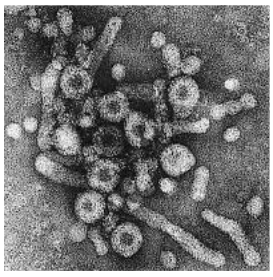
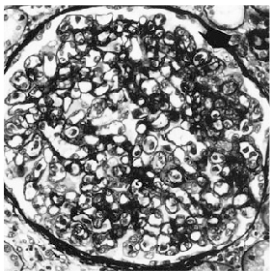
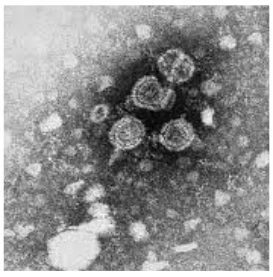
VIRAL HEPATITIS

An essential guide for nurses and health care professionals

THIRD EDITION

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PRAKASH
PRogrammed Approach to Knowledge And Sensitisation on Hepatitis

WHOCC on Viral Hepatitis and Liver Diseases

ilbs

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VIRAL HEPATITIS

An essential guide for nurses and health care professionals

An educational initiative of Project PRAKASH, ILBS

VIRAL HEPATITIS – An essential guide for nurses and healthcare professionals

Training Organiser: Institute of Liver & Biliary Sciences, New Delhi | www.ilbs.in

Under the Project
PRAKASH: **PR**ogrammed **A**pproach to **K**nowledge **A**nd **S**ensitization on **H**epatitis

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FOREWORD

Viral Hepatitis is a global concern especially endangering the population of developing countries. It is cited as an extremely common infection present among communities. Nearly 2 billion people are predicted to be suffering from HBC alone with over 325 million living as chronic carriers of HBV & HCV. Prevalence of HBV & HCV is considered higher among healthcare workers mainly attributable to occupational risk.

To be a factor in achievement of global standards in viral hepatitis, ILBS along with Cipla Foundation, established project PRAKASH in 2017 with an aim to strengthen healthcare care system by upskilling patient management skills of in-service healthcare professionals in management of viral hepatitis. The two components of the program – Hepatitis Induction Program & Hepatitis Update Program are made available for all level of healthcare workers. The program is in line with National Viral Hepatitis Control Program which uses both, the traditional cascade model of training and other platforms like e-learning and virtual classroom techniques. PRAKASH is an integrated initiative for prevention and control of viral hepatitis in India which would further contribute in achieving sustainable development goal (3.3) which aims to eliminate viral hepatitis by 2030.

This module on viral hepatitis for nursing professionals will describe the knowledge, skills and attitude that is required to deliver patient centered liver care. The course is intended to be used with other local policies and pathways around the scope of practice undertaken by nurses working at all levels. In addition to nurses this module will be useful for healthcare institutions as guiding document for capacity building in a way to be able to address this public health challenge of viral hepatitis in India.

I am highly excited to showcase the progress of project PRAKASH through this book. I congratulate the team of project PRAKASH for successfully putting up a wonderful course material which would serve as a ready reckoner for the learners.

Dr. S. K. Sarin,
Vice Chancellor, ILBS

PREFACE

Of many public health issues overwhelming the existing healthcare systems and workforces around the globe, viral hepatitis has established itself to be of great concern. Every year, hepatitis B and C alone accounts for more than 1 million deaths worldwide, 78% of the world's hepatocellular carcinoma and more than half of the fatal cirrhosis.

The purpose of this book is to provide guidance on recommended practices for viral hepatitis for nursing professionals to prevent or minimize adverse consequences of the disease. The book is addressed primarily to in-service nursing professionals who are involved in rendering healthcare services to viral hepatitis patients, it is correspondingly intended to provide guidance to healthcare institutions to plan and execute patient centric liver care. Likewise, the unit could be beneficial to other caregivers and professionals i.e. technicians, social workers, dieticians and counsellors involved in primary and secondary level of patient care services. The information is presented in a form readily accessible to the beneficiaries and essential guidance is given as detailed as possible.

This book is an uninterrupted effort to disseminate training on viral hepatitis and comprehensively covers the entire complexity associated with the disease. Diagnosis, prevention and management of the disease, nursing interventions as hepatitis counsellor, standard precautions, needle stick injury, bio-medical waste management, newer treatment advancement and mental health issues to name a few. This volume is our little contribution towards the battle against viral hepatitis elimination. Oversights and errors in this book are inevitable due to ever evolving literature. We look forward to criticism and suggestions from our readers.

The high prevalence of the disease has attracted worldwide attention and global and national policies have been formed to eliminate this deadly virus. The government agencies are forming long term systematic prevention and control strategies. There will be no doubt about the successful elimination of viral hepatitis, as we have been intensifying efforts to prevent and control the disease by improving screening, vaccination and treatment.

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ACKNOWLEDGEMENTS

Project PRAKASH is one of its kind initiatives undertaken by Institute of Liver & Biliary Sciences, New Delhi, supported by Cipla Foundation under its corporate social responsibility initiative. The first ever training program for nursing professionals on viral hepatitis in the country was commenced in 2017 with only 50 nurses enrolled in the program. Since then, the program has trained 8,000 healthcare professionals from 25 states across the country making it one of the most successful training programs in healthcare industry in India.

We express our profound gratitude to Dr. S. K. Sarin, Vice Chancellor, Institute of Liver & Biliary Sciences, New Delhi for believing in us and for being a wonderful mentor throughout. Thank you for encouraging and providing your invaluable support and guidance to the team.

Our deepest gratitude to all the faculties and educators for providing scientific content for the program. The revision of this module consumed huge amount of work, research and dedication which would not have been possible without the extensive contribution of Ms. Sarita Ahwal & Ms. Tarika Sharma (Lecturer, College of Nursing, ILBS). Therefore, we would like to extend our sincere gratitude to both of them.

The success of the project would not have been possible without the support that we have received from all of you. Last but not the least our thanks go to all the participants from different healthcare facilities across the country without who's enthusiastic participation this wonderful and memorable journey of project PRAKASH could not have been accomplished.

We heartily acknowledge contribution of the following individuals for their untiring efforts.

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ABBREVIATIONS & ACRONYMS

AALD	Alcohol Associated Liver Disease
AASLD	American Association for the Study of Liver Diseases
ACLF	Acute on Chronic Liver Failure
ADL	Activities for Daily Living
AIDS	Acquired Immune Deficiency Syndrome
AIH	Auto Immune Hepatitis
ALF	Acute Liver Failure
ALT	Alanine Aminotransferase
Anti-HAV	Hepatitis A Antibody
Anti-HBc	hepatitis B Core Antigen
Anti-HBe	Hepatitis B e Antigen
Anti-HBs	Hepatitis B Surface Antibody
Anti-HBV	Hepatitis B Antibody
Anti-HCV	Hepatitis C Antibody
Anti-HDV	Hepatitis D Antibody
Anti-HEV	Hepatitis E Antibody
APRI	Aspartate Aminotransferase to Platelet Ratio Index
ART/ARV	Antiretroviral Therapy
AST	Aspartate Aminotransferase
AVH	Acute Viral Hepatitis
BCG	Bacille Calmette-Guérin
BMWM	Bio-Medical Waste Management
BSG	British Society of Gastroenterology
CBC	Complete Blood Count
CBWTF	Common Bio-medical Waste Treatment and Disposal Facility
CCA	Cholangiocarcinoma
CD4	Cluster of differentiation 4
CDC	Center for Disease Control
cDNA	complementary Deoxyribonucleic Acid

CHB	Chronic Hepatitis B
CPCB	Central Pollution Control Board
CTP	Child-Turcotte-Pugh
DAAs	Direct Acting Antivirals
DALY	Disability-Adjusted Life Year
DILI	Drug Induced Liver Injury
DPT	Diphtheria-Pertussis-Tetanus
eGFR	Estimated Glomerular Filtration Rate
EL.U.	ELISA units
EOBs	Explaination of Benefits
ET Tube	Endotracheal Tube
FHF	Fulminant Hepatic Failure
FIB4	Fibrosis Stage >4
FiO	Fraction of inspired Oxygen
GCS	Glasgow Coma Scale
GI	Gastrointestinal
GPs	General Pysicians
HAV	Hepatitis A Virus
Hb	Hemoglobin
HBeAb	Hepatitis B Antigen and Antibody
HBeAg	Hepatitis B e Antigen
HBIG	Hepatitis B Immune Globulin
HBsAg	Hepatitis B Surface Antigen
HBV	Hepatitis B Virus
HCC	Hepatocellular Carcinoma
HCF	Health Care Facility
HCP	Health Care Professional/Personnel
Hct	Hematocrit
HCV	Hepatitis C Virus
HDV	Hepatitis D Virus
HE	Hepatic Encephalopathy
HEV	Hepatitis E Virus
HIV	Human Immuno-deficiency Disease
HPA	Health Protection Agency

HPS	Hepatopulmonary Syndrome
HRS	Hepatorenal Syndrome
ICP	Increased Intracranial Pressure
ICU	Intensive Care Unit
IDP	Internally Displaced Population
IDSA	Indian Direct Selling Association
IFN	Interferon
IFN-a	Interferon Alpha
Ig	Immunoglobulin
IgG	Immunoglobulin G
IgM	Immunoglobulin M
IM	Intramuscular
INR	International Normalized Ratio
IP&CT	Infection Prevention and Control Team
ITP	Immune Thrombocytopenic Purpura
IU	International Unit
IV	Intravenous
JAK2	Janus Kinase 2 gene
kPa	Kilopascal
LFT	Liver Function Tests
LMICs	Low-& Middle Income Countries
LMWH	Low Molecular Weight Heparin
LOLA	L-ornithine L-aspartate
MAP	Mean Arterial Pressure
MDR	Multiple Drug Resistant
MELD	Mayo End-stage Liver Disease
MMR	Measles, Mumps, and Rubella
MMWR	Morbidity and Mortality Weekly Report
MSM	Men having Sex with Men
NCP	Nursing Care Plan
NS5A	Non-Structural Protein 5A
NSI	Needle Stick Injury
OPV	Oral Poliovirus Vaccines
PaO	Partial Pressure of Oxygen

PCR	Polymerase Chain Reaction
pegIFN	Pegylated Interferon
PELD	Pediatric End-stage Liver Disease
PEP	Post Exposure Prophylaxis
PLHIV	People Living with HIV
PN	Parenteral Nutrition
PPCD	Paracentesis Circulatory Dysfunction
PPE	Personel Protective Equipment
PVT	Portal Vein Thrombosis
RNA	Ribonucleic Acid
ROM	Range of Motions
RT-PCR	Real-Time Reverse Transcriptase-Polymerase Chain Reaction
S. Creatinine	Serum Creatinine
SBP	Spontaneous Bacterial Peritonitis
SIRS	Systemic Inflammatory Response
SOFA	Sequential Organ Failure Assessment
STAT	Signal Transducer and Activators of Transcription
STD	Sexually Transmitted Diseases
STIs	Sexually Transmitted Infections
SVR	Sustained Virological Response
TIPS	Trans jugular Intrahepatic Portosystemic Shunt
TPO	Thrombopoietin
UIP	Universal Immunisation Program
USG	Ultrasound Sonography
WHO	World Health Organisation
Wks	Weeks
WNL	Within Normal Limits

ILBS

Institute of Liver & Biliary Sciences (ILBS) was started in 2010 as an autonomous institution under Government of National Capital Territory of Delhi (GNCTD) as a teaching hospital of liver and biliary diseases.

The vision of the institute is:

ILBS is committed to the highest levels of patient satisfaction, healthcare, staff and patient safety through continual improvement by ensuring:

- Evidence-based clinical practices of highest standard.
- Transparent management processes, facilitating patient satisfaction & ensuring dignity and rights of patients.
- Safe and conducive work environment for staff, and
- Establishing a dedicated centre of excellence in healthcare, teaching/training & research in the field of liver & biliary diseases.

The mission of the institute is:

To develop a facility with international standards, which could provide a comprehensive and most modern set up for the diagnosis and treatment, an advanced centre for dedicated research and resource for advanced training in the field of liver diseases, including liver transplantation, gall bladder and biliary diseases and allied specialties.

To serve as a torch-bearer model of health care in the country by amalgamating the skills and structure of academic universities, clinical and research acumen of the super-specialists and the managerial skills of the corporate world.

Our Values underpins the way we integrate values of clinical practice, education, research and skill development. Our core value focuses on:

- Integrity & ethical values for proper conduct.
- Focussed thinking by adopting a holistic approach employing various methods for liver-based therapies.
- Excellence in both clinical and research.
- Team work for enabling best patient care and collaborative initiative for capacity building.
- To be the torchbearers and pioneers to take on new challenges and developing solutions in both patient care and academic pursuit.

ILBS – WHOCC

ILBS has achieved the distinction of being a **World Health Organization Collaborating Centre (WHOCC) on liver disease and second on viral hepatitis**.

The collaboration between ILBS and WHO would enable systematic collection and analysis of community and hospital-based data on hepatitis A, B, C and E, including various aspects of transmission, prevention, and

treatment specific to low resource settings in India. Such data would help WHO in developing guidelines and recommendations on these aspects of diseases and formulate policies accordingly. The collaborating centre will also serve as a resource center for training of different categories of healthcare workers in relation to viral hepatitis and liver diseases.

1. Generate data, evidence-based policies
2. Capacity through quality training
3. Prevent transmission,
4. Increased access to treatment

BACKGROUND

Hepatitis is described as an inflammation of the liver. It may be caused by drugs, alcohol use, autoimmune diseases or certain medical conditions. But in most cases, it is caused by a virus which is known as viral hepatitis. The condition of hepatitis can be self-limiting, or it can cause fibrosis i.e., scarring, cirrhosis or liver cancer.

Viruses that infect hepatocytes are considered hepatotropic viruses. Five hepatotropic viruses known to cause hepatitis, have been described and have been named as hepatitis A, B, C, D, and E in historical order of their recognition. Worldwide, cases of hepatitis presumably caused by viruses other than these five also occur.[1] Hepatitis A and E virus are predominantly enterically transmitted pathogens and are responsible to cause both sporadic infections, epidemics of acute viral hepatitis (AVH) and are occasionally a healthcare infection prevention issue.[2] Hepatitis B, C and D virus are blood borne pathogens which predominantly spread via parenteral route and are notorious to cause chronic hepatitis, which can lead to grave complications including cirrhosis of liver and hepatocellular carcinoma (HCC).[3] HBV, HCV and HDV also pose a risk of healthcare-associated transmission or occupational exposure for healthcare personnel (HCP).[4,5] The infection prevention of each of the viral hepatitis contains specific recommendations.

