAg positive women. Hepatitis B immunoglobulin should also be added (PMTCT HepB)

- All new-born infants should be given birth dose of hepatitis B vaccine. Continue with three doses as part of routine childhood immunization at child welfare clinics starting from six weeks as part of DPT-HepB-Hib vaccine

- At risk populations such as health workers (including trainee students and newly recruited staff), partners and household members of Hepatitis B positive persons should be screened and those negative for hepatitis B vaccinated.

2) **Practice safe sex**

Use condoms appropriately. Avoid multiple partners

3) **Blood safety**

All blood should be screened for Hepatitis B and C before transfusion

4) **Infection Prevention and control measures**

Process all instruments/sharps (by decontamination with 0.5% chlorine, cleaning and high level decontamination or sterilization) before use at all health and non-health facilities. (refer to MOH IPC Policy guidelines 2015). Practice safe injections, use only sterile needles and syringes. Avoid sharing sharps (blades, needles and syringes) and tooth brushes etc with others

2.3 Role of diet and healthy lifestyle in preventing hepatitis

Eating balanced diet including lots of fruits and vegetables protects the liver. Agents that damage the liver such as alcohol and smoking are particularly harmful in patients who already have hepatitis B. For this reason, it is recommended that persons with hepatitis B avoid drinking alcohol and smoking.

Avoid multiple partners, practice safe sex, use condom, avoid sharing of sharps like blades and needles.

2.4 Screening

Periodic mass screening of persons at risk for Hepatitis B and C should be conducted by trained health staff. Persons should be counselled before and after screening. Only WHO pre-qualified testing reagents should be used (Refer to lab section). Viral Hepatitis Case Investigation Form (CIF) should be used to capture information on all persons screened (Refer to data management section). Only Persons who test negative should be vaccinated against the respective viral hepatitis e.g.

Hepatitis A, B and E vaccines. All persons who test positive should be referred to health facilities for care and treatment.

The following persons should be screened for Hepatitis B and C routinely.

- All health care professionals (additionally pre-employment and exit screening would be required)
- All health care trainees
- All pregnant women reporting at ante-natal care (for positive mothers Infants born to HBsAg positive women to be given hepatitis B vaccine and hepatitis B immunoglobulin (PMTCT HepB)
- First degree relatives and partners of known positives
- All donated blood
- All suspected cases reporting to health facilities.

3. Surveillance for Viral Hepatitis

3.1 Definition of Surveillance

Disease Surveillance is the ongoing systematic and regular collection, collation, analysis and interpretation of data on the occurrence, distribution and trends of a disease with sufficient accuracy and completeness and the dissemination of information to those who need to know to take action (disease control).

Importance of viral hepatitis Surveillance:

Surveillance of viral hepatitis is essential for generating information that may lead to:

- Early Detection of outbreaks, monitor trends in incidence and identify risk factors for new, incident infections. This is done through Surveillance for acute viral hepatitis in health facilities
- Forecasting acute viral hepatitis outbreaks
- Monitor trends of acute and chronic viral hepatitis cases and deaths
- Evaluate control measures that are being instituted
- Estimate the prevalence of chronic infections and monitor trends in sentinel groups. This is by keeping surveillance on chronic infections.
- Estimate the burden of sequelae i.e. Surveillance for cirrhosis and Hepatocellular carcinoma (HCC)

3.2 Sources of Surveillance Information

The following are the sources of surveillance information:

1. Acute viral hepatitis cases reporting to health facilities.
2. Reports from community based surveillance workers on outbreak of fever with jaundice cases
3. Analysis of daily/weekly/monthly routine surveillance data on acute and chronic viral hepatitis cases by health workers in the health facility (both outpatient and in-patient records).
4. Surveys-e.g. screening of populations at risk and identifiable groups (churches, schools etc)
5. Reports from print and electronic media
6. Rumours from communities

3.3 Types of Viral Hepatitis Surveillance

There are three domains of viral hepatitis surveillance namely, surveillance of acute hepatitis, surveillance of chronic infections and surveillance for sequelae i.e. the complications of chronic viral hepatitis such as hepatocellular carcinoma.

a) Surveillance of acute hepatitis is done to identify and understand the sources of new infections and prevent

them. This is done through collecting information on persons with acute hepatitis in health care settings.

b) Surveillance for chronic prevalent infections is done to estimate how common these are. That is done through approaching persons without signs and symptoms of acute hepatitis, mostly in biomarker surveys-by screening general populations, specific at risk population e.g. health workers, prisoners, commercial sex workers etc.

c) Surveillance for sequelae is done to measure the impact of control measures/treatment on mortality reduction. To this effect, data is captured on persons diagnosed with hepatocellular carcinoma or cirrhosis in tertiary centres.

3.4 Viral Hepatitis Standard Case Definition

Case definitions are a set of criteria used to determine whether a person has viral hepatitis. Viral Hepatitis is a weekly/monthly notifiable disease in Ghana. The following standard case definitions are used:

Acute Viral Hepatitis case definitions:

Suspected case:

- Any person with onset of an acute illness with signs or symptoms of:

- (a) acute illness (fever, jaundice, dark urine, anorexia, malaise, extreme fatigue right upper quadrant abdominal pain) and
- (b) hepatic injury (elevated liver enzymes)

Confirmed case: A suspected case that is laboratory confirmed by virus specific biomarkers

- Hepatitis A: IgM anti-HAV positive or positive RNA
- Hepatitis B: HBsAg, IgM anti-HBc positive
- Hepatitis C: Anti HCV positive AND IgM negative for HAV, HEV, and anti-HBc OR RNA positive/ Anti-HCV negative
- Hepatitis D: IgM anti-HBc positive plus anti-HDV positive (only as co-infection or super-infection of hepatitis B)
- Hepatitis E: IgM anti-HEV positive

Chronic Viral Hepatitis case definition (HBV and HCV):

Any person not meeting the case definition for acute viral hepatitis and has specific biomarkers.

Chronic Hepatitis B:

- HBsAg is the first serological marker to appear. Persistence of HBsAg for at least 6 months indicates chronic infection
- HBeAg is present or absent with positive anti HBcIgG or HBcIgM

Chronic Hepatitis C

- Serological evidence of past or present infection; Anti HCV positive
- Hepatitis C virus RNA present in a person with antibodies against hepatitis C (Anti-HCV positive)
- HCV RNA positive OR HCV Ag positive

NB: Antibody detection cannot differentiate between acute and chronic infection

3.5 Data management

For all suspected/confirmed acute or chronic Viral Hepatitis cases, some basic patient information should be collected using the Viral Hepatitis case-based investigation form (CIF) and summarized on the line listing form. The Viral Hepatitis data capture and reporting tools are annexed.

Data Capture and Entry

At Facility Level

Use of Case-based form: For each suspected Viral Hepatitis case reporting at all health facilities, the Disease Control /Surveillance Officers/designated Focal Persons are to ensure that blood specimen is collected and fill the Viral Hepatitis case-based investigation form (see annex 4). Provide a unique identifier (Epid. Number: Country code (CCC)-Region code (RRR)-District code (DDD)-Year code (YY)-Case Number (NNN): [CCC-RRR-DDD-YY-NNNN] to link the laboratory results with the patient clinical/epidemiological records. Keep a copy of the Viral Hepatitis case-based Investigation form at the facility, send copy to district level, and send a copy each to the region and National Viral Hepatitis Control Programme (national level) and the other copy together with the blood specimen sent to the referral laboratory (Regional Hospital Laboratory, Zonal Public Health Laboratory or National Public Health and Reference Laboratory. This Epid. Number is given by district level Disease Control/Surveillance Officer.

Use of DHIMS: Health Information Officers and Disease Control/Surveillance Officers at all health facilities should enter the summary data on suspected/confirmed acute/chronic Viral Hepatitis into the District Health Information Management System (DHIMS2) platform weekly.

The District Disease Control/Surveillance Officer and the Regional Surveillance Officer and Data Manager should validate

data entered.

Data on blood screened: The Disease Control/Surveillance Officer and Laboratory Officers should capture summary data on all blood screened for Viral Hepatitis B and C at the health facilities using the Viral Hepatitis Blood Donors Screening form (see annex 5). This should then be entered into the DHIMS2 platform monthly.

Cancer Registers: All persons diagnosed with hepatocellular cancer should be captured in a designated register at health facilities especially teaching hospitals. The District Disease Control/Surveillance Officer and the Regional Surveillance Officer in collaboration with Physician Specialist should complete the register and monthly enter summary data on the hepatocellular cancer cases and deaths into the DHIMS platform (refer National Cancer Register)

At District Level

The District Disease Control/Surveillance Officers enters the Case-based forms from health facilities into a computer programme, eg Epi-Info. They will also enter the laboratory data and tests results on the same database. The completed data base will then be sent to the regional level on a weekly/monthly basis.

At Regional Level

The data base received from the districts will be merged by the

Regional Data Manager in collaboration with the Regional Disease Control/Surveillance Officers into a single database and sent to the national level on a weekly/monthly basis. The Data Manager at the Regional level should check for data entry flaws and clean the data base on a weekly basis. He/She should make sure that clinical and laboratory data of each patient are linked, before analysis.