Viral hepatitis now ranks as the seventh leading cause of mortality worldwide. Although mortality due to communicable diseases has declined globally, the absolute burden and relative ranking of viral hepatitis as a cause of mortality has increased between 1990 and 2013.[6]

In South-East Asia, 100 million people are currently estimated to be living with hepatitis B, and 30 million with hepatitis C.[7] In India, viral hepatitis is now recognized as a serious public health problem. It places a huge social and economic burden on the affected individuals, families, as well as the health system. Viral hepatitis is a cause for major health care burden in India and is now equated as a threat comparable to the “big three” communicable diseases – HIV/AIDS, malaria and tuberculosis.[2] Around 400 million people all over the world suffer from chronic hepatitis and the Asia-Pacific region constitutes the epicentre of this epidemic.[6]

As per WHO and the latest estimates, in India, 40 million people are chronically infected with hepatitis B and six to 12 million people are chronically infected with hepatitis C. HEV is the most important cause of epidemic hepatitis, though HAV is more common among children. Most acute liver failures diagnosed are attributable to HEV.[2] There are many challenges in prevention and eradication of viral hepatitis in India.[8] Maintaining adequate sanitary and hygienic conditions can help tackle the problem associated with enterically transmitted pathogens like HAV and HEV.[2,8] Following a multipronged approach of active screening, adequate treatment, universal vaccination against HBV and educational counselling can help decrease the burden of liver diseases associated with HBV and HCV infection in India.[2,8] WHO's Draft Global Health Sector Strategy on Viral Hepatitis gives the much needed roadmap and targets to combat hepatitis. It provides realistic targets and action plans to eliminate hepatitis by 2030.[9] This is planned to be achieved by building capacities in the existing health care delivery system to reach the desired goal.[9]

In May 2016, the World Health Assembly adopted the first global health sector strategy on viral hepatitis, 2016-2021. The strategy highlights the critical role of universal health coverage and sets targets that align with

those of the Sustainable Development Goals. The strategy aims to eliminate viral hepatitis as a public health problem by reducing new viral hepatitis infections by 90% and reduce deaths due to viral hepatitis by 65% by 2030.[10] For World Hepatitis Day 2021, WHO is focusing on the theme "Hepatitis can't wait" to highlight the urgency of hepatitis elimination with a view to achieving the 2030 elimination targets.[10]

Standard precautions, which encompass both universal precautions and body substance isolation, are appropriate for prevention and spread of all types of viral hepatitis in the healthcare environment.[11] Vaccines are available for hepatitis A and hepatitis B. There is no vaccine available at the present time to protect against infection of hepatitis C & D virus; however, trials are currently underway. While there is a safe and effective anti-hepatitis E vaccine, at present it is only licensed for use in China. Given the recognition of HEV as a global pathogen, there is a need to develop HEV vaccines for use globally. Vaccines remain an important cornerstone in the battle to achieve dominance over hepatitis A, B, C, D, and E and thereby decrease morbidity and mortality from these infections in a cost-effective manner.[12,13]

PRAKASH

There are many challenges to prevent and eradicate viral hepatitis from the country. Health professionals in the country needs to join hands towards achieving the target of viral hepatitis elimination by 2030, a global call for action by WHO.

It is being felt that the knowledge of viral hepatitis, especially B and C is necessary for our doctors, nurses and laboratory technicians for better discharge of their duties to protect the patients and themselves from viral hepatitis infection. The above can only be achieved by building capacity in the existing healthcare delivery system by imparting knowledge of screening, diagnosis, and management of viral hepatitis amongst healthcare providers.

Project PRAKASH (PRogrammed Approach to Knowledge And Sensitization on Hepatitis), has been conceptualised and a delivery mechanism has been formalised so that comprehensive knowledge sharing among technical experts from ILBS and healthcare professionals across India could be done at a common platform. It is a training program for primary care physicians, and paramedical professionals to provide comprehensive training in screening, diagnostic and therapeutic services for viral hepatitis to general and high-risk population of the country.

The overall aim of the project PRAKASH is in harmony with the National Viral Hepatitis Control Program (NVHCP) i.e. capacity building of existing human resources in management of viral hepatitis and its complications. Both the programs are in line with each other with the intention of raising the awareness level about hepatitis infection across the nation thereby aligning the program with global mandate of viral hepatitis elimination by 2030 set by WHO.

ILBS being the only liver specialist institute has under taken this initiative with an aim to reduce the burden of viral hepatitis by conducting nationwide training of healthcare fraternity in management of viral hepatitis. Since its inception in 2017 the program has successfully trained more than 8,000 healthcare professionals from 500 healthcare institutions across 25 states and union territories of the country. The program has two major components: Hepatitis Induction Program (HIP) & Hepatitis Update Program (HUP).

The project aims at achieving below mentioned goals at the end of the program:

- Creating awareness among nursing professionals in management of viral hepatitis and to promote best practices while managing patients of viral hepatitis.
- Tracking the progress made on the training imparted and to create a model towards awareness and training for healthcare providers.
- To strengthen the role of nurses by supporting the nursing organizations within the sector to develop, deliver and evaluate education on blood-borne viruses as well as health professionals working in the field of viral hepatitis.
- To create a healthcare communal stage to discuss on need, methods and ways to minimize burden of viral hepatitis in the country.

Training objectives: This document provides technical guidance to in-service nursing professionals and other key stakeholders to understand and manage viral hepatitis in hospital settings. For healthcare facilities, this document can also serve as a checklist to identify any remaining gaps.

This document is intended to guide the diagnosis, management and prevention of viral hepatitis and it's complications and to ensure that patients can access appropriate treatment support without compromising safety of healthcare workers.

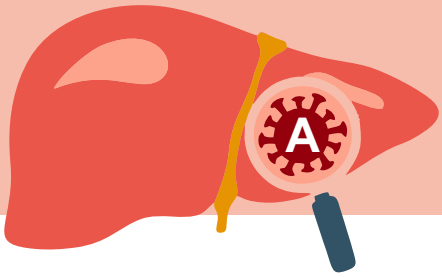
At the end of the training course, nursing professionals will be able to:

- Understand and interact with specialists about the epidemiology of viral hepatitis and their consequences.
- Understand the serological diagnosis of HAV, acute and chronic HBV, acute and chronic HCV, and hepatitis B and hepatitis D co-infection.
- Understand the need of family counselling and screening and addressing the mental health issues associated with the disease.
- Identify complications like cirrhosis, portal hypertension and liver cancer.
- To be thoroughly equipped with personal protective equipment's, post
- exposure prophylaxis, and bio-medical waste management guidelines so as to minimize risk of transmission among nursing professionals.
- Reaffirms standard precautions as the foundation for preventing transmission of infectious agents in hospital settings.
- Refer cases to appropriate referral centres.

COURSE SCHEDULE

DAY - 1
PRAKASH - Introduction Introduction to the program; key facts on viral hepatitis; national & international policies & do's and don'ts in a virtual classroom.
Viral Hepatitis A Key facts; epidemiology; clinical features; laboratory diagnosis of HAV; vaccination & treatment options.
Viral Hepatitis B Key facts; modes of transmissions; acute vs chronic infection; laboratory diagnosis & tratment; vaccination for various age groups; HBV in co-morbidities.
Viral Hepatitis C Epidemiology; symptoms; complications & transmission in HCV; diagnosis, treatment & prevention; percutaneous exposure among healthcare workers.
Viral Hepatitis D Co-infection with HBV; epidemiology; laboratory diagnosis; treatment & prevention.
Viral Hepatitis E Epidemiology; modes of transmission, clinical features; diagnosis, treatment & prevention.
DAY - 2
Patient & Family Counselling HBV & HCV of screening family; mental health disorder in viral hepatitis patients.
Viral Hepatitis in children Acute vs chronic viral hepatitis (A-E); treatment & prevention options.
Viral Hepatitis in pregnancy HAV & HEV in pregnancy; acute liver failure; vaccination & breast feeding of newborns.
NSI & PEP Standard precautions; injection safety; reporting of NSI; post exposure prophylaxis in case of a needle stick injury.
Bio-medical waste management Categorization & classification of wastes; segregation; treatment & disposal; spill management guidelines of blood & mercury spills.

HEPATITIS A



Key facts

- Hepatitis A is a viral liver disease that can cause mild to severe illness.[14,15]
- Hepatitis A virus (HAV) is transmitted through ingestion of contaminated food and water or through direct contact with an infectious person.[14,15]
- Almost everyone recovers fully from hepatitis A with a lifelong immunity. However, a very small proportion of people infected with hepatitis A could die from fulminant hepatitis.
- The risk of hepatitis A infection is associated with a lack of safe water, and poor sanitation and hygiene (such as dirty hands).
- Epidemics can be explosive and can cause substantial economic loss.
- A safe and effective vaccine is available to prevent hepatitis A.
- Safe water supply, food safety, improved sanitation, hand washing, and hepatitis A vaccine are the most effective ways to combat the disease.

Epidemiology

HAV is assigned its own genus, Hepatovirus, in the family Picornaviridae.[16] HAV is a nonenveloped, 27-nm single-stranded RNA virus that can be found by electron microscopy in the faeces of persons with this infection. Humans and primates are the only known natural hosts for HAV. Replication of HAV occurs in the hepatocytes, but the virus is not directly cytopathic.[16]

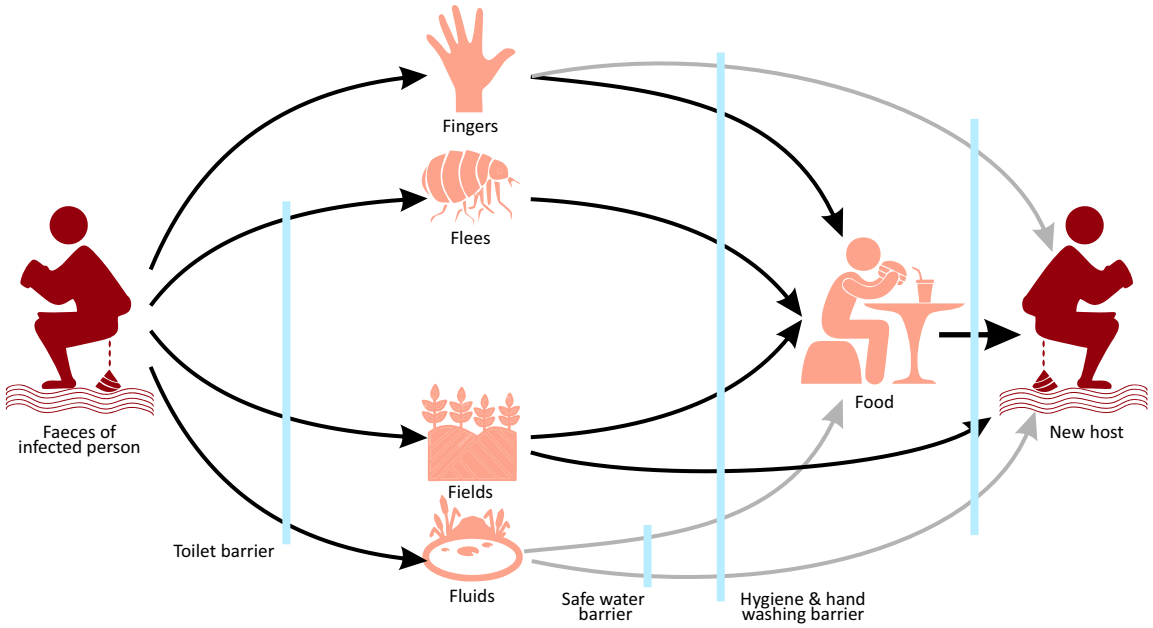
Scenario in India

HAV is responsible for several outbreaks of sporadic viral hepatitis in India.[2] However, in the recent times there has been a sero-epidemiological shift in HAV infection in India, with increasing incidence of infection being noted in the adult and adolescent population compared with children[2]. Studies have clearly demonstrated the higher seroprevalence of HAV in older children and established a clear link between improved living standard and decreased seropositivity of HAV[2].

Transmission

- HAV is transmitted principally by the faecal-oral route, with the highest level of virus in the faeces found in the 2 weeks prior to onset of jaundice or increased liver enzymes. This is also the period of highest infectivity.[17]
- Transmission is usually facilitated by intimate personal contact (household, sexual, etc.), poor hygiene, unsanitary conditions, or contaminated water, milk, or food, especially raw shellfish.[17]
- Additional risk factors of acquiring HAV[16]Childcare exposure (children, parents, or attendants) esp. day care workers who don't wash their hands after changing a diaper.
- Men who have sex with men (MSM)
- Occupation (e.g., sewage worker, paediatric nurse)
- Users of both injectable and non-injectable street drugs can get it by using dirty or used needles; Intravenous (IV) drug users
- HAV is rarely transmitted by blood or blood products (e.g., clotting factor concentrates) as a consequence of transient viremia in asymptomatic donors.

Figure 1: Transmission of Hepatitis A by feco-oral route



The "F-diagram" (faeces, fingers, flies, fields, fluids, food), showing pathways of fecal–oral disease transmission. The vertical blue lines show barriers: toilets, safe water, hygiene and handwashing.

Source: UNICEF Philippines and Luis Gatmaitan / 2014 / Gilbert F. Lavides - https://www.flickr.com/photos/gtzecosan/17125224489/in/set-72157648282032913

Who is at risk?

Anyone who has not been vaccinated or previously infected can get infected with hepatitis A virus. In areas where the virus is widespread (high endemicity), most hepatitis A infections occur during early childhood. Risk factors in intermediate and high endemicity areas include[17]:

- Poor sanitation;
- Lack of safe drinking water;
- Use of recreational drugs;
- Living in a household with an infected person;
- Being a sexual partner of someone with acute hepatitis A infection; and
- Travelling to areas of high endemicity without being immunized.

Pathogenesis

Infection with HAV occurs in the gastrointestinal tract. HAV is transiently detectable in blood as early as 4 weeks before symptoms.[18] It is detectable in faeces 2 to 4 weeks before and 1 to 3 weeks following the onset of jaundice.[18] Infected neonates may shed HAV in faeces for months[18]. There is no chronic HAV carrier state. HAV replicates in cytoplasm of hepatocytes, and then is shed in bile, which results in high titre of infectious HAV in faeces. Disease occurs as a result of host immune response, which causes hepatocyte injury. Development of antibodies to HAV confers lifelong immunity[18].