At National Level

The data bases received from the regions will be merged into a single national database using preferably Excel/Epi-Info before sharing with Health Developmental Partners on a monthly basis. The Data Manager at the National Viral Hepatitis Control Programme (NVHCP) should check for data entry flaws and clean the data base on a weekly basis. He/She should make sure that clinical and laboratory data of each patient are linked, before analysis. The National Public Health and Reference Laboratory (NPHRL) shall collate all Viral Hepatitis test done at all laboratories. The data from the NPHRL will be computerized using Excel/epi-info then sent to the NVHP where they will be linked to the clinical data using the Epid-number. The results will then be sent to the regions and districts where the specimen came from.

Data Reporting:

Acute Viral Hepatitis data should be reported weekly, whilst

Chronic Viral Hepatitis B and C is reported monthly throughout the year. Facilities and Districts should report weekly/monthly, even when no cases are recorded ("Zero reporting").

During outbreaks of Acute Viral Hepatitis, the reporting of cases and deaths should be done on a daily basis. The line list should be completed at the health facility level, compiled at district level and a copy sent to the regional and national levels, on a daily basis.

All summary data captured in DHIMS should be reported monthly.

Data analysis

The Disease Control/Surveillance Officers at each level should calculate the Incidence Rate for Acute Viral Hepatitis cases and Prevalence Rate for Chronic Viral Hepatitis B and C cases and Case Fatality Rate. The data should be analysed further by person (age, sex),), place (affected communities, districts) and time (weekly/monthly trends of cases and deaths). The results should be illustrated with tables, spot maps and graphs (epidemic curves) every week/month. The supervisors at regional and national levels should ensure that all districts keep an up-to-date weekly and monthly trend (epidemic curve) of Acute and chronicViral Hepatitis cases and deaths respectively.

Every month, the Data Manager of the NVHCP should make a map showing the distribution of cases and deaths by district, as well as the laboratory results by district.

4. Laboratory Diagnosis of Viral Hepatitis

For all suspected cases of Viral Hepatitis blood samples should be taken by Laboratory Officers and sent to the referral labs for testing on Viral Hepatitis A, B, C, D and E. The referral labs are all the 10 Regional hospital Laboratories, and all Public health Reference laboratories (Tamale, Sekondi-Takoradi, Kumasi, and Accra). The District and Regional Disease/ Surveillance Officers shall coordinate the collection and transportation of the blood samples..

4.1 Laboratory Diagnosis for Acute Viral Hepatitis

Table 1 below describes specimen collection, storage, transportation and laboratory test for confirmation of all types of Viral Hepatitis: Only WHO prequalified standard hepatitis testing kits/reagents should be used.

Table 1: Specimen collection, storage, transportation and laboratory test for confirmation of all types of Acute Viral Hepatitis

Diagnostic test	Hepatitis A: IgM anti-HAV positive or RNA positive Hepatitis B: +ve for Hepatitis B surface antigen (HbsAg) or IgM anti-HBc positive Hepatitis C: Anti-HCV positive or positive RNA Hepatitis D: HBsAg positive or IgM anti-HBc positive plus anti-HDV positive (only as co-infection or super-infection of hepatitis B) Hepatitis E: IgM anti-HEV positive
Specimen	Serum, whole blood or stool
When to collect the specimen	Specimens should be collected from suspected patient. IgM anti-HAV becomes detectable 5-10 days after exposure. HBsAg can be detected in serum from several weeks before onset of symptoms to days, weeks or months after onset; it persists in

	chronic infections. IgM anti-HBc positive usually disappears within 6 months.
How to prepare, store and transport the specimen	Use universal precautions to minimize exposure to sharps and any body fluid. Collect at least 5 mls of venous blood. • Let clot retract for 30 to 60 minutes at room temperature or centrifuge to separate serum from red blood cells. • Aseptically transfer serum into sterile, screw capped tubes. • Store serum at 4°C. • For storage >5 days, samples are held at -20°C Transport serum samples using appropriate packaging to prevent breakage or leakage.
Results	Results are usually available within 1 to 3 days from arrival at the laboratory.

4.2 Laboratory Tests for Chronic Viral Hepatitis

Chronic Viral Hepatitis B (HBV)

Basic initial laboratory investigations

The following laboratory tests should be requested after thorough history and physical examination in HBsAg positive individuals

Confirmed HBsAg Positive

a. Establish Chronicity: HBcIgG positive or Repeat HBsAg after 6 months if HBcIgG test is unavailable

b. Establish e antigen/antibody status: HBe Ag & Ab

c. Establish function activity: LFTs, Consider liver biopsy if indicated (see indications: include indications……..)

d. Determine the Level of viraemia – viral load:HBV DNA

e. Screen for complications using Alpha fetoprotein, Abdominal ultrasound, Coagulation profile, Full blood count

f. Screen for other co-infections: HCV Ab, HIV, HDV if available

g. Supportive investigation: determine blood urea and creatinine

Chronic Viral Hepatitis C (HCV)

Initial Investigations for HCV Patients

The screening test for HCV is HCV Ab test. Unlike HBV testing, a positive HCV screening test (anti-HCV Ab) does not equate to active infection. Also, the HCV testing is bedevilled with several false positive results. The following steps are recommended to establish active infection;

- Confirm HCV Ab testing
    - ELISA
- Confirm active infection
    - RNA testing; detectable RNA confirms active infection

      if RNA undetectable, no further testing is indicated
- Further testing for RNA positive cases
    - LFT
    - abdominal ultrasound
    - FBC
    - alpha fetoprotein
    - BUE and Cr
    - Screen for co-infections - HIV, HBV.

- Genotyping

  HCV genotyping is very important for decision on choice of treatment, duration, and outcome. In general genotype 1 is more difficult to treat, 2 & 3 are relatively easier, requiring shorter duration of treatment; genotype 4 is intermediate. The predominant genotype(s) in Ghana is not known at present; few studies suggest genotype 2. Reference studies

- Assess degree of inflammation and fibrosis particularly in genotype 1.
  - Liver biopsy is the gold standard.
  - Aspartate aminotransferase-to-platelet ratio index (APRI) Score
  - Fibrosis-4 (FIB4) score
  - Fibroscan

5. Care and Treatment for Viral Hepatitis

5.1 Acute Viral Hepatitis

Management of acute viral hepatitis is mainly supportive and often may not require hospitalization or medication.

It is important to establish which virus is involved, as the risk of progression differs as indicated below:

Hepatitis A: This is usually self-limiting. The rate of fulminant hepatic failure (FHF) is very low; there is a 1% fatality rate in those over the age of 40 years.

Hepatitis B: self-limiting in 95% of adult cases; but for children under the age of five it is self limiting in only 5-15%

Hepatitis C: self-limiting in 5-30% of cases

Hepatitis D: requires the presence of HBV and follows the course of HBV.

Hepatitis E: self-limiting. The overall mortality rate in FHF is 1–3%;however in pregnant women the rate is 15–25%. Pregnant women, children and adults above the age of 40 years and those with background chronic liver disease are at increased risk of developing a more severe disease.

The next session will discuss the five hepatotropic viruses.

5.1.1 Acute Hepatitis A Infection

Hepatitis A virus (HAV) is an RNA-containing virus of the Picorna viridae family. The average incubation period is 28 days, but it can vary from 15 to 45 days.

Hepatitis A transmission is feco-oral and therefore poor hygiene and sanitation enhance its transmission. At risk group include children, participants in oro-anal sex, consumers of high-risk foods (e.g., raw shellfish) day-care employees and families of children in day-care. HAV infection confers a lifelong immunity.

Diagnosis of Hepatitis A infection: HAV is reliably diagnosed by anti-HAV immunoglobulin M (IgM). The presence of anti-HAV immunoglobulin G indicates a previous infection or immunity.

Management of HAV infection

HAV infection is self-limiting and treatment should be conservative and supportive. There is no specific medication for HAV infection. Hygiene is very important. Hands should always be washed after bathroom use.

Prognosis: The risk of FHF is very low (0.01–0.1%), but increases with age, pregnancy and in those with pre-existing liver disease. In patients above the age of 40 years, there is a 1% mortality rate.

5.1.2 Acute Hepatitis B Infection

Hepatitis B virus (HBV) is a DNA-containing virus of the Hepadnaviridae family. The virus is present in most body fluids of individuals with acute or chronic hepatitis. In Ghana, HBV is often transmitted vertically (infected mother to child) or horizontally among young children playing together (through biting and scratching). Other modes of transmission are through unsafe injections, unsafe blood/blood products and non-sterile instruments (scarifications). Sexual transmission is less common.

The incubation period for HBV is 60 days, and it can vary from 28 to 160 days. Approximately 30% of infections among adults present as icteric hepatitis, and 0.1– 0.5% of patients develop fulminant hepatitis. Infection resolves in 1%, 5%, 30% and 95% in neonates, under 1 year old, under 5 year old and adults respectively, with loss of serum HBsAg and subsequently the appearance of anti-HBs (HBsAb).

Diagnosis of Acute HBV Infection: Acute HBV infection is confirmed by a positive HBsAg and HBcIgM tests and a negative HBcIgG test.

A follow-up re-check of HBsAg should always be carried out 6 months after the acute onset to confirm clearance.

Management of Acute HBV Infection: Treatment is often conservative and supportive. In fulminant hepatitis, meticulous intensive care may improve the survival, but orthotopic liver transplantation is the only therapy that has been shown to improve patient outcomes.