Clinical features

Infection by HAV is generally self-limited and can produce effects that range from a lack of symptoms to death

from fulminant hepatitis.[18] The likelihood of clinically apparent disease associated with HAV infection increases with age. In children less than 6 years of age, most infections (70%) are asymptomatic[18], and if illness does occur, it is usually anicteric. Among older children and adults, infection is usually symptomatic, with jaundice occurring in more than 70% of patients.[18] After an average incubation period of 28 days (range, 15 to 50 days), most HAV-infected persons developed nonspecific constitutional signs and symptoms followed by gastrointestinal symptoms. Typically, these include fever, malaise, anorexia, nausea, abdominal discomfort, dark urine, and jaundice, all of which usually last less than 2 months.[18] There is no evidence of chronic liver disease or persistent infection following infection. However, 15 to 20% of the patients may have prolonged or relapsing disease lasting up to 6 months[19,20], and HAV can be detected in serum for as long as 6 to 12 months after infection[21]. Fulminant hepatitis is a rare complication of hepatitis A. The risk of acute liver failure ranges from 0.015 to 0.5%, and the highest rate occur among young children and older adults with underlying chronic liver disease.[22,23]

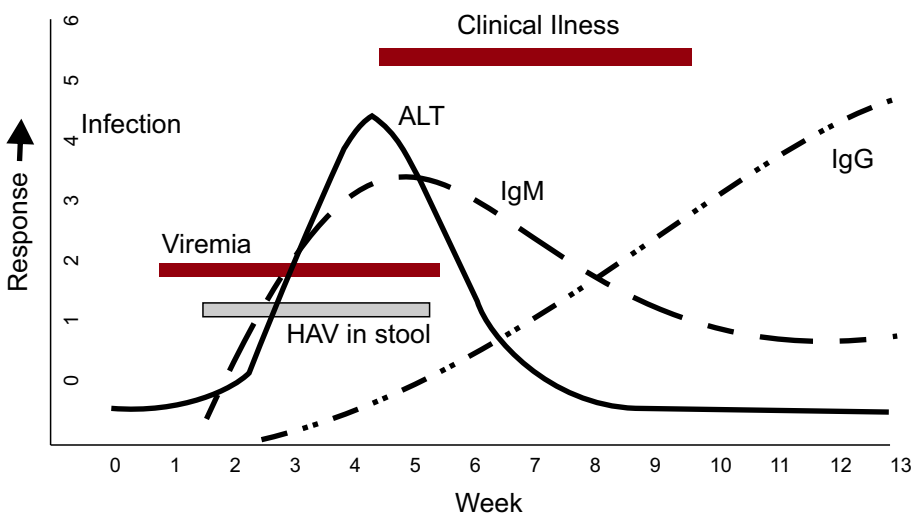
Laboratory diagnosis

Clinical features of acute hepatitis are not specific for HAV infection, so serological diagnosis is necessary (Figure).[18] Immunoglobulin M antibodies to HAV (IgM anti-HAV) are used to detect acute HAV infection, are detectable within 3 weeks of exposure, and are present at the onset of jaundice. Titre declines over 4 to 6 weeks and is usually not detectable after 6 to 12 months. Immunoglobulin G anti-HAV (IgG anti-HAV) is also detectable at onset of jaundice and remains positive lifelong, indicating immunity to HAV.[24]

Molecular diagnosis

The amplification of HAV RNA by reverse transcription, followed by PCR of the cDNA, is the most sensitive technique for screening clinical specimens. Studies using reverse transcription PCR (RT-PCR) have demonstrated that HAV RNA can be detected in blood earlier than antibodies and that the viremia may be present for a much longer period during the convalescent phase of hepatitis A than was previously thought. Amplification of viral RNA by nested PCR is currently the most sensitive and widely used method for the detection of HAV RNA in different types of samples (serum, plasma, saliva, fecal suspension and environmental samples).[25] Different studies have shown that in particular, HAV load is strongly correlated with the severity of hepatitis A.[26]

Figure 2: Clinical course of Hepatitis A



Source: http://www.ncbi.nlm.nih.gov/pubmed/15123984. Accessed January 14, 2019.

Treatment

Supportive care (e.g., fluids and nutrition) is the only known management for acute Hepatitis A.[28] Recovery from symptoms following infection may be slow and take several weeks or months. Therapy is aimed at maintaining comfort and adequate nutritional balance, including replacement of fluids that are lost from vomiting and diarrhea.[28] Liver transplantation should be considered in case of fulminant hepatic failure.[28]

Prevention

- Public health and personal hygiene measures, including hand washing or hand sanitizer, may effectively interrupt further transmission. Risk of transmission of HAV is transient and occurs during the prodrome.[29]
- Standard precautions are appropriate to prevent healthcare-associated transmission in most instances. With diapered or incontinent patients, the addition of contact precautions is recommended.
- Postexposure prophylaxis should be considered in instances such as household or sexual contacts or in outbreak situations such as common source exposure in an infected food handler or a case of HAV in a childcare center. HAV vaccine is recommended for unvaccinated adults aged 40 or younger with recent (within 2 weeks) exposure to HAV. For persons over 40 with recent (within 2 weeks) exposure to HAV, immune globulin (Ig) is preferred over vaccine. A dose of 0.02 mL/kg intramuscular (IM) protects for up to 3 months.
- Improved sanitation and hepatitis A immunization are the most effective ways to combat the disease.
- Adequate supplies of safe drinking water and proper disposal of sewage within communities combined with personal hygiene practices, such as regular hand washing reduces the spread of HAV.
- Several hepatitis A vaccines are available internationally. All are similar in terms of how well they protect people from the virus and their side-effects. No vaccine is licensed for children below one year of age.

Vaccination

Patients having chronic illness are more likely that they will have serious complications from certain diseases. Immunization provides the best protection against vaccine preventable diseases. Vaccination forms a cornerstone in preventing HAV and both inactivated and live attenuated vaccines are available for use. Active immunization with either licensed single antigen HAV vaccine (HAVRIX, manufactured by GlaxoSmithKline; VAQTA, manufactured by Merck & Co., Whitehouse Station, NJ) or combination TWINRIX (manufactured by GlaxoSmithKline, Rixensart, Belgium), which contains both HAV (in a lower dosage) and HBV antigens, is generally safe and effective.[30]

Table 1: Havrix & Vaqta vacine comparison

Vaccine#	Age group	Dose	Volume	#Dose	Schedule
Havrix (GlaxoSmithKline [GSK])	1-18 years	720 El.U.*	0.5 ml	2	0,6-12 months
	19 years and older	1440 El.U.*	1.0 ml	2	0,6-12 months
Vaqta (Merck & Co.)	1-18 years	25 U**	0.5 ml	2	0,6-18 months
	19 years and older	50 U**	1.0 ml	2	0,6-18 months

*Completion of the hepatitis A series with the same product is preferable. However, if the originally used product is not available or not known, vaccination with either product is acceptable.

**The 2 vaccines have similar immunogenicity but local tolerance was better with Vaqta11

Indian Academy of Paediatrics recommends two doses for any of the licensed vaccines which have to be given 6 months apart to children aged 1 year or older.[31] The dose recommended is 720 ELU for those aged <19 years and 1440 ELU for those above.[31] Protective titres of antibodies are seen in almost 100% after the second dose of injection. More than 95 percent of adults generate protective antibodies within a month of HAV vaccination. Adverse reactions are minor and usually include local pain and swelling.[31] Immunization should be offered to select adult populations that are either at risk for fulminant presentation or at high risk of acquiring HAV. These groups include:[30]

- Those travelling to countries or areas with recent or ongoing hepatitis A outbreak or epidemic
- Homosexuals (MSM)
- IV drug users
- have a chronic liver disease such as hepatitis B or hepatitis C
- are being treated with clotting-factor concentrates
- Persons who work with HAV in experimental laboratory settings (not routine medical laboratories), and
- Food handlers when health authorities or private employers determine vaccination to be appropriate

Pre-Exposure Prophylaxis

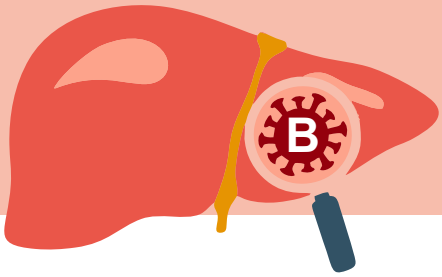
- Immune-globulin is recommended for all susceptible travellers to developing countries. IG is especially important for persons who will be living in or visiting rural areas, eating or drinking in settings of poor or uncertain sanitation, or who will have close contact with local persons (especially young children) in settings with poor sanitary conditions[32,33,34,35].
- For travellers, a single dose of IG of 0.02 ml/kg of body weight is recommended if travel is for less than 3 months. For prolonged travel or residence in developing countries, 0.06 ml/kg should be given every 5 months.

Post-Exposure Prophylaxis

- For post exposure IG prophylaxis, a single intramuscular dose of 0.02 ml/kg is recommended.
- IG should be given as soon as possible after last exposure; giving IG more than 2 weeks after exposure is not indicated.
- Specific recommendations for IG prophylaxis for hepatitis A depend on the nature of the HAV exposure.
- Close personal contact: IG is recommended for all household and sexual contacts of persons with hepatitis A.
- **Day-care centers**: Day-care facilities attended by children in diapers can be important settings for HAV transmission[19,20,21,22]. IG should be administered to all staff and attendees of day-care centers or homes if
  - one or more children or employees are diagnosed as having hepatitis A, or
  - cases are recognized in two or more households of center attendees. When an outbreak (hepatitis cases in three or more families) occurs, IG should also be considered for members of households that have children in diapers.
- **Institutions for custodial care**: Living conditions in some institutions, such as prisons and facilities for the developmentally disabled, favour transmission of hepatitis A. When outbreaks occur, giving IG to residents and staff who have close contact with patients with hepatitis A may reduce the spread of disease.
- **Hospitals**: Routine IG prophylaxis for hospital personnel is not indicated. Rather, sound hygienic practices should be emphasized. Outbreaks of hepatitis A occur occasionally among hospital staff, usually in association with an unsuspected index patient who is fecally incontinent. Large outbreaks have occurred from contact with infected infants in neonatal intensive care units. In outbreaks, prophylaxis of persons exposed to faeces of infected patients may be indicated.

- **Common-source exposure**: IG use might be effective in preventing foodborne or waterborne hepatitis A if exposure is recognized in time. If a food handler is diagnosed as having hepatitis A, common-source transmission is possible. IG should be administered to other food handlers. However, IG administration to patrons may be considered if all of the following conditions exist:
  - the infected person is directly involved in handling foods without gloves that will not be cooked before they are eaten, and
  - the hygienic practices of the food handler are deficient or the handler has had diarrhoea, and
  - patrons can be identified and treated within 2 weeks of exposure.

HEPATITIS B



Key facts

- Hepatitis B is a viral infection that attacks the liver and can cause both acute and chronic disease.[36]
- The virus is transmitted through contact with the blood or other body fluids of an infected person.
- An estimated 296 million people are living with chronic hepatitis B virus infection (defined as hepatitis B surface antigen positive). Around 1.5 million [1.1–2.6 million] people are newly infected with hepatitis B virus.
- 6 million [4–11 million] children younger than five are living with hepatitis B virus infection (WHO, 2021).[37]
- Hepatitis B is an important occupational hazard for health care workers.
- However, it can be prevented by currently available safe and effective vaccine.

Hepatitis B is infection of liver caused by hepatitis B virus. The infection is called acute when a person first becomes infected with HBV. The infection becomes chronic (long term) when a person has symptoms, such as liver swelling for 6 months or longer. Acute HBV infections are more common in adults. Infants and young children have a higher risk for chronic HBV. Hepatitis B is a potentially life-threatening liver infection caused by the hepatitis B virus which is a major global health problem.[36,38,39] It can cause chronic infection and puts people at high risk of death from cirrhosis and liver cancer. A vaccine against hepatitis B has been available since 1982 and is 95% effective in preventing infection and the development of chronic disease and liver cancer caused due to hepatitis B.[40]

Modes of transmission

Figure 3: Modes of transmission of Hepatitis B virus

	Child to child (also adult to child): Infected children and most chronically infected adults look healthy. Transmission occurs during play through cuts, bites, scrapes, scratches or contact with wounds **(Most common mode of transmission in india.)**
	Pre-natal transmission: from mother to baby, usually at the time of birth
	Through unsafe blood transfusion and organ transplant

	Through drug users sharing needles, or through unsafe injections or other unsafe medical procedures.
	Through unprotected sexual contact

Source: Epidemiology of Hep B and HIV diseases in India Dr. Pradeep Haldar AC(I) SEPIO meeting 18-20 May 2011

HBV is transmitted through contact with infected blood or body fluids across breakages in skin/mucous membranes and unprotected sexual intercourse.[36,38,39]

HBV is 100 times more infectious than Human Immuno-deficiency Virus. Unlike HIV, HBV is able to remain active on surfaces (e.g. table tops, razor blades, blood stains etc.) for about a week without losing infectivity[36,38,39].

Outcomes of HBV infection

Hepatitis B disease is the inflammation of the liver cells caused by hepatitis B virus. The outcomes of HBV infection are age-dependent and include acute (short term and clinically apparent) hepatitis B and chronic (long-term and mostly unapparent) disease.[41,42,43] The infecting dose of virus and the age of the person infected are important factors that correlate with the severity of acute or chronic hepatitis B. Only a small proportion of acute HBV are actually recognized clinically.[41,42,43]

Acute HBV infection

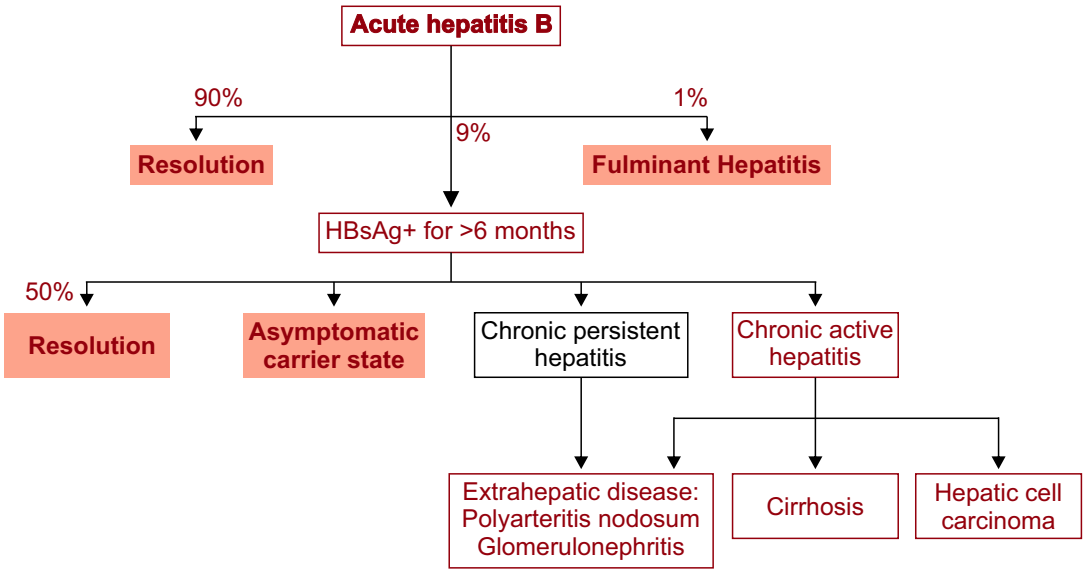
- Acute hepatitis B occurs in approximately 1% of perinatal, 10% of early childhood (1-5 years old) and about 30% late (more than 5 years old) HBV infections.[44,45] The course of acute hepatitis B is extremely variable and the incubation period ranges from 2-5 months.