Prognosis: Full recovery with development of anti-HBs provides long-term immunity.

5.1.3 Acute Hepatitis C Infection

Hepatitis C virus (HCV) is an RNA-containing virus of the Flaviviridae family. The incubation period varies from 14 to 160 days. Transmission is from blood to blood and blood products. HCV may potentially be transmitted sexually, mainly in individuals with other sexually transmitted diseases. The perinatal transmission rate is around 5%, much lower than the rates for HIV and HBV. Breastfeeding does not pose a risk. Health-care workers are at risk, mostly due to nosocomial transmission (needle stick injury carries a 3% HCV risk). Also at risk are individuals in prisons and persons born in countries with high rates of endemic disease.

Most acute infections are asymptomatic, but if symptoms occur, they usually last 2– 12 weeks.

Diagnosis of acute HCV infection

Distinguishing acute from chronic HCV can be challenging. The presence of HCV antibodies signifies exposure; however in an acute infection, HCV antibody may remain undetectable up to 4 weeks. Testing for HCV RNA is the best method of diagnosing acute HCV, particularly if it is then followed by the development of anti-HCV.

NB: Anti-HCV is not protective and does not confer immunity.

Management of Acute HCV Infection: Early identification of HCV is important, because there is evidence that early intervention with standard interferon alpha can markedly reduce the risk of chronic infection from 80% to 10%. NB: There is no vaccine for HCV.

Prognosis of Acute HCV infection

Without treatment majority will progress to chronicity. Unfortunately, most acute infections are missed as they are asymptomatic, and the opportunity to treat is therefore rare.

5.1.4: Acute Hepatitis D infection

Hepatitis D virus (HDV) is a defective single-stranded RNA virus of the Deltaviridae family. It is an incomplete RNA virus that needs the hepatitis B surface antigen to transmit its genome from cell to cell. It therefore only occurs in people who are positive for the hepatitis B surface antigen. The mean incubation period varies from 60 to 90 days, but it can vary as widely as 30 to 180 days.

The mode of transmission of HDV is similar to that of HBV. HDV infection can occur either as a co-infection with HBV or as a super-infection in those with chronic HBV. HBV /HDV Co-infection leads to severe acute disease, indistinguishable from acute HBV and with a relatively low risk of chronicity. Super-infection usually develops as acute exacerbation of chronic hepatitis with a high risk of progression to chronic liver disease.

Diagnosis of Acute HDV Infection

Positive HDV Ag and HDV-RNA (PCR) confirm a diagnosis of acute HDV infection. The anti-HDV (IgM class) appears 30–40 days after the first symptoms.

Management is conservative and supportive.

5.1.5 Acute Hepatitis E Infection

Hepatitis E virus (HEV) is an RNA-containing virus of the Caliciviridae family. The average incubation period is 40 days, and it can vary from 15 to 60 days. HEV is transmitted primarily by the faeco–oral route, and faecally contaminated drinking water is the most frequent vehicle for transmission. Transmission may occur vertically. Transmission between persons is minimal.

Diagnosis of acute Hepatitis E infection

HEV antigen and IgM/IgG antibody testing.

Acute hepatitis E treatment

Treatment is conservative and supportive.

Prognosis of Acute HEV Infection

The prognosis is generally good, except in pregnant women. Pregnant women with acute hepatitis E infection have an approximately 15% risk of fulminant liver failure. The mortality rate is high, ranging from 5% to 25% in different studies. HEV infection causes mortality in up to 25% of pregnant women in the third trimester of pregnancy.

NB 1. Acute Hepatitis E infection should be considered as a differential for HELLP syndrome.

NB 2. There has been reported evidence that HEV can progress to chronicity in the Genotype 3 sub-type but this guideline will not address that aspect

5.2 Chronic Hepatitis B

Chronic hepatitis B (CHB) is defined as persistence of hepatitis B surface antigen (HBsAg) for six months or more. The major complications of CHB are cirrhosis and hepatocellular carcinoma

5.2.1 Transmission

Most infections are acquired via perinatal (vertical) or horizontal transmission during childhood. Other routes of transmission include contaminated blood transfusion or contact with infected body fluids (sexual transmission, contaminated needles and unsterilized instruments used for circumcisions, tattoos and manicure).

HBV is highly infectious, compared to HCV; a tiny innoculum of blood or blood products may cause infection. More than 90% of childhood infections become chronic whereas only 5 to10% of acute adult infections become chronic. This emphasizes the importance of perinatal HBV vaccination in Ghana.

5.2.2 Natural history and Terminology

There are 4 phases of chronic hepatitis B infection namely 1) Immune tolerant 2) Immune Clearance/active 3) Immune control/inactive and 4) Immune escape/reactive. See table 2.

Table 2: Natural and Terminology for Chronic Hepatitis B

	Immune tolerant	Immune clearance /active	Immune control /inactive	Immune escape /reactivation
ALT	Normal	High	normal	High
HBeAg Status	Positive	Positive	Negative	Negative
Viral load	Very High	High	Low	High
Liver Histology	Normal	Active Necro-Inflammation	Normal	Active Necro-Inflammation
Comments	Common & prolonged following perinatal or childhood infections	Common following adult infection	Spontaneous HBsAg loss at 1-3%/year	Linked to mutations
Treatment	No	Yes	No	Yes

5.2.3 Who should be investigated or screened?

Ideally all persons reporting for medical care should be screened. Screening during blood donation and routine medical examination are particularly recommended.

The following categories of patients are at higher risk and must be screened:

- Abnormal liver function tests (LFT's) particularly elevated ALT of unknown cause
- Patients with cirrhosis, or suspected hepatocellular carcinoma (HCC)
- Spouses or children of HBsAg or anti-HCV positive patients
- HIV and HCV positive patients
- Acute kidney injury / Chronic kidney disease (CKD) patients, especially if haemodialysis is planned

The following people must be screened to prevent transmission:

- Healthcare workers
- Blood donors
- Patients with haemoglobinopathies
- Pregnant women

- Pre-school children and before hepatitis B vaccination
- Any person offering to be screened (voluntary screening).

5.2.4 Pre-and Post-test Counselling

It is important that patients are fully informed, in simple comprehensible language in the following areas:

- The main mode of transmission, possibility of transmission to non-immune spouse, children and close household relatives
- Health implications of chronic hepatitis B infection
- Reassure that not all will develop complications
- Avoidance of certain health risks e.g. Alcohol use, unprotected indiscriminate sex.
- Vaccination of non-immune partner and household.
- Stress on long term follow up if positive
- No dietary restrictions

5.2.5 Basic initial laboratory investigations

The following laboratory tests should be requested after thorough history and physical examination in HBsAg positive individuals

Phase 1: Confirmed HBsAg Positive

- Establish Chronicity: HBcIgG positive or Repeat HBsAg after 6 months if HBcIgG test is unavailable
- Request hepatitis B profile
    - HBe Ag and HBeAb
    - HBsAg and HBsAb
    - HBc Ab (IgG an IgM)
- Explain the significance of parameters identified in the profile
- Establish function activity: LFTs, Consider liver biopsy if indicated (see indications……..)
- Determine the Level of viraemia – viral load
- Screen for complications: Alpha fetoprotein, Abdominal ultrasound, Coagulation profile, Full blood count
- Screen for other co-infections: HCV Ab, HIV and HDV
- Supportive: determine blood urea and creatinine

Phase 2: Pretreatment Counselling

- The FINANCIAL IMPLICATIONS of treatment must be discussed including affordability (consider delition).

- Accessibility and availability of antivirals
- Need for long term follow up
- Objectives of treatment and the likely outcomes must be discussed namely:
    - Normalization or improvement of hepatic damage in the long term
    - Virological clearance
    - Prevention or delay of further liver damage and progression to Chronic liver disease and HCC
    - HBeAg seroconversion
    - HBsAg seroconversion ideal but seldom achieved (with current therapy)
    - Overall improvement of the quality of life
    - Some of the misinformation by lay public must be discouraged.
    - The guilt feeling of those affected must be dispelled.
- It must be stressed that most patients are healthy; treatment is aimed at preventing future complications in a small minority at risk.
- Un-recognised forms of treatment including herbs should be avoided.

- Drug compliance is vital. The protracted treatment schedule and the need for rigorous compliance must be stressed.

- Side effects of therapy should be discussed with the patient. The importance of avoiding other drugs unless indicated must be emphasized.

Diet and lifestyle: The patient is encouraged to eat balanced diet normally but avoid those foods that upset him / her. Healthy lifestyle including regular exercises, treating any concurrent illnesses e.g. diabetes, and the avoidance or reduction of alcoholic beverages must be encouraged.

Patients who do not qualify for treatment must be given explanation and be reassured. Likewise treatment failure must be explained.

5.2.6 Patients Follow-up

All patients including those not needing immediate treatment require long term follow-up to identify any changes in clinical status and to identify early any complications.

Depending on HBeAg status, 3-6 monthly viral load (VL) and LFTs in the first year and thereafter according to results. Abdominal ultrasound (USG) 6-12 monthly.