Common symptoms include:

- Fever (Mild/ absent)
- Loss of appetite
- Tiredness
- Pain in muscles, joints
- Nausea, diarrhoea, vomiting
- Pain abdomen
- Headache
- Dark urine
- Pale stools
- Jaundice

- Most acute cases result in recovery except about 1% progresses to fulminate hepatitis. Fulminant hepatitis has a very high mortality of about 70%.[44,45]

Figure 4: Clinical outcomes of Hepatitis B infection[46]



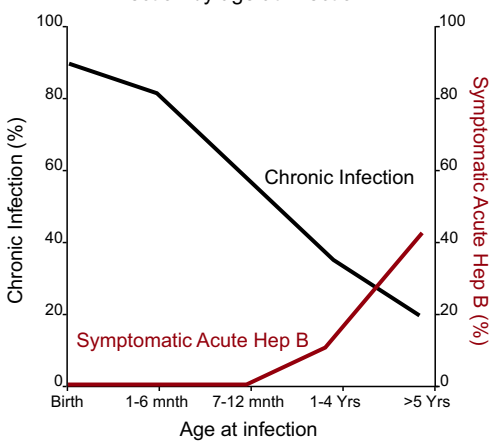
Source: Burrell CJ, Howard CR, Murphy FA. Fenner and White's Medical Virology.

Chronic hepatitis B infection

Chronic HBV infection is one of the most common and persistent viral infections in humans. If infection occurs in infancy, 99% remain asymptomatic. 90 % of these become chronic carriers[48,49]. In contrast, 30% of those infected during childhood (1-5 years) and 6% of those infected during adulthood become chronic carriers. Persons with chronic HBV infection have a 15-25% risk of dying prematurely due to HBV related liver cirrhosis and cancer.[44,45,49] The example in the table below demonstrates, out of 100 persons infected at different ages, the number of persons at risk of developing chronic HBV infection and complications.

In Africa and Asia, liver cancer is second only to tobacco as the most frequent cause of cancer deaths among adult males, most of which are attributed to HBV infection.[44,48,49]

Figure 5: Outcome of Hepatitis B virus infection by age at infection[50,51]

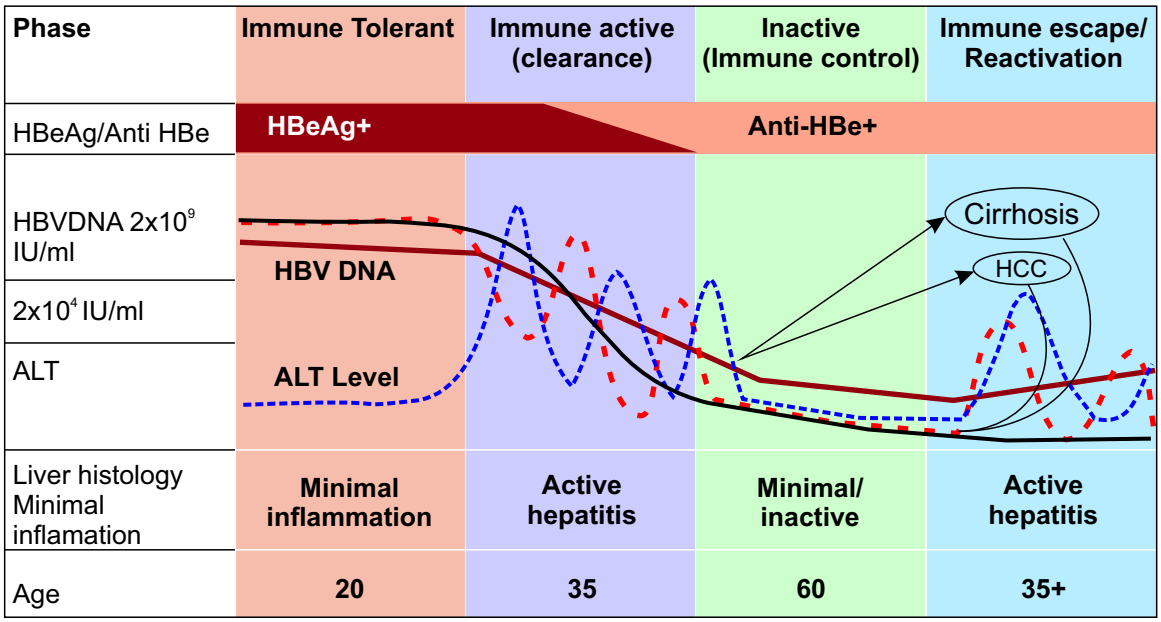


Source: Morse SA. Atlas of Sexually Transmitted Diseases and AIDS. Saunders/Elsevier; 2010.

Type	IF Infected	THEN chronic HBV infection	AND Cirrhosis/ Carcinoma*
Infant	100	90% = 90	15% of 90 = 14
Child (1-5 Yrs)	100	30% = 30	15% of 30 = 5
Adult	100	6% = 6	15% of 6 = 1

**assuming the lower rate of 15% complications*

Figure 6: Natural history of Hepatitis B infection



Immune Tolerant	Immune active (clearance)	Inactive (Immune control)	Immune(escape/ reactivation)
This phase is seen in HBV transmission at birth/1-2 years of life. HBeAg +ve and high viral load (107 IU/mL) but no elevation of transaminases and minimal activity in liver as there is no immunological response.	With increased immune response HBVDNA level decreases. Liver enzymes fluctuate. Active inflammation in liver ending in HBeAg negative and HBeAb +ve (HBeAg seroconversion) Ongoing activity could progress to fibrosis and liver cirrhosis with HCC.	HBeAg remains negative in 70-85% with low viral load <2 x 103 IU/mL with persistently normal liver enzymes but hepatitis activity may continue in some Fibrosis/cirrhosis noted in those who had progressed in immune active phase.	Progression from HBeAg negative inactive phase to HBeAg negative hepatitis B with mutation in core or core promoter region of HBV genome resulting in HBeAg negative but with continued HBV replication and progression in liver disease.

Source: Modified from Hepatitis B Virus Infection, Yun-Fan Liaw, Chia-Ming Chu, Lancet 2009; 373 : 582-92

Clinical features

The incubation period ranges from 30 to 180 days (mean=75 days).[52,52,54,55] Prodromal urticarial rash, arthritis, and fever occur in 5 to 10 percent of adults.[54] Neonates or young children are usually asymptomatic. Acute HBV is more insidious and prolonged than HAV. Fulminant hepatic failure is rare but can be fatal without liver transplantation.[36,54] Symptoms are similar to HAV. In acute HBV (Figure 8), HBsAg, HBeAg, and HBV DNA are detectable in serum 2 to 7 weeks before onset of symptoms.[36,38,39,54] When symptoms occur, immunoglobulin M anti-HBV core (IgM anti-HBc) and ALT, aspartate aminotransferase (AST), and bilirubin levels all rise.[54,56,57]

ALT levels generally exceed AST and are usually elevated 10- to 20-fold from normal. Bilirubin elevations vary with severity. Prolonged prothrombin time (international normalized ratio [INR] ≥ 1.5) or hypoalbuminemia imply severe hepatic injury and may portend fulminant hepatic failure. Acute HBV resolves slowly (weeks to months) following detection of immunoglobulin G anti-HBc (IgG anti-HBc), anti-HBe, and anti-HBs, and disappearance of HBeAg and HBsAg. IgM anti-HBc may persist for months then disappear.[54,56,57]

In **chronic hepatitis** (Figure), HBsAg, HBeAg, and HBV DNA are detected for more than 6 months, and ALT and AST levels fall but do not always return to normal. These persons remain infectious for others; those with HBeAg are highly infectious and are at greatest risk of developing cirrhosis or hepatocellular carcinoma. Persons who have human immunodeficiency virus or other forms of immunosuppression (e.g., dialysis patients) and who acquire HBV infection are more likely to develop chronic HBV and associated liver complications than are those without these comorbid conditions.

Figure 7: Typical serological course of hepatitis B virus infection with recovery[50,51]

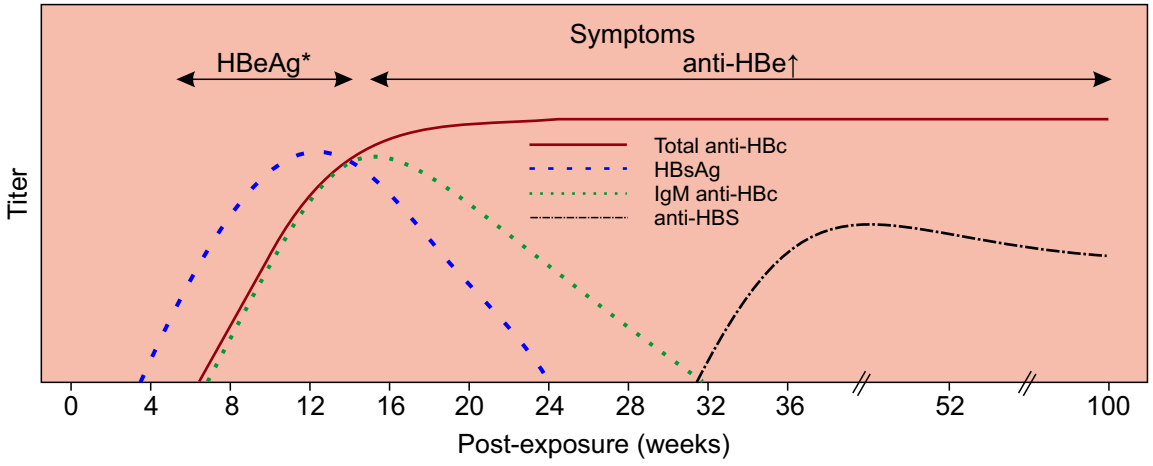
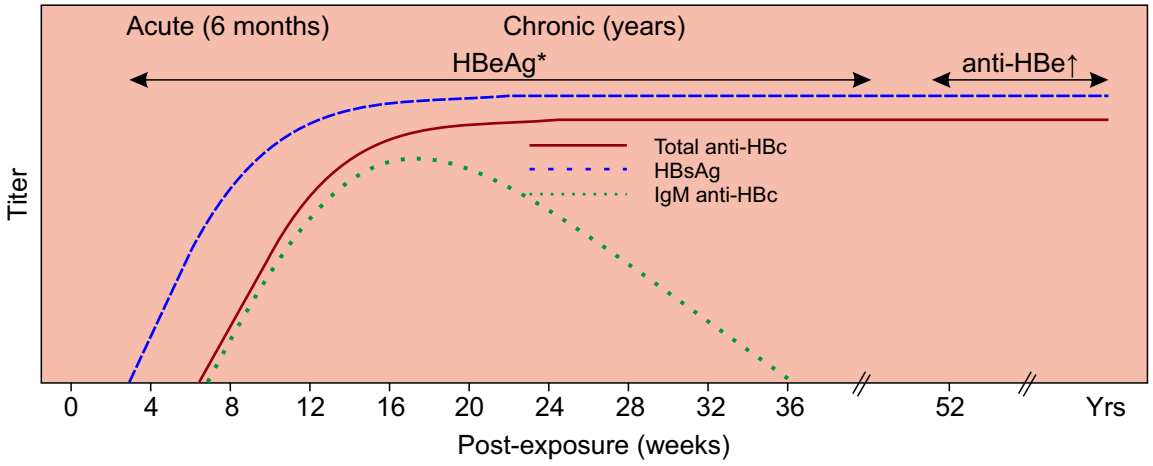


Figure 8: Typical serological course of acute hepatitis B virus infection with progression to chronic HBV infection[50,51]



Laboratory diagnosis

- In prodromal or preicteric HBV disease, HBsAg, HBeAg, and HBV DNA are detectable in serum (see Figure), with HBsAg becoming positive 1 to 10 weeks after an exposure and before the onset of symptoms.[58,59,60,61] Finding HBeAg and high concentration of HBV DNA signify high rates of HBV replication and heightened infectivity. With onset of symptoms, rise in levels of aminotransferase and bilirubin, IgM anti-HBc becomes positive. This is the ideal test to determine whether an acute hepatitis is due to hepatitis B, since the titre rises with onset of symptoms and falls below detectable levels after several months, so it is not positive in those with chronic hepatitis B. As acute illness wanes over a period of weeks, aminotransferase and other biochemical monitors improve. HBeAg, HBV DNA, and HBsAg may disappear. IgG anti-HBc, anti-HBe, and anti-HBs are detectable.[58-61]
- In chronic HBV, biochemical abnormalities may persist, and a positive serum test for HBsAg for more than 6 months is diagnostic of chronic hepatitis B. IgG anti-HBc remains detectable, but IgM anti-HBc declines. Eventually HBV DNA and HBeAg may disappear, and this signifies an asymptomatic carrier. In active chronic infection, transaminases and HBV DNA remain elevated. These patients can either be HBeAg positive or HBeAg negative. HBeAg positive patients can spontaneously convert to anti-HBe, typically with an acute rise in transaminases, then return to normal, along with a fall in HBV DNA and improved liver inflammation level. IgG anti-HBc persists for life in both chronic active HBV and in persons who have cleared an acute infection. Persons with chronic HBV (particularly HBeAg positive and HBV DNA positive) remain infectious for others.[58-61]

Table 2: Significance of serological markers[62]

Antigen or antibody	Presence in serum	Inference	Explanation
HBsAg (hepatitis B surface antigen also known as the Australia antigen, is the surface antigen on outer lipoprotein coat)	Yes, 30-60 days after exposure	Infection and infectivity	HBV envelope protein and excess coat particles detectable in the blood in acute and chronic hepatitis B infection. It indicates current hepatitis B infection.
HBcAg (Hepatitis B core antigen)	Difficult to detect. Detected in the liver tissues with acute or chronic infection	Hepatitis B infection	HBV core protein. The core protein is coated with HBsAg and therefore not found free in serum
HBeAg (Hepatitis B e antigen; core related protein that is secreted out in serum)	Yes, with high virus titres and during rapid replication of virus	High infectivity	Viral protein found in the high replicative phase of hepatitis B. HBeAg is usually a marker of high levels of replication with wild-type virus but is not essential for viral replication
Anti-HBs (Hepatitis B surface antibody)	Yes, during convalescence after acute infection or following hepatitis B vaccination	Past infection and immunity	Antibody to HBsAg. Develops in response to HBV vaccination and during recovery from acute hepatitis B, denoting

Anti-HBe	Yes	Low infectivity	Antibody to HBeAg. Detected in persons with lower levels of HBV replication but also in HBeAg-negative disease (HBV that does not express HBeAg)
Anti-HBc (Hepatitis B core antibody)	Yes	Both acute and chronic infection	Antibody to hepatitis B core (capsid) protein. Anti-HBc antibodies are not neutralizing antibodies and are detected in both acute and chronic infection
IgM anti-HBc	Yes	Recent infection (<6 months)	Subclass of anti-HBc. Detected in acute hepatitis B but can be detected by sensitive assays in active chronic HBV
IgG anti-HBc	Yes	Past or current infection with HBV	Subclass of anti-HBc detected in past or current infection. If it and HBsAg are both positive (in the absence of IgM anti-HBc), this indicates chronic HBV infection.

Treatment

The goal of treatment is to prevent the disease from getting worse and leading to more serious liver problems. Treatment may help improve the function of your liver and decrease your symptoms of liver disease. HBV may last a short time and go away on its own without treatment. HBV may become chronic, leading to liver damage and disease.[48,52,63,64,65]

- **Antiviral medicines**: Antiviral medicines may be given to help stop the virus from spreading in the patient's body.[64,65]
- **Immune-globulin**: Hepatitis B immune globulin is medicine given if a patient has been exposed to HBV. Immune globulin helps body fight the HBV infection. HBIG is also given to new-born babies who were exposed to HBV while in the womb of a HBV positive mother.
- **Liver transplant**: Some patients may need liver transplant if they have severe liver disease or liver failure.

Table 3: Whom to treat & whom to monitor

Whom to treat	Whom not to treat
As a priority, all adults, adolescents and children with CHB and evidence of compensated or decompensated cirrhosis should be treated, regardless of ALT levels, HBeAg status or HBV DNA levels	Antiviral therapy is not recommended and can be deferred in persons without evidence of cirrhosis, and with persistently normal ALT levels and low levels of HBV replication (HBV DNA <2000 IU/mL), regardless of HBeAg status or age. Where HBV DNA testing is not available: Treatment can be deferred in HBeAg-positive persons aged 30 years or less and persistently normal ALT levels.
Treatment is recommended for adults with CHB who, do not have evidence of cirrhosis, but are aged more than 30 years (in particular), and have persistently abnormal ALT levels and evidence of high-level HBV replication (HBV DNA >20 000 IU/mL), regardless of HBeAg status.	Continued monitoring is necessary in all persons with CHB, but in particular those who do not currently meet the recommended criteria for whom to treat or not treat, to determine if antiviral therapy may be indicated in the future to prevent progressive liver disease. These include persons without cirrhosis aged 30 years or less, with HBV DNA levels >20 000 IU/ mL but persistently normal ALT.

Prevention

- Getting vaccinated against HBV is the best way to decrease the risk and prevent the disease[11,12,54]
- The HBV vaccine is given in 3 doses over a period of 6 months.
- Some people may not show any response to vaccines. After vaccination, you may need a blood test to check your response to vaccine.

Table 4: Hepatitis B vaccine schedule in India

The hepatitis B vaccination schedule in Universal Immunisation Program includes birth dose within 24 hour of delivery, followed by 3 more doses of hepatitis B vaccine along with Diphtheria-Pertussis-Tetanus (DPT) vaccine. Birth dose should be provided for all institutional deliveries, within 24 hours of birth. Subsequently, 3 doses should be provided at 6, 10, and 14 weeks age along with three doses of DPT & Oral poliovirus vaccines (OPV).

Prospective of birth dose
Vaccination Schedule:

Age	Vaccines		
Birth	HepB	BCG	OPV0
	birth dose		zero dose
6 weeks	HepB1	DPT1	OPV1
10 weeks	HepB1	DPT2	OPV2
14 weeks	HepB1	DPT3	OPV3

The following people should be vaccinated against HBV:[12,40,45]

- Any person not already vaccinated against HBV, healthcare workers and workers in others care facilities.
- New-born babies born to women with HBV- All new-born babies should be vaccinated shortly after birth and have additional doses as directed by a caregiver.
- People living in care facilities and inmates of correctional facilities.
- People who have decreased liver function or who are infected with hepatitis C, hepatitis D or HIV.
- People who inject illegal drugs.
- People with kidney failure, receiving haemodialysis treatment. More or higher doses of the vaccine may be needed for people with kidney failure.
- People with more than one sexual partner or men having sex with other men.
- People who have had a sexually transmitted disease (STD) before should also be vaccinated.

Those people who are HBV positive should:[45,65,66]

- Cover any open cuts/scratches. If blood from a wound gets on a surface, clean the surface with bleach right away.
- Dispose of any items with blood or body fluids properly.
- Do not donate blood, sperm or organs to others.
- Do not share items that may have infected blood or body fluids on them (includes toothbrushes, razors or personal injection items, such as needles).
- Tell household and sexual contacts that you have HBV. All close contacts should be vaccinated. If contacts have not had the vaccination, they may need to start treatment to help prevent infection.
- Also inform medical or dental caregivers you have HBV when getting any kind of treatment.
- When having sex, always use a condom, even if you have acute HBV and your infection goes away, you can still spread the virus for up to 6 months.

Hepatitis B vaccine

- Recombinant hepatitis B vaccines of three intramuscular doses of hepatitis B vaccine induces an adequate antibody response in greater than 90% of healthy adults and in greater than 95%of infants, children, and adolescents from birth through 19 years of age.[67,68]
- The deltoid (arm) is the recommended site for hepatitis B vaccination of adults and children; immunogenicity of vaccine for adults is substantially lower when injections are given in the buttock.
- Larger vaccine doses (two to four times normal adult dose) or an increased number of doses (four doses) are required to induce protective antibody in a high proportion of haemodialysis patients and may also be necessary for other immune compromised persons (such as those on immunosuppressive drugs or with HIV infection).
- Primary vaccination comprises three intramuscular doses of vaccine, with the second and third doses given 1 and 6 months, respectively, after the first.
- Adults and older children should be given a full 1.0 ml dose, while children less than 11 years of age should usually receive half (0.5 ml) dose.
- An alternative schedule of four doses of vaccine given at 0, 1, 2, and 12 months has been approved for one vaccine for post-exposure prophylaxis or for more rapid induction of immunity.
- Hepatitis B vaccine should be given only in the deltoid muscle for adults and children or in the antero-lateral thigh muscle for infants and neonates.
- For patients undergoing haemodialysis and for other immunosuppressed patients, higher vaccine doses or increased numbers of doses are required.
- Vaccine doses administered at longer intervals provide equally satisfactory protection, but optimal protection is not conferred until after the third dose.

- If the vaccine series is interrupted after the first dose, the second and third doses should be given separated by an interval of 3-5 months. Persons who are late for the third dose should be given this dose when convenient.
- Side effects and adverse reactions: The most common side effect observed following vaccination with each of the available vaccines has been soreness at the injection site.
- Need for vaccine booster doses:
  - ✓ Up to 50% of adult vaccines who respond adequately to vaccine may have low or undetectable antibody levels by 7 years after vaccination.
  - ✓ For adults and children with normal immune status, booster doses are not routinely recommended within 7 years after vaccination, nor are routine serologic testing to assess antibody levels necessary for vaccine recipients during this period.
  - ✓ For infants born to hepatitis B-carrier mothers, booster doses are not necessary within 5 years after vaccination.
  - ✓ The possible need for booster doses after longer intervals will be assessed as additional information becomes available.
  - ✓ For haemodialysis patients, the need for booster doses should be assessed by annual antibody testing, and booster doses should be given when antibody levels decline to less than 10 mIU/ml.

Groups recommended for pre-exposure vaccination:

- ➢ With occupational risk: HBV infection is a major infectious occupational hazard for health-care and public-safety workers. If those tasks involve contact with blood or blood-contaminated body fluids, such workers should be vaccinated.
- ➢ Clients and staff of institutions for the developmentally disabled.
- ➢ Staffs who work closely with clients should also be vaccinated.
- ➢ The risk in institutional environments is associated not only with blood exposure but may also be consequent to bites and contact with skin lesions and other infective secretions.
- ➢ Susceptible clients and staff who live or work in smaller (group) residential settings with known HBV carriers should also receive hepatitis B vaccine.
- ➢ Staff of non-residential day-care programs (e.g., schools, sheltered workshops for the developmentally disabled) attended by known HBV carriers have a risk of HBV infection comparable to that among health-care workers and therefore should be vaccinated.
- ➢ Haemodialysis patients.
- ➢ Sexually active homosexual men.
- ➢ Recipients of certain blood products: Patients with clotting disorders who receive clotting-factor concentrates.
- ➢ Household and sexual contacts of HBV carriers.
- ➢ Adoptees from countries of high HBV endemicity: Families accepting orphans or unaccompanied minors from countries of high or intermediate HBV endemicity.
- ➢ Other contacts of HBV carriers.
- ➢ Sexually active heterosexual persons, with multiple sexual partners.
- ➢ International travellers.

Post-exposure prophylaxis for hepatitis B

- Prophylactic treatment to prevent hepatitis B infection after exposure to HBV should be considered in the following situations: perinatal exposure of an infant born to an HBsAg-positive mother, accidental percutaneous or per mucosal exposure to HBsAg-positive blood, sexual exposure to an HBsAg-positive person, and household exposure of an infant less than 12 months of age to a primary care giver who has

acute hepatitis B.[67-69]

- For an infant with perinatal exposure to an HBsAg-positive and HBeAg-positive mother, a regimen combining one dose of HBIG at birth with the hepatitis B vaccine series started soon after birth is 85%-95% effective.
- For accidental percutaneous exposure, a regimen of two doses of HBIG, one given after exposure and one a month later, is about 75% effective in preventing hepatitis B in this setting.
- For sexual exposure, a single dose of HBIG is 75% effective if given within 2 weeks of last sexual exposure.
- The efficacy of IG for post-exposure prophylaxis is uncertain. IG no longer has a role in post-exposure prophylaxis of hepatitis B because of the availability of HBIG and the wider use of hepatitis B vaccine.
-

Table 5: Post-exposure prophylaxis for hepatitis B infection

Exposed person	Treatment when source is found to be		
	HBsAg positive	HbsAg negative	Source not tested or unknown
Unvaccinated	HBIGX1 and initiate hepatitis B vaccine	Initiate hepatitis B vaccine	Initiate hepatitis B vaccine
Previously vaccinated known responder	**Test for anti-HBs** If adequate, no treatment If inadequate, hepatitis B vaccine booster dose	No treatment	No treatment
Previously vaccinated known non-responder	HBIG X 2 or HBIG X 1 plus 1 dose of HB vaccine	No treatment	If known high risk source, may treat as if source were HBsAg positive
Response unknown	**Test for anti-HBs** If adequate, no treatment If inadequate, HBIG X 1 plus hepatitis B vaccine booster dose	No treatment	**Test fot anti-HBs** If adequate, no treatment If inadequate, hepatitis B vaccine booster dose

Source: Sharma T, Chaudhary A, Singh J. Needle stick injuries and postexposure prophylaxis for hepatitis B infection.JASCP.2021. 2(1), 4-8

Perinatal exposure and recommendations[67-69]

- All pregnant women should be routinely tested for HBsAg during an early prenatal visit in each pregnancy.
- This testing should be done at the same time that other routine prenatal screening tests are ordered.
- In special situations (e.g., when acute hepatitis is suspected, when a history of exposure to hepatitis has been reported, or when the mother has a particularly high-risk behaviour, such as intravenous drug abuse), an additional HBsAg test can be ordered later in the pregnancy.
- No other HBV marker tests are necessary for the purpose of maternal screening, although HBsAg-positive mothers identified during screening may have HBV-related acute or chronic liver disease and should be evaluated.
- If a woman has not been screened prenatally or if test results are not available at the time of admission for delivery, HBsAg testing should be done at the time of admission, or as soon as possible thereafter. If the mother is identified as HBsAg-positive greater than 1 month after giving birth, the infant should be tested for HBsAg. If the results are negative, the infant should be given HBIG and hepatitis B vaccine.

- Following all initial positive tests for HBsAg, a repeat test for HBsAg should be performed on the same specimen, followed by a confirmatory test using a neutralization assay. For women in labour who did not have HBsAg testing during pregnancy and who are found to be HBsAg-positive on first testing, initiation of treatment of their infants should not be delayed by more than 24 hours for repeat or confirmatory testing.
- Infants born to HBsAg-positive mothers should receive Hepatitis B vaccine (0.5 ml) intramuscularly once they are physiologically stable, preferably within 12 hours of birth. The first dose should be given concurrently with HBIG but at a different site. If vaccine is not immediately available, the first dose should be given as soon as possible. Subsequent doses should be given as recommended for the specific vaccine. Testing infants for HBsAg and anti-HBs is recommended when they are 12-15 months of age to monitor the success or failure of therapy. If HBsAg is not detectable and anti-HBs is present, children can be considered protected. Breast-feeding poses no risk of HBV infection for infants who have begun prophylaxis.
- Household members and sexual partners of HBV carriers identified through prenatal screening should be tested to determine susceptibility to HBV infection, and, if susceptible, should receive hepatitis B vaccine.
- Obstetric and paediatric staff should be notified directly about HBsAg-positive mothers so that neonates can receive therapy without delay after birth and follow-up doses of vaccine can be given. Programs to coordinate the activities of persons providing prenatal care, hospital-based obstetrical services, and paediatric well-baby care must be established to assure proper follow-up and treatment both of infants born to HBsAg-positive mothers and of other susceptible household and sexual contacts.
- In highly endemic populations, universal vaccination of new-borns with Hepatitis B vaccine is the recommended strategy. HBsAg screening of mothers and use of HBIG for infants born to HBV-carrier mothers may be added to routine hepatitis B vaccination. More extensive programs of childhood hepatitis B vaccination should be considered if resources are available.

Acute exposure to blood that contains (or might contain) HBsAg

Exposed person has not been vaccinated or has not completed vaccination:[67-72]

- Hepatitis B vaccination should be initiated.
- A single dose of HBIG (0.06 ml/kg) should be given as soon as possible after exposure and within 24 hours, if possible.
- The first dose of hepatitis B vaccine should be given IM at a separate site (deltoid for adults) and can be given simultaneously with HBIG or within 7 days of exposure.
- Subsequent doses should be given as recommended for the specific vaccine.
- If the exposed person has begun but not completed vaccination, one dose of HBIG should be given immediately, and vaccination should be completed as scheduled.
- Exposed person has already been vaccinated against hepatitis B, and anti-HBs response status is known.
- If anti-HBs level is adequate, no treatment is necessary.
- If anti-HBs level is inadequate, a booster dose of hepatitis B vaccine should be given.
- Exposed person has already been vaccinated against hepatitis B, and the anti-HBs response is unknown.
- The exposed person should be tested for anti-HBs.
- If the exposed person has adequate antibody, no additional treatment is necessary.
- If the exposed person has inadequate antibody on testing, one dose of HBIG (0.06 ml/kg) should be given immediately and a standard booster dose of vaccine given at a different site.

Patient education

- Key points in counselling and preparing the patient prior to initiation of therapy. Preparing to start treatment: Patients should be counselled about the indications for treatment, including the likely benefits and side-effects, willingness to commit to long-term treatment, and need to attend for follow-up monitoring both on and off therapy; the importance of full adherence for treatment to be both effective and reduce the risk of drug resistance; and cost implications.
- Measurement of baseline renal function and assessment of baseline risk for renal dysfunction should be considered in all persons prior to initiation of antiviral therapy

- Seek help immediately if:
  - ✓ You have a sudden, severe headache and head pressure.
  - ✓ You have new or increased bruising or red or purple dots on your skin. You may also have bleeding that does not stop easily.
  - ✓ Your abdomen is swollen.
  - ✓ You have severe nausea or cannot stop vomiting.
  - ✓ You see blood in your urine or stool, or you vomit blood.
  - ✓ You have new or increased yellowing of your skin or the whites of your eyes.
  - ✓ You have severe pain in your upper abdomen.
- Limit or avoid alcohol: Alcohol can increase your liver damage and can damage your brain and heart.
- Quit smoking: Smoking harms your lungs, blood and heart. You are more likely to have a heart attack, lung disease and cancer if you smoke. You will help yourself and those around you by not smoking.