5.2.7 Treatment of Chronic Hepatitis B Infections

Goals of Treatment:

- To achieve clearance of HBV viraemia
- To prevent or delay chronic liver disease progression
- To minimize risk of hepatocellular carcinoma
- To prevent transmission of HBV infection
- To improve quality of life and survival of affected patients.

Treatment End points: HBsAg seroconversion is the ideal end point but this is not commonly achieved with all forms of current therapy (Table 3).

Table 3: Treatment End Points for Chronic Hepatitis B

	HBeAg positive	**If HBeAg negative**
End points	ALT Normalization	ALT Normalization
	HBV DNA viral suppression	HBV DNA viral suppression
	HbeAg Seroconversion	HBsAg Seroconversion
	HBsAg Seroconversion	

5.2.8 Who Should Be Treated

The following categories of patients should be treated:

- All patients with chronic ACTIVE HBV infection (HBeAg Positives and HBeAg Negatives)
- All HBV related cirrhosis or advanced fibrosis (APRI Score >2) patients with detectable viraemia

Criteria for HBeAg Positives CHB (see algorithm Figure 2)

- Persistently elevated ALT (>2x ULN)
- Viral load > or = 20,000 IU/ml
- Moderate – severe inflammation or fibrosis on liver histology

Criteria for HBeAg Negative CHB (see algorithm Figure 3)

- Persistently elevated ALT (>2x ULN)
- Viral load > or = 2,000 IU/ml
- Moderate – severe inflammation or fibrosis on liver histology

Figure 2: Algorithm for HBeAg positive patients

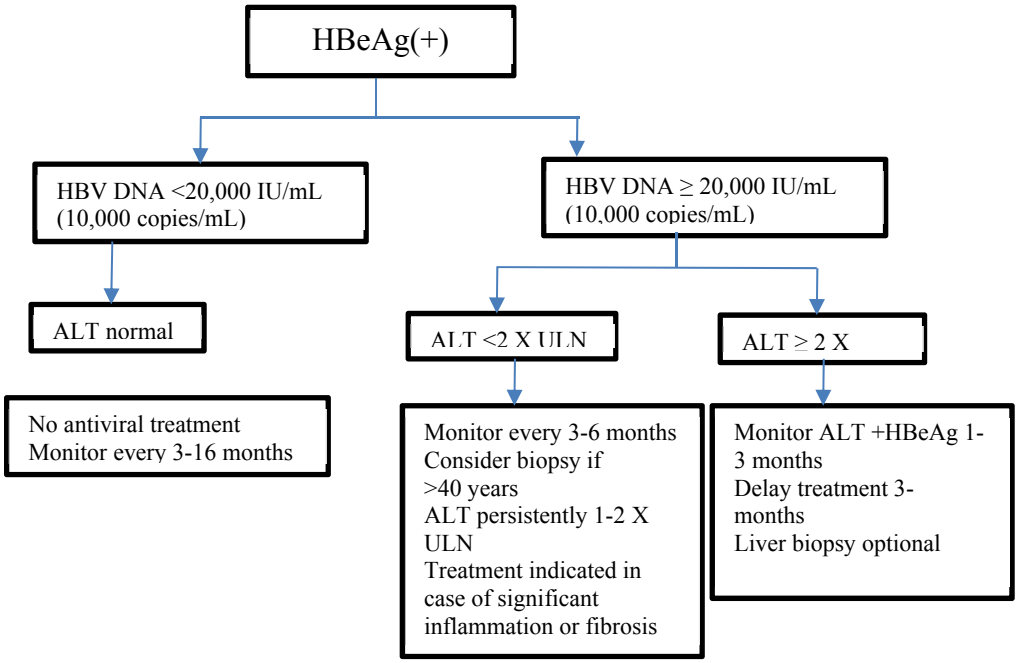
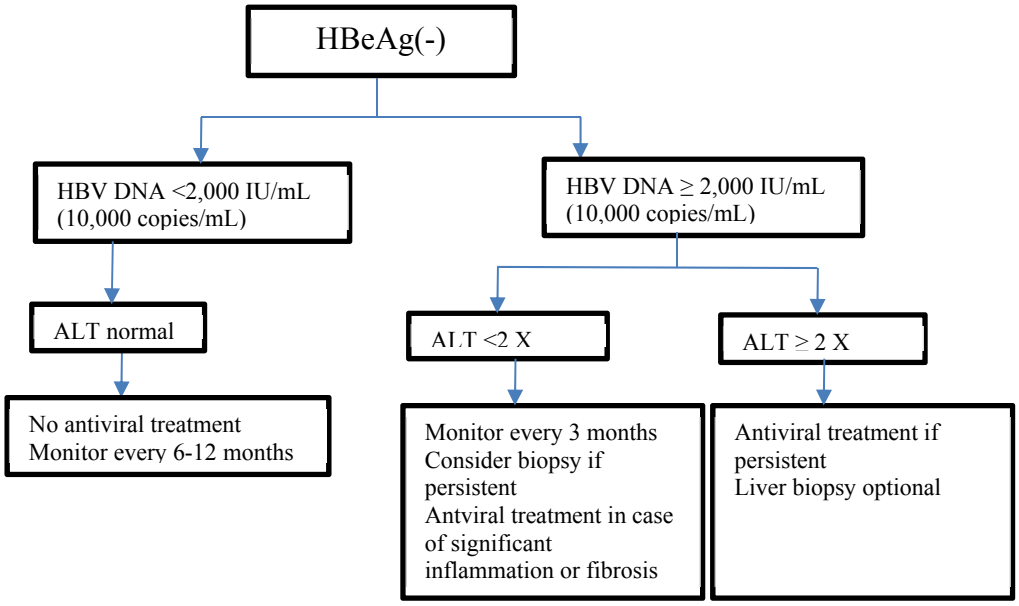


Figure 3: Algorithm for HBeAg negative patients



5.2.9 Antiviral Therapy for Chronic Hepatitis B

Until the introduction of interferons in the mid 80s no effective treatment was available. Conventional interferons (α-2a & 2) were given by injection three times a week for a period of 1-6 months. The response rate was low and currently not recommended. Conventional interferon therapy use was also limited by its side effect profile Reference.

Approved Antiviral Agents

1. Pegylated interferons: This is conventional interferon modified by pegylation to have longer half-life and therefore used as a once a week injection. They have been shown to increase and sustain the response rates in both HBeAg-ve and HBeAg+ve patients with a defined duration of treatment. See table 3 for comparative analysis.

2. Lamivudine: This is a nucleoside analogue with antiviral activity against HBV. It has been shown to have better on-therapy viral suppression rates than conventional interferons but low off-therapy sustained viral suppression rate. It also has a significantly increased risk of treatment failure due to emergence of resistant mutants. The best results with lamivudine are obtained when the duration is indefinite provided there is no development of resistance.

It is no more recommended as a first line option for HBV treatment.

3. Tenofovir dixopoxil fumarate: Is a nucleotide analogue with very potent activity against HBV replication with a high genetic barrier.

4. Entecavir: Is a nucleoside analogue with very potent activity against HBV replication with a high genetic barrier.

5. Other approved anti-HBV drugs:

1. Adefovir

2. Telbivudine

Recommended drug therapy for HBV treatment are Tenofovir/Entecavir and Peg Interferon.

Table 4: Comparison of different treatment options in CHB

	Treatment duration	**Advantages**	**Disadvantages**
Conventional Ifnα	Defined (4 – 6 months)	• Finite treatment duration • Durable HBeAg seroconversion • No resistance	• Inferior response rates compared to pegylated interferons. • Poor tolerability. • Less favourable safety profile. • Expensive • Injection (sc)
Pegylated Ifnα-2a (Pegasys®)	Defined(• 48 weeks)	• Finite treatment duration • Favourable response rates in both HBeAg+ve and HBeAg-ve disease. • More durable HBeAg seroconversion. • HBsAg loss in HBeAg+ve& -ve disease. • No resistance	Response rates may be low in HBeAg-ve. • Low tolerability • High cost • Less favourable safety profile. • Injection (sc)
Lamivudine, Adefovir	Potentially indefinite	• Well tolerated • Safe in patients with compensated or decompensated liver disease. •Cheaper (Lam Only)? • Oral administration.	• HBeAg seroconversion less durable. • ALT flare up on discontinuation may be serious. • Increasing drug resistance with long term therapy.

	Treatment duration	Advantages	Disadvantages
			• Expensive (Adefovir)
Tenofovir, Entecavir	Potentially indefinite	• Well tolerated • Potent against? • Better resistance profile against? • Cheaper (TDF only). • Oral administration	• High cost (entecavir) • Caution in renal impairment. • Caution in decompensated liverdisease. • Flare up hepatitis may occur on discontinuation.

Recommended First Line Antiviral Therapy for Chronic Hepatitis B

The current recommended 1st line antiviral therapy include; Tenofovir, entecavir and peg-interferon. Tenofovir is the recommended first choice treatment for chronic hepatitis B. Entecavir is used infrequently because of the very high cost. However entecavir is the drug of choice for children 2-11year. Peg – interferon α-2a (Pegasys) is used in well selected category of patients (very high ALT, moderate –severe necro-inflammatory changes on liver histology and moderately high viral loads)

NB Peg Inteferon is contraindicated in children under 12 years of age.

Monitoring during treatment

The aim of monitoring while on treatment is to assess adherence, evaluate effectiveness of therapy, check for evidence of progression of liver disease, adverse events and assess for indications for stopping treatment.