Monitoring

Table 6: Monitoring of hepatitis B infection: parameters & frequency[62]

Interval (Months)	3 Months			6 Months			9 Months			12 Months		
HBeAg/Anti HBe		✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
HBVDNA		✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
ALT	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
AST										✓		✓
CBC (Platelet)										✓	✓	✓
APRI/FIB4/Fibro Scan										✓	✓	✓
USG				✓						✓	✓	✓
Serum Creatinine											✓	
eGFR											✓	
Phosphate											✓	
Urine Protein: Creatinine Ratio											✓	

	Not on Treatment
	Treatment
	Discontinue Treatment

- The disease is complex and has sequelae, resolution as well as drugs side effects. Hence, three types of monitoring is necessitate.[9,11,65,73]
- Monitoring for disease progression and treatment response in persons with CHB prior to, during and post-treatment.[9,11,65,73]
- Monitoring for tenofovir or entecavir side-effects
- Monitoring for hepatocellular carcinoma

Table 7: Monitoring, treatment and discontinuation of treatment in hepatitis B virus infection[62]

Note on treatment	On treatment	Discontinued treatment
Frequent monitoring with monthly ALT and 3 monthly HBeAg/Anti HBeAg and HBVDNA quantitative would be required in those with fluctuating ALT and HBVDNA 2000-20,000 IU/mL, who are as yet not on treatment.[9,11,65,73] In active chronic B with persistently normal ALT and HBVDNA <20,000IU/mL, may be monitored annually.	More frequent 3-6 monthly assessment is required initially in those with advanced liver disease in the first year.	Careful long-term monitoring for reactivation with serial 3-6 monthly HBeAg, ALT and HBVDNA levels is mandatory in those who have discontinued treatment for consideration of retreatment.

Special Situations

HBV positive pregnant woman

- All pregnant women with HBV should be evaluated for the need of treatment for hepatitis B and any associated liver disease and given advice about prevention of transmission. Only a proportion of those with hepatitis B virus infection (pregnant or otherwise) need treatment.[9,11,65,73]
- Hepatitis B in a pregnant woman is not a reason for considering termination of pregnancy. Similarly, the need for caesarean delivery should be decided based on obstetric indications, and not on the presence of HBV infection.[9,11,65,73]
- Administration of hepatitis B vaccine to pregnant women with HBV provides no benefit either to the mother or the baby.

Care of the baby of a HBV positive pregnant woman

Immuno-prophylaxis of hepatitis B virus infection

- The new born baby should be administered a timely first dose (the 'birth dose') of hepatitis B vaccine (monovalent) as soon as possible after birth, ideally within 24 hours. Even within this time duration, the earlier it can be administered, the better. If, for some reason, the birth dose is not administered within 24 hours, it should still be administered as soon as it is possible and not omitted. This dose is administered intramuscularly in the anterolateral thigh. This birth dose must be followed by timely administration of 3-doses of hepatitis B-containing vaccine e.g. monovalent hepatitis B vaccine, tetravalent combination vaccine with DPT (DPT-Hep B) or a pentavalent vaccine (DPT+HepB+Hib). The hepatitis B vaccine birth dose followed by these three doses is the most effective method for prevention of mother-to-child transmission of hepatitis B.
- Hepatitis B immunoglobulin (HBIG) may provide some additional protection in situations where risk of transmission is particularly high – i.e. babies born to mothers with hepatitis B who also have detectable

HBeAg and/or high viral load. However, additional benefit provided by it, over properly-administered hepatitis B vaccine (as described above) is small. Also, HBIG is costly and has limited availability. If a decision is taken to administer HBIG (0.5 ml or 100 international units, intramuscular), this should be done as soon after birth as possible (and within 12-24 hours) and in a limb other than the one in which hepatitis B vaccine has been administered.

- Data on benefit and risks of administering anti-hepatitis B drugs to the pregnant women for prevention of mother-to-child transmission are unclear.

Breast feeding

A mother who has hepatitis B may breast feed her baby, unless there is an exuding injury or disease of the nipple or surrounding skin. The advantages of breast feeding far outweigh the risk, if any, of transmission of hepatitis B to a baby who has received hepatitis B vaccine.

Timing of testing

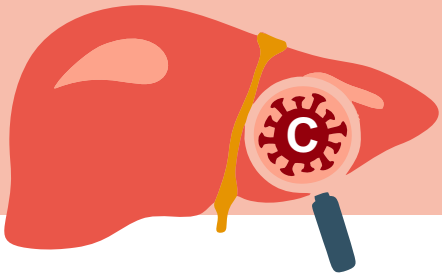
If it is felt that the baby needs to be tested for hepatitis B, this should be done only after 1 year of age. Any positivity before this age is difficult to interpret and may resolve spontaneously over time.

Co-morbidities

HIV and Hepatitis B co-infection

- The natural history of both diseases is affected when a person is co-infected with both HIV and Hep B and this has implications on management of both diseases. Current evidence suggests that human immunodeficiency virus infection has an adverse impact on HBV-related liver disease progression, with higher serum HBV DNA polymerase activity, lower rates of loss of serum hepatitis B e antigen, and increased risk of cirrhosis, liver-related mortality, and hepatocellular carcinoma at lower CD4 T-cell counts. HBV infection is more likely to be chronic in those with HIV infection. In some cohorts, liver disease has emerged as a leading cause of death in HIV-infected persons co-infected with either hepatitis B or C, as mortality due to other HIV-related conditions has declined following the introduction of antiretroviral therapy (ART).
- Similarly, the HBV infection also negatively impacts the progression of HIV infection leading to faster immune deterioration and higher mortality. Other studies have suggested that HBV is associated with a rapidly progressive course of HIV infection. A retrospective analysis indicated that the risk of death in 64 individuals co-infected with HIV and HBV was approximately two-fold higher than that in individuals with HIV mono infection. Prospective observational cohort among those with primary HIV infection showed that HBV co-infection is an independent predictor of immunologic deterioration in such group of patients. In another large prospective multicentre cohort by Chun et al among 2352 (PLHIV) with sero-conversion window of less than 3 years, co-infected persons with Hepatitis B were associated with two times higher risk of AIDS/death, higher among HBV co-infected patients compared to HBV mono-infected patients
- The HIV-Hepatitis co-infected persons show faster CD4 decline, slower CD4 recovery following ART, increased incidence of AIDS and non-AIDS events, increased rate of ARV toxicity and increased chances of Immune reconstitution hepatitis. In one of the large cohort studies of more than 5000 co-infected persons, the relative risk of liver related deaths was found to be 17 times higher than those with HBV mono-infected patients.
- Other challenges among co-infected include cross-resistance between HIV and HBV drugs, increased liver injury, either due to direct hepatotoxicity or to ART-related immune-reconstitution hepatitis, with elevation of ALT; if ART does not cover both HIV and HBV infections adequately, fulminant hepatitis is an eventuality.

HEPATITIS C



Key facts

- Hepatitis C is a liver disease caused by the hepatitis C virus: the virus can cause both acute and chronic hepatitis, ranging in severity from a mild illness lasting a few weeks to a serious, lifelong illness.[62,64]
- The hepatitis C virus is a bloodborne virus and the most common modes of infection are through exposure to small quantities of blood. This may happen through injection drug use, unsafe injection practices, unsafe health care, and the transfusion of unscreened blood and blood products.
- Globally, an estimated 71 million & in India around 12 million people have chronic hepatitis C infection.
- Worldwide, up to 8% of pregnant women are infected with hepatitis C virus (HCV).[74] Little is known about hepatitis C virus infection in pregnant women in India. The seroprevalence of anti-HCV antibody in the healthy general population of India was found to be 1.5 per cent each in 234 voluntary blood donors and 65 pregnant women.[75,76]
- A significant number of those who are chronically infected will develop cirrhosis or liver cancer.
- WHO estimated that in 2019, approximately 290 000 people died from hepatitis C, mostly from cirrhosis and hepatocellular carcinoma (primary liver cancer).[77]
- Antiviral medicines can cure more than 95% of persons with hepatitis C infection, thereby reducing the risk of death from liver cancer and cirrhosis, but access to diagnosis and treatment is low.
- There is currently no vaccine for hepatitis C; however, research in this area is ongoing.

Epidemiology

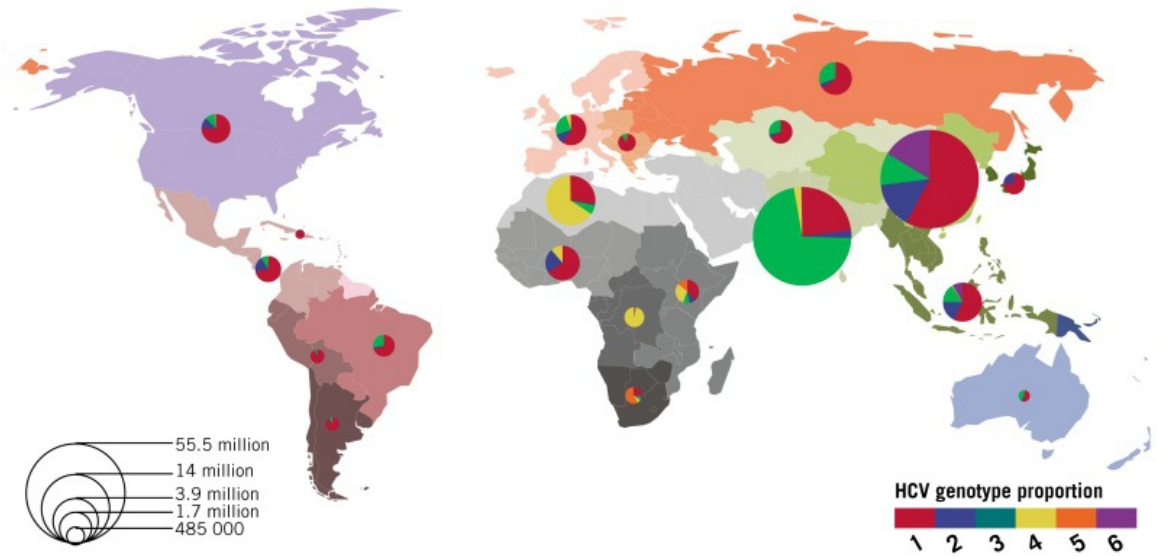
Hepatitis C virus (HCV) is a small (55–65 nm in size), enveloped, positive-sense single-stranded RNA virus of the family Flaviviridae. Hepatitis C virus is the cause of hepatitis C and some cancers such as liver cancer and lymphomas in humans. Hepatitis C is also called non-A or non-B hepatitis. It is the inflammation of the liver caused by hepatitis virus C. Similar to hepatitis A and Hepatitis B virus, hepatitis C virus (HCV) attacks and damages the liver. CDC estimates worldwide there are 3-4 million people infected with HCV every year.[78]

WHO estimated that Globally, an estimated 58 million people have chronic hepatitis C virus infection, with about 1.5 million new infections occurring per year. Approximately 2,90,000 people died from hepatitis C, mostly from cirrhosis and hepatocellular carcinoma (primary liver cancer) in 2019.[79]

Aside from the burden of HCV infection secondary to liver-related sequelae, HCV causes an additional burden through comorbidities among persons with HCV infection, including depression, diabetes mellitus and chronic renal disease. A proportion of these morbidities is directly attributable to HCV and is therefore referred to as extra hepatic manifestations. These manifestations are likely to be affected by treatment. The World Health Assembly recognized that viral hepatitis is a major public health problem and passed two initial resolutions in 2010[81] and 2014.[82] WHO estimated that approximately 1.5 million new HCV infections occur every year, mostly because of injecting drug use and unsafe health care.80 Worldwide, HCV infection may be caused by one of six major HCV genotypes (Fig. 2.1).[82] However, in many countries, the genotype distribution remains unknown.[83]
Hepatitis C virus causes both acute and chronic infection. Acute HCV infection is usually asymptomatic and is

only very rarely (if ever) associated with life-threatening disease. About 15–45% of infected persons spontaneously clear the virus within 6 months of infection without any treatment.[84] The remaining 60–80% of persons will develop chronic HCV infection. Of those with chronic HCV infection, the risk of cirrhosis of the liver is between 15–30% within 20 years.[85,86] The high variability and the limited knowledge of the structure of the hepatitis C virus envelope glycoproteins are challenging hurdles for vaccine design.[83]

Figure 9: Worldwide distribution of HCV genotypes



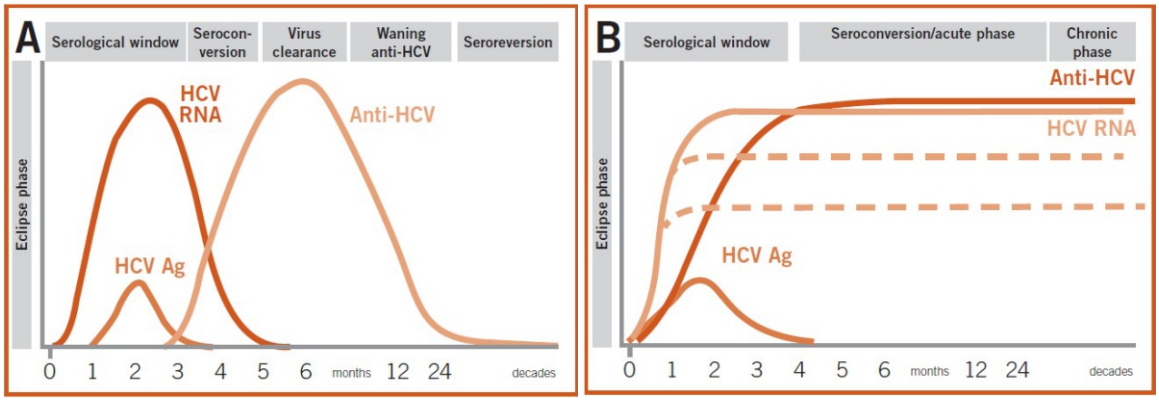
Source: WHO guidelines on hepatitis B & C

Symptoms

The most common symptom of hepatitis C is fatigue (feeling more tired than usual). The patient may present with one or more of the following:[87,88]

- Dark orange-coloured urine or clay coloured stool
- Fever
- Itchy skin
- Jaundice (yellowing of the skin or the whites of the eyes)
- Joint pain, body aches or weakness
- Loss of appetite, nausea or vomiting
- Pain in the right side of abdomen
- Extra hepatic manifestations of HCV include cryoglobulinemia (cryoglobulins are single or mixed immunoglobulins that undergo reversible precipitation at low temperatures) glomerulonephritis, thyroiditis and Sjogren syndrome, insulin resistance, type-2 diabetes mellitus, and skin disorders such as porphyria cutanea tardy and lichen planus.
- Persons with chronic HCV infection are more likely to develop cognitive dysfunction, fatigue and depression. These outcomes may be associated with replication of the virus in the brain; however, the causal link between these manifestations and chronic HCV infection is not certain.

Figure 10: Approximate time course of virological and immunological markers of HCV infection with (A) Self-resolving HCV infection, and (B) Chronic HCV infection



Source: WHO guidelines for hepatitis B & C testing.

Complications

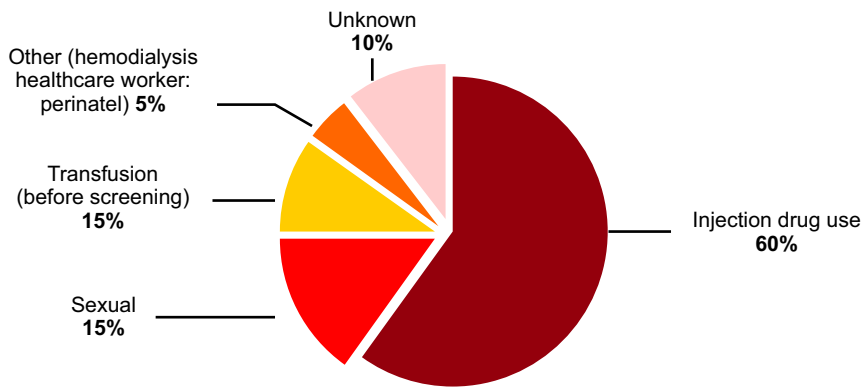
- Liver cirrhosis
- Liver cancer
- Liver failure
- Kidney disease

Transmission

Hepatitis C virus is carried in the blood and other body fluids, such as semen or vaginal fluids. Hepatitis C virus may spread by any of the following:[78,91]

- Childbirth: passed from a pregnant woman to her baby during delivery
- Needle stick injury
- Long term dialysis
- Blood transfusion or an organ transplant before June 2001
- Sharing items that may have infected blood on them, such as razors, toothbrushes or nail-clippers
- Sharing infected needles to use illegal or street drugs
- Using dirty needles or instruments for tattooing, body piercing or other procedures
- HCV can also be transmitted by sexual route

Figure 11: Hepatitis C infection by source



Source: Centers for Disease Control and Prevention. Viral Hepatitis Surveillance - United States, 2016.

Vertical transmission

The overall rate of mother-to-child transmission of HCV from HCV-infected, HIV-negative mothers has been estimated at 3%-5%.[92,97] However, in an overview of 77 prospective cohort studies with at least 10 mother-infant pairs, the overall rate was 1.7% if the mother was known to be anti-HCV positive. If the mother was known to be viremic, that is HCV-RNA-positive, the rate was 4.3%.[98] At least one-third of infants acquire HCV infection during the intrauterine period; the perinatal transmission is estimated to be as high as 40%-50%, whereas postpartum transmission is rare.[99,100] The detection of HCV RNA in the serum of infants in the first 24 h of life suggests that early intrauterine infection may be possible.[100] The diagnosis of perinatal transmission should be considered in children born to HCV-positive mothers when: HCV RNA is detected in at least two serum samples at least 3 month apart during the first year of life; and/or when testing of antibodies against HCV is positive after 18 month of age.[100]

There is an interesting observation reported by the European Paediatric Hepatitis C Virus Network from a multicentre prospective study of HCV-infected pregnant women and their infants.[100] In that study girls were twice as likely to be infected as boys. This sex association is an intriguing finding that probably reflects biological differences in susceptibility or response to infection. Co-infection with HIV increases the rate of mother to child transmission up to 19.4%.[98] The weighted rate of transmission is 8.6% in mothers who are anti-HCV positive and injecting drug users, compared with 3.4% in anti-HCV-positive mothers without known injecting drug use. A meta-analysis including 2382 infants estimated that the risk of HCV vertical transmission was 2.[82] from anti HCV+ /HIV+ co-infected mothers compared with anti HCV+ /HIV- mothers.[101,102] Vertical transmission of HIV and HCV separately is most likely from HIV/HCV-coinfected mothers; however, transmission of both infections is less frequent.[103] Numerous risk factors for vertical transmission have been studied.

In general, high viral load defined as at least 2.5 × 106 viral RNA copies/mL, HIV co-infection, and invasive procedures are the most important factors.[103] In general, maternal peripheral blood mononuclear cell infection by HCV, membrane rupture > 6 h before delivery, and procedures exposing the infant to maternal blood infected with HCV during vaginal delivery are associated with an increased risk of transmission.[104] Abnormal ALT levels in mothers in the year before pregnancy may reflect a more severe liver disease and may help in identifying mothers with an increased risk of vertical transmission.[103] Finally, a Japanese study suggested that maternal liver dysfunction, large blood loss at delivery, and vaginal delivery were potential novel risk factors for mother to child transmission of HCV.[97]

A consensus for management of HCV-infected pregnant women and their children by the European Paediatric Network has indicated that although several risk factors for vertical transmission have been identified, none are modifiable and there are currently no interventions available to prevent such transmission.[105] Based on the current evidence, it would be prudent to avoid amniocentesis, instrumented vaginal delivery, and prolonged rupture of membranes. A recent meta-analysis including 641 mother-infant pairs showed that caesarean section does not decrease perinatal HCV transmission from HCV-RNA+ /HIV- mothers to infants.105 Thus, elective caesarean delivery should not be offered, and breast feeding should not be discouraged. HCV/HIV co-infected women should be offered elective caesarean section to prevent HCV/HIV transmission and avoid breastfeeding where safe alternatives are available.[105]

Hepatitis C transmission risk by exposure type

Table 8: HCV transmission of exposure type

Exposure		Risk per exposure (unless otherwise stated)
Needle stick	Healthcare setting, source patient (serology) known	0-10%. Average 1.8% Increased risk if - hollow needle, deep injuries, co-infection with HIV, high viral load.[107,108,109,108,110,111,112]
	Healthcare setting, source patient unknown, or unable to test source patient (serology unknown)	Unknown source – negligible risk.[112] Risk assessment required
	Community setting	Risk not accurately determined.112 Risk assessment required. If local PWID population has a sero-prevalence of 50-90%, the estimated risk of HCV transmission in a community needle stick injury is 1.62%.[113]
Exposure prone procedure by infected healthcare worker		0-3.7%74 Risk may increase to 6% for certain procedures, e.g. open-heart surgery.[114] Risk assessment required.
Non-healthcare related occupational sharp injuries		Risk not accurately determined, but transmission possible.[117,118] Risk assessment required.
Tattoos		Risk not accurately determined. Pooled odds ratio 2.73 (95% CI 2.38-3.15).[119] Risk assessment required. Increased risk if larger tattoos or tattoos in non-professional locations
Mucous membrane exposure to blood		Very low risk. Case reports only.[120,121] Risk assessment required
Intact skin exposed to blood		No recognised risk
Non-intact skin, body fluid exposure		Very low risk. Case report describes transmission of HIV and HCV from co-infected source.[122] Risk assessment required.
Human bite injuries		Very low risk.[123] Case reports only. Risk assessment required. Possible higher risk of transmission of HCV than HIV if the source.[124]
Sexual exposures	Heterosexual exposures in general	Inefficient transmission, but transmission possible as seen in stable heterosexual relationships, and in those with history of multiple sexual partners.[125-130] Possible increased risk of transmission if source co-infected with HIV.[125]
	MSM	Inefficient transmission.[131,132] Co-infection with HIV increases the risk of transmission.[125,133-135] No recognised risk.

Diagnosis

- **Enzyme immunoassay**: This test checks for HCV antibodies
- **Genotyping**: Blood test that tests the genotype of the hepatitis C virus
- **Hepatitis C profile serological test**: This checks the number and activity of HCV in the blood
- **Liver biopsy**: Small piece of liver is removed and sent to a lab for tests
- **Liver function tests**: to check the enzymes and other substances made in the liver
- **Hepatitis C infection is diagnosed in 2 steps:** Screening for anti-HCV antibodies with a serological test; if the test is positive for anti-HCV antibodies, a different test is needed to confirm chronic infection because about 30% of people infected with HCV spontaneously clear the infection by a strong immune response without the need for treatment.[62,64,78,106]
- **Window period:** Assays designed solely to detect antibodies to HCV inevitably have a window period of infectivity in early infection, during which antibodies may be undetectable. HCV RNA is typically not used to determine exposure to HCV, in spite of its short window period (1–2 weeks after the onset of acute infection) primarily because of cost. There are some situations with occult HCV infection, i.e. HCV RNA detectable in the absence of any serological markers (i.e. HCV seronegative), which may be due to underlying immunosuppression in, for example, HIV-infected populations.[62,64,78,106]

Treatment

Whom to treat

Any individual diagnosed to have infection with hepatitis C virus (viremia+) needs treatment. The duration of treatment will depend on the several situations such as, cirrhosis versus non-cirrhosis, presence of decompensation (ascites, variceal bleeding, hepatic encephalopathy, or infection(s), treatment naïve versus treatment experienced (to pegIFN, DAAs, etc). [62,64,78,106]

Anti-viral medicine:

All patients of Hepatitis C should be initiated on treatment.[62,64,78] Direct acting antivirals are available for treatment of Hepatitis C and form the backbone of therapy in addition to existing pegylated interferons and ribavirin. The DAAs, target three important regions within the HCV genome: NS3/4A protease, NS5A and NS5B RNA-dependent polymerase. These medicines have led to higher sustained virological responses (SVRs) than interferon-based regimens, are shorter in treatment duration, are orally administered and have fewer side effects. The mechanism of action of the Direct Acting Antivirals (DAAs) are shown in the figure below.

Table 9: List of DAAs lincensed for treatment

Protease Inhibitors	NSSA Inhibitors	Polymerase inhibitor (NS5B), nucleotide analogue	Polymerase inhibitor (NS5B), nucleoside analogue
Asunaprevir Paritaprevir Simeprevir	Daclatasvir Ledipasvir Velpatasvir	Sofosbuvir	Dasabuvir

Figure 12: Mechanism of action of the Direct Acting Antivirals (DAAs) on HCV[136]

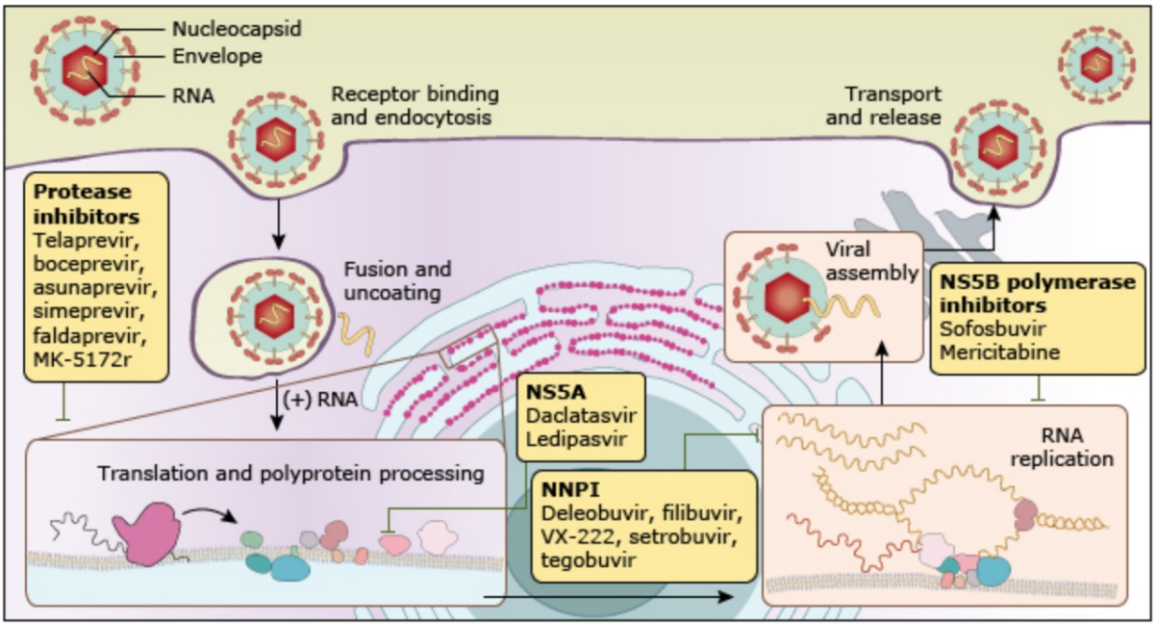


Table 10: Treatment options available in the National Viral Hepatitis Control Program

Regimen type	Category of patients	Drugs and dose	Treatment duration
I	Patient without Cirrhosis (uncomplicated)	Sofosbuvir(400mg) & Daclatasvir(60mg)	84 days (12 wks.)
II	Patient with cirrhosis-compensated (Child-Pugh A)	Sofosbuvir(400mg) + Velpatasvir(100mg)	84 days (12 wks.)
III	Patient with cirrhosis- decompensated (Child-Pugh B and C) **	Sofosbuvir(400mg) + Velpatasvir(100mg) & Ribavirin (600-1200mg**)	84 days (12wks)
IV	In Ribavirin intolerant patients	Sofosbuvir(400mg) + Velpatasvir(100mg)	168days (24wks)

Table 11: Monitoring schedule framework for the treatment og HCV patients[137]

Time	Regimen: Only DAAs (non-cirrhotic usually)			Regimen: DAAs and Ribavirin (cirrhotic usually)		
	CBC, S. Creatinine, LFT	Adherence and side effects	HCV RNA	CBC, S. Creatinine, LFT	Adherence and side effects	HCV RNA
Baseline	Yes		Yes	Yes		Yes
Week 1				Yes	Yes	
Week 2				Yes	Yes	
Week 4	Yes	Yes		Yes	Yes	
Week 8				Yes	Yes	
Week 12				Yes	Yes	
Week 12 after completion of treatment (SVR-12)			Yes	Yes		Yes

CBC, complete blood counts; LFT, liver function tests; SVR, sustained viral response

Sustained Virological Response (SVR)

- At the end of treatment, the patient should be checked for HCV RNA and if it is not detectable then SVR is achieved.[62,64,78]
- If SVR is not achieved, then patient should be referred to a higher centre for further testing (resistance testing) and treatment. [62,64,78]
- SVR should also be checked at 6 months and 12 months post treatment to look for relapse of infection.[62,64,78]

Hepatitis C therapy in the era of the newer direct-acting antiviral agents has radically changed our treatment schemes by achieving very high rates of sustained virological response. However, treatment with direct antiviral agents fails in a subgroup of patients. The expressions “difficult-to-cure” and “difficult-to-treat” are used indistinctly in the literature, which renders challenging establishing a reason why some patients cannot be freed from infection.[138-141] We shall use the term “difficult-to-cure patient” to refer to failures related to virological characteristics, and the term “difficult-to-treat patient” to failures associated with one of the following three reasons:

- poor adherence;
- early therapy discontinuation because of an unlikely side effect or a not so unlikely clinically relevant interaction; and
- loss to follow-up, in close relationship to poor adherence, which precludes the assessment of SVR endpoint attainment (Table I).