At each visit check for adverse events (Insert a table for adverse event)

At 12 weeks perform the following test: Insert a table for monitoring on therapy for all the medications

- HBV DNA viral load
- Liver Function Tests (LFTs)
- FBC (optional)
- BUE and Cr
- HBsAg quantification for patients on PEG * *(End of Treatment Response)

At 24 weeks perform the following test:

- HBV DNA Viral Load)
- Liver Function Test
- FBC if indicated
- BUE & Cr
- HBsAg quantification

At 48 weeks perform the following test:

- HBV DNA Viral Load
- Liver Function Test
- FBC, Thyroid function tests (pegylated interferon).
- HBsAg quantification

At least annually thereafter

- HBV DNA Viral Load
- Liver Function Test
- Abdominal ultrasound
- FBC
- BUE & Cr

Insert tabular form of monitoring PEG vs NUCs

Table 5: Recommended drugs for the treatment of CHB and their doses in adults

Drug	**Dose**
Tenofovir	300 mg once daily
Tenofovir plus emtricitabine	Tenofir 245 mg; emtricitabine 200mg
Entecavir (adult with compensated liver disease and lamivudine naive)	0.5 mg once daily
Entecavir (adult with decompensated liver disease)	1 mg once daily
Telbivudine	600 mg once daily
Lamivudine	300 mg once daily
Adefovir	10mg once daily
Pegylated interferon alpha-2a	180ug once per week
Pegylated interferon alpha-2b	0.5 or 1.0ug per kg per week

Non –responders / treatment failure

Recommendation: Switch to a more potent NUCs or "add on" therapy; Lamivudine switch to Tenofovir

Relapsers relook at the concept of relapsers in HBV infection

5.2.10 Antiviral Therapy for Special Groups

HBV and Pregnancy:

All pregnant women should be screened for HBV infection during ANC. Acute HBV infection during pregnancy should be managed as for the non-pregnant population. However acute infections are more likely to be fulminant. In such situation ,antiviral therapy may be considered on a case by case basis. Chronic HBV is not at increased risk of progression during pregnancy. Evaluation remains the same as for the non-pregnant population.

HBV DNA should be tested at the end of the 2nd trimester and persons with viral loads greater than 100,000 IU/ml and no other contraindication for treatment should be started on antiviral therapy and continued throughout the 3rd trimester. Treatment in this case is stopped upon delivery and monitored thereafter.

Tenofovir is currently the safest and preferred drug for HBV treatment in pregnancy. Entecavir has not been studied adequately in pregnancy. Peg-interferon is contraindicated in pregnancy.

Nb: The Risk Of Mother To Child Transmission Is Not Influenced By The Mode Of Delivery

New born babies to HBsAg positive mothers MUST receive the monovalent HBV vaccine preferably within 24hr and also the HBIG soon after delivery but preferably not more than 72hours. The injections should be given on the different sites of lateral thigh. The baby thereafter should be enrolled into the National EPI to complete routine childhood immunizations.

Prior to immunosuppressive therapy

ALL HBsAg + persons scheduled for immunosuppressive therapy who otherwise do not qualify to start treatment must start antiviral therapy or prophylaxis at least one week before starting chemotherapy. Treatment should be with the most potent nucleos(t)ide available and must be continued for upto 6 months after cessation of chemotherapy.They should be monitored with monthly LFT and 3 monthly Viral loads.

Renal dialysis and Transplant patients

HBV is prevalent in persons with CKD including renal transplant recipients. All such patients should be tested prior to initiation of renal dialysis and sero- negative patients should be vaccinated in consultation with a gastroenterologist.

All the nucleoside analogues require dose adjustments and should be used with caution. Renal function monitoring should be done in consultation with a nephrologist during therapy. Interferons are not recommended.

Liver transplant

All potential liver transplant recipients should be tested for HBV. Sero-negative persons should be vaccinated. Positive individuals should be started on treatment prior to transplant and continued thereafter, with monitoring of viral load and liver function, as recommended for the general population. Interferons are not recommended.

HIV/HBV coinfection content should follow this section(Refer to ART guidelines)

5.3 Chronic Hepatitis C

Hepatitis C virus (HCV) belongs to the family of flaviviruses with several known genotypes. The HCV is a small, positive-stranded RNA-enveloped virus. It has a highly variable genome, which has been classified into six distinct genotypic groups. Existing direct-acting antiviral (DAA) treatments are significantly more effective on certain genotypes than others; thus it is important to know a patients genotype prior to initiating treatment. HCV is infectious but less so than Hepatitis B.

5.3.1 Transmission

Transmission is via contact with contaminated blood and blood products. It was regarded as the major cause of transfusion induced hepatitis prior to the advent of screening of blood products. Practices such as persons who inject drugs (PWID), sharing of needles and unsterilized scarification and tattooing are likely routes of transmission. Sexual transmission is possible but uncommon. Also through child birth; from infected mother to child.

Hepatic damage from HCV infection is thought to be an immune mediated cytotoxic T cell response. Approximately 20% and10% of persons with HCV infection, develop cirrhosis and hepatocellular carcinoma (HCC) respectively after about 10 – 20 years. They may also develop extra hepatic manifestations such as kidney disease, arthritis and skin disorders. There is no immunity after infection, unlike HBV and this is due to the diversity and numerous strains of the HCV. Currently there are no vaccines against HCV infection.

5.3.2 Initial Investigations for HCV Patients

The screening test for HCV is HCV Ab test. High quality WHO prequalified tests should be used for screening. Unlike HBV testing, a positive HCV screening test (anti-HCV Ab) does not equate to active infection. However, the HCV testing is bedevilled with several false positive results. The following steps are recommended to establish active infection;

- Perform HCV serology testing (HCV Ab testing)
- If HCV Ab positive, confirm active infection by nucleic acid testing;
    - Detectable Ribonucleic acid (RNA) confirms active infection
    - If RNA undetectable, no further testing is indicated
- Further testing for RNA positive cases
    - FBC
    - LFT
    - Genotyping
    - Screen for co infections
    - Alpha fetoprotein
    - BUE and Creatinine and

- Abdominal Ultrasound
- ,Screen for co-infections - HIV, HBV, TB
- Genotyping

The predominant genotype(s) in Ghana is not known at present; However the WHO global distribution of genotypes suggests that Ghana falls within the area where genotypes Assess degree of inflammation and fibrosis particularly in genotype 1 (see table xx).

- Aminotransferase/platelet ratio index (APRI) Score
- FIB-4
- FibroScan

Table 6: Selected non-invasive tests to assess liver fibrosis

Test	Components	Requirements
APRI	AST, platelets	Simple serum and haematology tests
FIB-4	Age, AST, ALT, platelets	Simple serum and haematology tests
FibroTest	gGT, haptoblobin, bilirubin, A1 apolipoprotein, α2-macroglobulin	Specialized test. Testing at designated laboratories
FibroScan	Transient elastography	Dedicated equipment

Figure 4: APRI and FIB-4 Formulas

APRI= [(AST (IU/L)/AST_ULN (IU/L)) X 100] / platelet count (10^9/L)

FIB-4 = age (yr) X AST (IU/L)/platelet count (10^9) X [ALT (IU/L)$^{1/2}$

ULN: upper limit of normal

In resource-limited settings, it is suggested that APRI or FIB-4 be used for assessment of hepatic fibrosis rather other non-invasive tests that require more resources such as elastography or FibroTest.

5.3.3 Indications for treatment

- All persons with active HCV infection i.e. detectable RNA are candidates for treatment if there are no contraindications.
- Prioritize treatment to persons with moderate to severe fibrosis, risk of HCV transmission e.g. IVD users , Men having sex with men (MSM), women in their reproductive ages and persons with extrahepatic manifestations

5.3.4 Pretreatment Management

- Education / counselling: natural history of disease, modes of transmission, prevention, assurance of effective treatment and cost of therapy
- Vaccinate against hepatitis A and B if seronegative
- Weight loss if appropriate. Obesity increases likelihood of liver

fibrosis

- Stop smoking / avoid use of illicit drugs
- Recommend abstinence from alcohol
- Assess for and manage depression if present in interferon based treatment
- Consider referral to support groups

Goals of Therapy

Primary goal of treatment is to eradicate the virus. The secondary goals are to:

- Slow disease progression
- Minimize risk of liver cancer
- Reverse liver damage
- Enhance quality of life
- Prevent transmission of virus
- Reduce extra-hepatic manifestations

5.3.5 Antiviral Therapy for Chronic Hepatitis C

Until 2011, standard of care was combination therapy of PEG-

interferon with Ribavirin for all genotypes globally (Table 5). Subsequently, there has been a paradigm shift with the development of several new drugs/ direct acting antiviral agents (DAA)e.g., sofosbuvir, ledipasvir, daclatasvir etc. where these are not available interferon based treatment may be used.

Tables 7 and 8 give the recommended preferred and alternative treatment durations in with or without cirrhosis, respectively.

Table 7: Summary of recommended preferred regimens with treatment durations

Table 7a: Persons without cirrhosis

Genotypes	**Daclatasvir/ sofosbuvir**	**Ledispasvir/ sofosbuvir**	**Sofosbuvir/ ribavirin**
1	12 weeks	12 weeks[a]	
2			12 weeks
3	12 weeks		24 weeks
4	12 weeks	12 weeks	
5		12 weeks	
6		12 weeks	

Table 7b: Persons with cirrhosis

Genotype	Daclatasvir /sofosbuvir	Daclatasvir /sofobuvir/ribavirin	Ledipasvir /sofosbuvir	Ledispasvir /Sofosbuvir /Ribavirin	Sofosbuvir /ribavirin
1	24 weeks	12 weeks	24 weeks	12 weeks[b]	
2					16 weeks
3		24 weeks			
4	24 weeks	12 weeks	24 weeks	12 weeks[b]	
5			24 weeks	12 weeks[b]	
6			24 weeks	12 weeks[b]	

[a] Treatment may be shortened to 8 weeks in treatment-naïve persons without cirrhosis if their baseline HCV RNA level is below 6 million (6.8 log) IU/mL. The duration of treatment should be shortened with caution

[b] If platelet count <75 X 10^3/μL, then 24 weeks treatment with ribavirin shoud be given

Table 7c: Summary of recommended alternative regimens with treatment durations

Genotypes	Simeprevi/ Sofosbuvir	Daclatasvir/ Sofosbuvir	Sofosbuvir/pegylated interferon/ribavirin
1	12 weeks[a]		
2		12 weeks	
3			
4	12 weeks		
5			12 weeks
6			12 weeks

[a] If genotype 1a-infected patient, is positive for the Q80K variant, a simeprevir/sofosbuvir regimen should not be chosen. For genotype 1a-infected patients, treat with ombitasvir/paritaprevir/ritonavir/dasabuvir and ribavirin, for genotype 1b-infected patients, treat with ombitasvir/paritaprevir/ritonavir/dasabuvir

Table 7d: Persons with cirrhosis

	*	**		
Genotypes	**Daclatasvir/ sofosbuvir**	**Simeprevir/ sofosbuvir**	**Simeprevir/ Sofosbuvir/ Ribavirin**	**Sofosbuvir/ Pegylated inferon/ Ribavirin**
1		24 weeks[a]	12 weeks[a]	
2	12 weeks			
3				12 weeks
4		24 weeks	12 weeks[a]	
5				12 weeks
6				12 weeks

*Can be prescribed to persons with compensated or decompensated cirrhosis

**These regimens should be prescribed only to persons with compensated cirrhosis because they can cause liver failure and death when prescribed to persons with decompensated cirrhosis. Therefore, they shoud be used only in settings where specialized care is available and where the degree of cirrhosis (compensated vs decompensated) can accurately be assessed

[a] If genotype 1a-infected patient is positive for the Q80K variant, simeprevir/sofosbuvir regimen should not be chosen

New drugs are at various stages of development and may be added on as and when they are approved.

Where interferon is being used the following apply:

Contra-indications for Interferon Therapy

1. Hypersensitivity to Interferon alpha or any active ingredients
2. Severe psychiatric disturbances e.g. depression, psychosis
3. Auto-immune hepatitis
4. Decompensated cirrhosis e.g. ascites, encephalopathy
5. Cardiac failure,
6. Uncontrolled seizure disorders
7. Pregnancy
8. Pre-existing uncontrolled thyroid disorders

5.3.6 Co-Infections

HBV, HIV, HCV and HDV share similar transmission routes. Concurrent infection with these viruses usually results in more severe and progressive liver disease, and a higher incidence of cirrhosis, HCC and mortality. Coinfected persons are therefore more likely to need treatment. In general, the dominant virus responsible for liver disease should be identified and initial treatment targeted toward this virus. For example, if HCV is dominant, treatment should first be given to achieve HCV clearance and cure, followed by determination of whether treatment for hepatitis B is warranted based on ALT and

HIV/HCV Co-Infection

In 2015, WHO updated its HIV treatment recommendations to recommend treatment for all persons living with HIV regardless of WHO clinical stage or CD4 cell count. The choice of ART for persons with coinfection is the same as for those with HIV alone. However, persons coinfected with HIV are at higher risk of developing side-effects of HCV therapy, and should be monitored more closely. Before starting HCV therapy, careful consideration of drug-drug interactions (DDIs) is essential. It is important for clinicians to consider potential DDIs in choosing regimens, as DDIs vary both in number and clinical significance, depending on the medicines prescribed. Where DDIs are likely, ARV drug substitutions should be made before commencement of HCV therapy. It is particularly important to be aware of HIV infection when considering ritonavir-based therapies (i.e. paritaprevir) in order to avoid singledrug therapy of HIV infection, which could lead to drug resistance to ARVs. Table 8 summarizes the first-line ART regimens and Table 8.6 summarizes the DDIs between HIV ART medicines and HCV medicines.

Table 8: Summary of first-line ART regimens for adults, adolescents, pregnant and breastfeeding women and children

Category of patients	Preferred firstline regimens	Alternative first-line regimens
Adults	TDF + 3TC (or FTC) + EFV	AZT + 3TC + EFV (or NVP) TDF + 3TC (or FTC) + DTG[a] TDF + 3TC (or FTC) + EFV 400[a] TDF + 3TC (or FTC) + NVP
Pregnant/breastfeeding women	TDF + 3TC (or FTC) + EFV	AZT + 3TC + EFV (or NVP) TDF + 3TC (or FTC) + NVP
Adolescents	TDF + 3TC (or FTC) + EFV	AZT + 3TC + EFV (or NVP) TDF (or ABC) + 3TC (or FTC) + DTG[a] TDF (or ABC) + 3TC (or FTC) + EFV400[a] TDF (or ABC) + 3TC (or FTC) + NVP
Children aged 3 to 10 years of age	ABC + 3TC + EFV	ABC + 3TC + NVP AZT + 3TC + EFV (or NVP) TDF + 3TC (or FTC) + EFV (or NVP)
Children younger than 3 years of age	ABC or AZT + 3TC + LPV/r	ABC or AZT + 3TC + NVP

Source: Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection. WHO, 2015

3TC-lamivudine; ABC: abacavir; AZT: zidovudine; DTG: dolutegravir; EFV: efavirenz; EFV400: EFV at lower dose (400mg/day); FTC: emtricitabine; LPV: lopinavir; NVP: nevirapine; r: ritonavir; TDF: tenofovir

[a] Safety and efficacy data on use of DTG and EFV400 in pregnant women, people with HIV/TB coinfection, and children and adolecents younger than 12 years of age are not yet available

Persons with HIV/HCV co-infection generally have more rapid progression of liver fibrosis, especially those with a CD4 cell count of <200 cells/mm3. Furthermore, even among patients in whom ART leads to successful control of HIV infection (i.e. undetectable HIV viral load), the risk of hepatic decompensation among co-infected patients is higher than among patients with HCV monoinfection. For these reasons, all persons with HIV/HCV coinfection should be considered for HCV treatment. Treating such patients in the past with interferon and ribavirin combination therapy was very difficult, as many patients had to discontinue treatment due to side-effects such as depression or weight loss as well as severe anaemia,thrombocytopenia and neutropenia. Furthermore, SVR rates in patients with coinfection were lower than among HCV-monoinfected patients. Outcomes of HCV therapy with DAAs in persons with HIV coinfection are comparable to those with HCV monoinfection. Thus, DAA therapy has substantially simplified the treatment of persons with HIV and HCV coinfection. There are fewer DDIs between DAAs and ARV medicines, and SVR rates with DAA-based therapy among persons with HIV coinfection are higher than 95%, even for those with prior HCV treatment failure or advanced fibrosis. Therefore, there is no longer a need to consider HIV/HCV coinfected patients as a

special, difficult-to treat patient population. The need to check for DDIs between HIV and HCV medications, however, needs to be emphasized (*see* Table 8).

It is advisable to first initiate treatment for HIV and achieve HIV suppression before starting HCV treatment, although there are some circumstances where it may make sense to treat HCV infection first and then initiate therapy for HIV. This could include persons with moderate-to-severe fibrosis at risk of rapid liver disease progression if the HIV infection is not associated with significant immunosuppression at the time of treatment. Also, in view of the short duration of HCV treatment, the risk of DDIs between HCV and HIV medicines and the increased risk of ART-related hepatotoxicity in the presence of HCV infection, treating HCV infection first can simplify subsequent ART depending on the regimen available locally. Persons coinfected with HIV are at higher risk of developing side-effects of HCV therapy, and should be monitored more closely. Before starting HCV therapy, careful consideration of DDIs is essential. Where DDIs are likely, ARV drug substitutions should be made before commencement of HCV therapy. It is particularly important to be aware of HIV infection when considering ritonavir-based therapies (such as ombitasvir/paritaprevir/ritonavir/dasabuvir) in order to avoid single-drug treatment of HIV infection, which could lead to drug resistance to ARVs. Given that many countries will not have access to a wide range of HCV therapies and may have limited opportunities for retreatment, it is critical that coinfected patients be carefully assessed and any drug interactions that may either reduce efficacy or increase the risk of side-effects avoided.

Potential harmful effects of ARV drugs include their hepatotoxic effects. Several studies have shown that hepatotoxicity as a result of ART may be worsened in the presence of concomitant HCV infection *(223–225)*.

However, the highest rates of hepatotoxicity have been observed with ARV drugs that are no longer commonly used or recommended, including stavudine (d4T), didanosine (DDI), nevirapine (NVP) or full-dose ritonavir (600 mg twice a day). For most HIV/HCV-coinfected persons, including those with cirrhosis, the benefits of ART outweigh concerns regarding drug-induced liver injury.

Raised liver enzymes may be the result of ART-induced drug toxicity and/or opportunistic infections, making interpretation of liver enzyme elevations more problematic than for patients with HCV infection alone. ALT and ASTshould be monitored at 1 month after ART initiation and then every 3–6months. A significant elevation of AST/ALT may prompt careful evaluation for other causes of liver function impairment (e.g. alcoholic hepatitis, hepatobiliary disease), and may require short-term interruption of the ART regimen or specific drug suspected of causing the elevation.

HBV/HCV Co-Infection

It is important to check for the presence of HBV infection before starting HCV treatment. HBV and HCV coinfection may result in an accelerated disease course; HCV is considered to be the main driver of disease and should treated first.

Persons co-infected with HBV and HCV can be treated with antiviral therapy for HCV; SVR rates are likely to be similar to those in HCV-monoinfected persons. During treatment and after HCV clearance, there is a risk of reactivation of HBV, and this may require treatment with concurrent anti-HBV antiviral therapy. DDIs must be checked before initiating treatment.

TB/HCV Co-Infection

People at increased risk of infection with HCV are also often at increased risk of infection with TB. Therefore, screening for active TB should be part of the clinical evaluation of patients being considered for HCV treatment. WHO recommends a four-symptom screening algorithm to rule out active TB.

If the patient does not have any one of the following symptoms – current cough, fever, weight loss or night sweats – TB can be reasonably excluded; otherwise, the patient should undergo further investigations for TB or other diseases.

Most of the DAAs interact with metabolic pathways in the liver, which increases and/or decreases the drug level of DAAs when co-administered with antimicrobial medicines such as rifabutin, rifampin and rifapentin. Therefore, concurrent treatment of HCV infection and TB should be avoided. Active TB should generally be treated before commencing therapy for HCV. Furthermore, in persons with HCV infection being treated for TB, it is important to monitor liver function tests, as the risk of antimycobacterial-induced hepatotoxicity is higher in patients with TB/HCV coinfection than in those with TB monoinfection, although the risk of severe hepatotoxicity is rare.

Concurrent treatment of HCV infection and multidrug-resistant TB is

particularly complicated because of many DDIs between DAAs and second-line antimicrobials. There are limited data on the management of persons coinfected with HCV, HIV and TB, but such cases need sound clinical judgement in order to reduce the additive side-effects, pill burden and DDIs. Clinicians need to be aware of the risk of reactivation of TB if the person, particularly if HIV coinfected, receives interferon-based

therapy, as interferon-based therapy could increase the incidence of active TB.

5.3.6 Special Considerations for specific conditions

Cirrhosis

The spectrum of disease in those infected with HCV extends from mild fibrosis to compensated then decompensated cirrhosis and HCC. Between 15% and 30% of persons infected with HCV will go on to develop cirrhosis of the liver within 20 years and a proportion of these will progress to HCC. The risk is markedly increased in those who consume excess alcohol and in those co-infected with HBV and/or HIV, particularly those who do not have access to ART. Persons with cirrhosis have the least time available for treatment, the most to lose and much to gain from achieving SVR. Treatment of HCV infection should be commenced before the onset of decompensated disease because medical management is more complicated and some HCV medicines can precipitate liver failure and death if administered at this stage.

Regular clinical examination and monitoring of serum bilirubin, albumin and coagulation profile are necessary in persons with cirrhosis on interferon based treatment in order to detect decompensated disease. The treatment of such persons with interferon-containing regimens carries a higher risk of serious side-effects, and the use of haemopoietic factors is recommended in settings where these are available .

Use of certain DAA regimens among persons with cirrhosis has been shown and efficacious, especially in those with compensated

disease. The addition of ribavirin to treatment increases the risk of SAEs, most notably those related to anaemia, and requires additional monitoring.Simeprevir and mbitasvir/paritaprevir/ritonavir/dasabuvir are not approved for use in patients with decompensated liver disease. Daclatasvir, ledipasvir and sofosbuvir have been studied in persons with decompensated cirrhosis and their use has been demonstrated to be both feasible and effective.

However, a proportion of patients with decompensated liver disease will deteriorate on treatment and currently there are no pretreatment predictors to identify these patients. Therefore, treatment of patients with decompensated liver cirrhosis should be considered only in centres with the expertise to manage complications and ideally where access to liver transplantation is available.

Assessment and follow up for the progression of disease and for evidence of HCC is an essential part of the care of persons with HCV-related cirrhosis. Compensated cirrhosis may also progress over time to decompensated cirrhosis associated with ascites, oesophageal and gastric varices, and eventually to liver failure, renal failure and sepsis, all of which are life threatening. The diagnosis of decompensated liver disease is based on both laboratory and clinical assessment, and therefore a careful medical examination of patients must be made before starting treatment. Persons with cirrhosis (including those who have achieved an SVR) should be screened for HCC with six-monthly ultrasound examination and α-fetoprotein estimation, and should have endoscopy every 1–2 years to exclude oesophageal varices.

Chronic Kidney Disease

There is an unmet need for DAA treatment in patients with severe renal disease (eGFR <30 mL/min/1.73 m2) and those requiring haemodialysis. Sofosbuvir, which is used in many approved regimens, does not have the safety and efficacy data to support its use in these situations. Preliminary pharmacokinetic and clinical study data suggest that the use of ombitasvir/paritaprevir/ritonavir and dasabuvir is feasible and the early results suggest possible efficacy.

Future regimens are also looking at addressing this unmet need.

Both ribavirin and pegylated interferon require dose adjustment in persons with renal failure. Pegylated interferon α2a is cleared by the liver and pegylated interferon α2b via the kidneys. While a theoretical accumulation of pegylated interferon α2b could occur in persons on haemodialysis, no differences have been reported clinically.

In persons with severe renal disease (eGFR <30 mL/min/1.73 m2), including those on haemodialysis, a reduced dose of pegylated interferon α2a 135 μg once a week is recommended. The dose of ribavirin must also be decreased as the risk of anaemia-related adverse events is high. In persons with renal impairment receiving chronic haemodialysis, ribavirin may be administered at a dose of 200 mg daily or 200 mg every other day. Plasma ribavirin is removed by haemodialysis with an extraction ratio of approximately 50%.

Patients receiving ARV drugs in combination with tenofovir and sofosbuvir may require enhanced renal monitoring (*see* section 9.2).

Women of child bearing age

None of the DAAs have been evaluated among pregnant women. Thus, women with childbearing potential should be counseled that they require effective contraception during treatment and for six months after completion of therapy. Interferon can induce pregnancy termination and ribavirin is associated with fetal abnormalities. These two medicines are thus contraindicated in pregnant women and those with childbearing potential unless effective contraception (i.e. two forms of contraception)

can be guaranteed during treatment and, for women taking ribavirin, for 6 months after completing therapy. Ombitasvir/paritaprevir/ritonavir-based regimens have DDIs with certain hormonal contraceptives and should be used with caution. Pre-treatment pregnancy tests should be conducted prior to treatment initiation.

Children and aldolescents

None of the DAAs have been approved for use among children; thus, the only approved treatment for children remains pegylated interferon/ribavirin, which is recommended for children older than 2 years. Clinical trials are urgently needed to provide the necessary safety and efficacy data to allow regulatory approval of DAAs among children. The product literature for pegylated interferon reports that paediatric subjects treated with ribavirin combination therapy had a delay in weight and height increases after 48 weeks of therapy compared with baseline. However, by the end of 2 years of follow up, most subjects had returned to baseline normative growth curve percentiles for weight and height (mean weight-for-age percentile was 64% at baseline and 60% at 2 years' post-treatment; mean height percentile was 54% at baseline and 56% at 2 years' post-treatment).

People who inject drugs

Injecting drug use is prevalent in many countries around the world, affecting people in low-, middle- and high-income countries. Globally, approximately 67% of PWID have evidence of HCV infection (i.e. anti-HCV antibodies); 10 million of 16 million people in 148 countries *(19).* PWID are at increased risk of HCV-related

and mortality, and therefore require specialized care *(54)* and should be considered as a priority for HCV treatment. In reality, many PWID with HCV infection are unaware that they are infected and HCV treatment rates among them are very low *(213).* This is due to a number of reasons, including the criminalization of drug use, as well as discrimination and stigma in healthcare settings. When caring for PWID, the central tenets of respect and non-discrimination should be followed, and additional adherence and psychological support given as required

Extrahepatic manifestations

Some patients with chronic HCV infection may suffer from extrahepatitic illnesses, with a symptomatic spectrum vary from fatigue to permanent organ damage such as such as renal disease, peripheral neuropathy, arthropathy, cryoglobulinaemia, lymphoproliferative disorders and peripheral and central nervous system vasculitis. These illnesses resolve following SVR by antiviral treatment. Interferon free treatment appear safe and effective in HCV patients with extrahepatic manifestations.

Please can we capture the use of HBV vaccine and HBV immunoglobulin

Please can we also capture the special patient populations (e.g. pregnant and breast feeding women and children)

REF

6. Supervision, Monitoring and Evaluation

Supervision of Viral Hepatitis programme activities will be conducted at all levels of the health system namely; health facilities, sub-district, district and regional level. This will be done by trained supervisors every quarter.

The key indicators to be monitored monthly and evaluated annually are:

- Incidence of HAV, HBV, HCV, HDV and HEV infection
- Prevalence of HBV and HCV infection.
- Infrastructure for testing.
- Vaccination coverage
- Needle and syringe distribution
- Injection safety
- Proportion of persons diagnosed

- HBV and HCV treatment coverage
- Cure rate for HCV
- Viral suppression for HBV
- Mortality Rate for HBV and HCV
- Prevalence of Liver Cirrhosis and Hepatocellular Carcinoma
- Mortality Rate for Liver Cirrhosis and Hepatocellular Carcinoma

Table 9: Hepatitis Indicators and Targets

Indicator	Numerator	Denominator	Source of data	Target
HBV Vaccination	Number of persons vaccinated	Target population	EPI	90%
HBV MTCT Birth dose	Number of neonates vaccinated	Number of newborns	EPI	50%
Safe Injection				
Harm Reduction				
HBV Treatment	Total Number of chronic HBV patients on treatment	Total Number of chronic HBV patients that requires treatment	Health facilities Treatment centres	5million treated by 2020 80%

Indicator	Numerator	Denominator	Source of data	Target
HCV Treatment	Total Number of chronic HCV patients on treatment	Total Number of chronic HCV patients that requires treatment	Treatment centres	3million treated 2020 80%

7. References

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8. Annexes

Annex 1: Post-exposure management of healthcare workers after occupational exposure to Hepatitis B infection

*HCW status	Post-exposure testing		Post-exposure prophylaxis		Post-vaccination anti-HBs
	Source patient	*HCW anti-HBs	§HBIG	HBV vaccination	
Documented responder(antibody titres >10IU and	No action required				

> 3 doses received)					
Documented non-responder (after >6 doses)	Positive	-	§HBIG twice (I month h apart)	-	No
	Negative	-	No action required		
Response unknown (after >3 doses)	Positive / Unknown	<10 mIU/mL	§HBIG once	Revaccinate	Yes
	Negative	<10 mIU/mL	None	Revaccinate	Yes
	Any result	>10 mIU/mL	No action required		

Unvaccinated/ incomplete vaccination	Positive / Unknown	-	HBIG once	Complete vaccination	Yes
	Negative	-	None	Complete vaccination	Yes

*HCW: Healthcare worker

§HBIG: Hepatitis B Immunoglobulin as soon as possible when indicated (0.06mL/Kg IM) or consult product literature

Anti-HBs titre should be performed 1-2 months after last dose of HBV vaccination series but ~ 4-6 months after HBIG to avoid detection of passively administered anti-HBs

Responder: person with anti-HBs > 10 mIU/mL after 3 or more HBV vaccination doses

Non-responder: person with anti-HBs < 10 mIU/mL after 6 or more HBV vaccination doses

N.B. All HCWs who have anti-HBs < 10 mIU/mL, unvaccinated or incomplete vaccination and sustain exposure to a source patient who is HBsAg-positive/ unknown HBsAg status should undergo HBsAg screening as soon as possible after exposure and follow up testing ~ 6 months later (HBsAg + anti-HBc).

Annex 2: Hepatitis B and C (HBV and HCV) Viral Markers and their significance

Virus	Markers*	Significance
	HBV DNA	Markers of HBV replication. Present in acute and chronic infections, and for both wild type and pre-core mutant* HBV infections
	HBsAg	First serological marker to appear. Persistence for at least 6 months indicates chronic infection
	Anti-HBs	Detectable after HBsAg clearance and indicates complete recovery or immunity after immunisation with vaccine
HBV	Anti-HBcIgM	Serological marker for acute infections. Single distinctive marker for recent infection
	Anti-HBcIgG	Indicates previous infection; not associated with recovery of immunity
	HBeAg	Serological marker for both acute and chronic infection. Remains positive during active viral replication but may be negative during mutant viral

Virus	Markers*	Significance
		replication.
	Anti-HBe	Signals a cessation or minimal HBV replication. Prognostic marker for eventual improvement in hepatic pathology
HCV	Anti-HCV	Indicates active or past HCV infection
HCV	HCV RNA	Marker for active HCV infection

*HBV DNA-Hepatitis B virus genomic DNA; HBsAg-Hepatitis B surface antigen: Anti HBs-Antibody to hepatitis B surface antigen; Anti HBcIgM-Early antibodies to hepatitis B core antigen; Anti HBcIgG-Late antibodies to hepatitis B core antigen; HBeAg-Hepatitis B e antigen; Anti HBc-Antibodies to hepatitis B c antigen; Anti HCV - Antibody to hepatitis C virus; HCV RNA-Hepatitis C genomic RNA. In acute HBV infections, markers present are HBsAg, HBeAg and antiHBcIgM with or without HBV DNA. In chronic HBV infections, HBeAg is present with anti HBcIgG. Fully resolved HBV infection has no antigens present, but with all antibodies except anti HBcIgM. Pathogenicity of pre-core mutants are similar to wild type and can replicate in the presence of anti Hbe.

Annex 3: Viral Hepatitis Monthly Reporting Form, GHANA

Reporting Region_____Reporting District_____
District Code_____

Year ____ Month_____

Officially Expected Number of Reports_____ Number of Reports received_____

Number of Reports received on time_____

C=cases; D= Deaths; LC= Lab. Confirmed; HAV=Hepatitis A; HBV=Hepatitis B; HCV=Hepatitis C; HDV=He
HEV=Hepatitis E

Reporting Sub-District/ Health Facility	Suspected Viral Hepatitis			Acute Viral Hepatitis									
				HAV		HBV		HCV		HDV		HEV	
	C	D	LC	C	D	C	D	C	D	C	D	C	D
Total													

*Lab test negative for Viral Hepatitis A,B,C,D and E

Name of Person Reporting: _____

Telephone No.: _____

Date Received at next level: ____/____/_____

Name of Person Receiving:_____

Telephone N _____

Annex 4: Viral Hepatitis Case Investigation Form

No.	**VIRAL HEPATITIS CASE INVESTIGATION FORM, GHANA**	
	Variable/Description	Response
1	Epid. Number	
2	Reporting District	
3	Reporting Region	
4	Reporting health facility	
5	Date form received at national level (day/month/year)	
6	Name(s) of patient	
7	Date of birth (day/month/year)	
8	Age in years	
9	Age in months	
10	Patient's residence: village/neighbourhood	
11	Town/City	
12	Urban/Rural	
13	District of Residence	
14	Region	
15	Sex (M/F)	
16	Date seen at health facility (day/month/year)	
17	Date health facility notified district (day/month/year)	
18	Date of onset (day/month/year)	
19	Number of vaccine doses	
20	Date of last vaccination (day/month/year)	
21	Type of vaccine	
22	Blood Transfusion Yes/No	
23	History of Surgery Yes/No	
24	Received injection Yes/No	
25	Skin piecing and tattooing Yes/No	
26	Drinking unsafe water Yes/No	

27	Contact with Jaundiced patient Yes/No	
28	In-patient or Out-patient?	
27	Outcome (1=Alive; 2=Dead; 3=Unknown)	
28	Final classification (1=Lab Confirmed; 2=Confirmed by Epidemiological linkage; 3=Discarded (lab negative); 4= Pending (Suspected with specimen lab results	
29	Date form sent to district (day/month/year)	
30	Date received form at district (day/month/year)	
Laboratory Investigation Report		
31	Date specimen collection (day/month/year)	
32	Date specimen sent to Lab (day/month/year)	
33	Type of Specimen (specify)	
32	Date lab received specimen (dd/mm/yyyy)	
33	Specimen condition 1=adequate (good) 2=not adequate (not good)	
34	Lab Results: Hepatitis A: IgM anti-HAV Hepatitis B: HBsAg or IgM anti-HBc Hepatitis C: Anti-HCV Hepatitis D: HBsAg or IgM anti-HBc plus anti-HDV Hepatitis E: IgM anti-HEV and/or IgG anti-HEV	
35	Other lab results	
36	Date lab sent results to district (dd/mm/yyyy)	
37	Date district received lab results (dd/mm/yyyy)	
38	Name of Reporting Officer: Title: Function of reporting officer: Contact Phone No.: Email:	

Annex 5: Viral Hepatitis (Blood Donors Screening)

District/Health Facility Monthly Reporting Form, GHANA

Reporting District_____ District Code_____

Year _____ Number of Reports received on time_____

Officially Expected Number of Reports_____ Number of Reports received_____

HAV=Hepatitis A; HBV=Hepatitis B; HCV=Hepatitis C; HDV=Hepatitis D; HEV=Hepatitis E

REPORTING SUB-DISTRICT / Name of Facility	Number of Blood Donors Screened	Number of blood donors Positive for Viral Hepatitis					Number of Blood Donors Negative for Viral Hepatitis
		HAV	HBV	HCV	HDV	HEV	

Name of Person Reporting: Telephone No.:

_____ _____

Date Received at next level: Name of Person Receiving:

____/____/_____ _____

Telephone No.:

_____