We usually categorize therapy failure according to the time of its development: within-treatment recurrence (virological rebound or breakthrough), post-treatment recurrence (relapsing infection), and primary absence of response. The virological causes of therapy failure (Table II) may be categorized as:

- genotyping errors;
- genetic recombination phenomena;
- treatment-resistant variants (whether pre-extant or acquired following initial exposure to DAAs);

- persistent infection, usually with the emergence of new predominant isolates;
- reinfection; and
- superinfection.

Table12: Difficult-to-cure patients

Difficult-to-cure patients with IFN-based therapies	Difficult-to-cure patients at present (IFN-free therapy)
➢ Genotype 1 ➢ High viral load ➢ Untoward Il28B polymorphism ➢ Absence of response to prior therapy ➢ Compensated cirrhosis ➢ Coinfection with HIV	➢ Genotype 3, particularly in previously treated or cirrhotic individuals ➢ Compensated cirrhosis ➢ DAA therapy failure

Surgery

A liver transplant may be done if the liver stops functioning. The diseased liver is replaced with a whole or a part of a healthy donated liver.

Counselling messages for screening test results:[91]

- All patients should be provided information on the meaning of their test results by the attending clinicians/trained health care workers/peer counsellors.
- Providing Pre-test information: through media such as posters, brochures, websites and short video clips shown in waiting rooms. This would include information on viral hepatitis and the benefits of testing for hepatitis B or C; the meaning of a positive and negative test result; a brief description of prevention options; confidentiality of the test result; the practical implications of a positive test result, including the when and where of treatment available.

Post-test information/counselling for a non-reactive hepatitis C screening test:

- Explain the meaning of the non-reactive antibody test, ensuring that the patient understands a negative antibody test does not protect him/her from future infection in the event of risk-taking behaviours.
- Discuss that if the patient was recently exposed (6 months), he/she may be in a window period and recommend repeat screening in 6 months, and provide information on hepatitis C prevention, risk and harm reduction.
- Encourage the patient to make healthy choices and to get vaccinated against hepatitis B, if appropriate.

Post- test counselling and linkages to treatment services for a reactive hepatitis C screening test:

- Explain the meaning of the reactive antibody test and counsel on the need for diagnostic testing (hepatitis C RNA test) to confirm a diagnosis of chronic hepatitis and other tests for staging of liver disease.
- Explain that the patient is most likely chronically infected and provide basic hepatitis C disease and treatment information. Make an active referral to the viral hepatitis treatment units.
- Discuss the importance of minimizing risk behaviours to avoid transmitting hepatitis C infection to others and encourage notification and screening of needle sharing and sexual partners.
- Encourage and offer HBV and HCV testing for family members, including children, and sexual partners.
- Discuss healthy liver practices, including stopping or reducing alcohol intake and getting vaccinated against hepatitis A and B, if appropriate.

- Adherence counselling by trained pharmacist:
  - **Pill count**: the total number of pills/doses dispensed, and the total number of pills/doses returned at monthly visits for each drug for the entire treatment duration for all patients;
  - **Patient self-reports**: it helps to determine reasons for non-adherence
- Though the majority of patients can be initiated the treatment for hepatitis C, there are several situations in which it is recommended to refer the patient to a specialized center. These include:
  - Patients with decompensated cirrhosis
  - Treatment experienced patients
  - Patients on chemotherapy with deranged liver enzymes
  - Patient with impaired renal function
  - Patient with HCC
  - Paediatric patients
  - Thalassaemic patients

Prevention

Prevention of hepatitis C includes:[142]

- Caregivers should wear personal protective equipment's (masks, gloves, gowns or safety goggles) when handling blood products and instruments
- Consider the risks of getting hepatitis C before having tattoos or body piercing
- If patients use illegal drugs, never reuse or share needles or syringes
- Do not share toothbrushes, razors or other personal care items
- Mothers infected with hepatitis C should stop breastfeeding if their nipples are cracked or bleeding
- Always use condoms while having sex

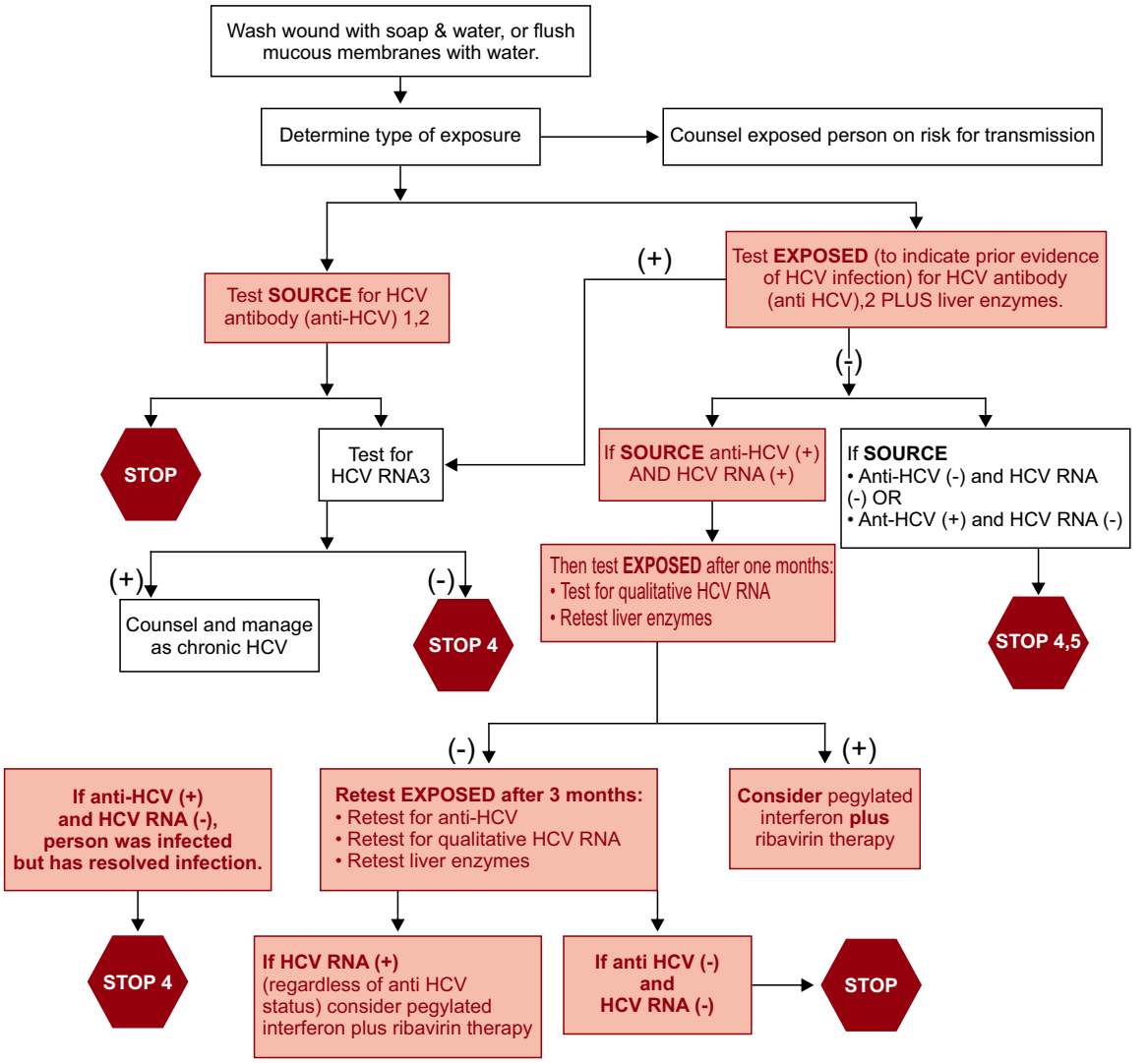
Healthcare personnel potentially exposed to hepatitis C virus

Exposure to viral hepatitis has long been recognized as an occupational risk for healthcare personnel, with recommendations previously established for the management of occupational exposures to hepatitis C virus. This algorithm, which is based on current laboratory guidance, updates the 2001 HCV testing algorithm for healthcare personnel.[145,146] Postexposure prophylaxis (PEP) of hepatitis C is not recommended, as outlined in the 2001 MMWR on management of healthcare personnel who have occupational exposure to blood and other body fluids.[146] After a needlestick or sharps exposure to HCV-positive blood, the risk of HCV infection is approximately 1.8%.[146] If the healthcare worker does become infected, follow AASLD/IDSA guidelines (www.hcvguidelines.org) for management and treatment of hepatitis C.

*** Test the source for HCV RNA**: If the source is HCV RNA positive, or if HCV infection status unknown, follow the algorithm. If it is not possible to test source for HCV RNA, then test for antibodies to HCV (anti-HCV) and screen HCW exposed to anti-HCV positive source. Note that persons with acute infection may test HCV RNA positive but anti-HCV negative.

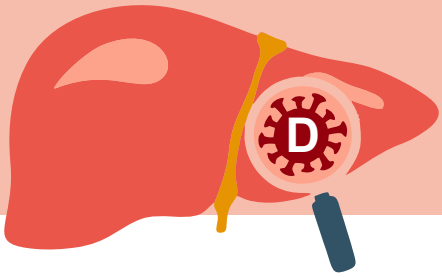
†In a nationally representative population sample with low (1%) HCV infection prevalence, 22% of anti-HCV positive results were determined to be false-positive. An additional 10% had indeterminate results in a confirmatory assay; most were likely to be false-positive. Among the subset of persons testing anti-HCV screening reactive and subsequently HCV RNA negative, 50% of the anti-HCV tests were false-positive.[3]
‡Anti-HCV testing at >= 6 months with reflex to HCV RNA test, if positive, could also be done.

Figure 13: Post exposure management of hepatitis C[143,144]



1. If source is unavailable or refuses testing, treat exposed as if source was anti-HCV (+) and HCV RNA (+).
2. Since immunosuppressed persons can be negative for hepatitis C antibody despite viremia, qualitative HCV RNA testing should be performed.
3. Qualitative HCV RNA by PCR or TMA.
4. Person was HCV infected at one time and spontaneously cleared the virus. Person is NOT able to transmit HCV at that time.
5. Advice and counsel EXPOSED person if SOURCE person is anti-HCV (+) only.

HEPATITIS D



Key facts

- Hepatitis D is also known as hepatitis delta agent and was discovered in 1977.[147]
- Hepatitis D virus (HDV) is a virus that requires hepatitis B virus (HBV) for its replication.
- Hepatitis D virus (HDV) affects globally nearly 5% of people who have a chronic infection of hepatitis B virus (HBV).
- HDV infection occurs when people become infected with both hepatitis B and D simultaneously (co-infection) or get hepatitis D after first being infected with hepatitis B (super-infection).
- Worldwide, the number of HDV infections has decreased since the 1980s, mainly due to a successful global HBV vaccination programme.
- The combination of HDV and HBV infection is considered the most severe form of chronic viral hepatitis due to more rapid progression towards liver-related death and hepatocellular carcinoma.

Epidemiology

Description

HDV is an RNA virus with the smallest genome of all known animal viruses.[148] This genome encodes a single antigen, which is expressed in two forms. HDV resembles plant satellite viruses but no other animal viruses. HDV has some genetic heterogeneity that varies geographically. It depends on simultaneous infection with HBV for its hepatotropism and transmission and is thus considered a parasite of HBV.[147,148]

Incidence

Approximately 5,000 to 7,500 new HDV infections occur per year in the United States, principally among IV drug users.[149] The incidence of HDV among patients with haemophilia has declined since the 1980s as a result not only of screening blood and plasma donors for HBV infection but also of solvent-detergent or heat inactivation of viruses in clotting factors and the development of recombinant factors VIII and IX.[149]

Prevalence

In a study published in the Journal of Hepatology in 2020, conducted in collaboration with WHO, it was estimated that hepatitis D virus affects nearly 5% of people globally who have a chronic infection with hepatitis B virus and that HDV co-infection could explain about 1 in 5 cases of liver disease and liver cancer in people with HBV infection. The study has identified several geographical hotspots of high prevalence of HDV infection including Mongolia, the Republic of Moldova, and countries in western and central Africa.[79]

HDV is endemic in Italy and other countries in the Mediterranean basin, western Asia, northern South America, and certain Pacific islands64,65. In western Europe and North America, the seroprevalence of HDV in blood donor populations ranges from 1.4 to 8 percent.[149-151] The highest prevalence in the United States is among injection drug users (20 to 67 percent of HBV-infected persons).[149-151] In Taiwan, 91 percent of HBsAg-positive injection drug users are also seropositive for HDV. Historically, 48 to 80 percent of United States patients with haemophilia were seropositive for HDV markers, but this rate is declining. Groups at

intermediate risk of HDV infection include haemodialysis patients and institutionalized persons. HCP are at risk of acquiring HDV infection via sharps injuries.

Transmission

HDV is transmitted principally by percutaneous exposure, but unlike HBV infection, HDV is inefficiently transmitted by sexual intercourse.[149,151,152] Perinatal transmission is very rare, and no cases have been documented in the United States.[151,152] It is not transmitted by the faecal-oral route or casual contact, though routes of transmission in countries in which HDV infection is endemic are not always clear.[151]

Pathogenesis

HDV infection and hepatotropism depend on simultaneous infection with HBV, as the viral envelope for hepatitis delta virus is the Hepatitis B surface antigen.[154] HDV replicates only in hepatocytes and may be cytopathic. HDV and HBV may co-infect a susceptible host; a person who is already a chronic HBsAg carrier can be superinfected with HDV.[154]

Clinical features

The incubation period of HDV ranges from 30 to 180 days.[155] Simultaneous co-infection with HBV and HDV usually manifests much like acute HBV alone, though there may be a biphasic elevation of ALT with HDV infection.[155] In 90 to 95 percent of cases of acute co-infection, the hepatitis is self-limited, and HBV and HDV are eliminated.[155]

However, fulminant hepatic failure occurs more frequently than is seen with HBV alone. Approximately 5 percent of co-infections result in chronic HBV and HDV infection, a rate that is similar to that of HBV infection alone.[155,156] Superinfection with HDV in a patient who is a chronic HBsAg carrier often causes more severe acute hepatitis than is seen with HBV/HDV co-infection. Moreover, HDV superinfection results in chronic HDV in greater than 90 percent of survivors of the acute infection.[155,156] In 10 to 15 percent of these, especially among IV drug users, hepatic damage may progress to cirrhosis and liver failure within 1 to 2 years.[157] Most of the others with chronic HDV have more slow progressive liver disease resembling chronic HBV. HCC is less common in patients with chronic HDV infection than it is with chronic HBV or HCV.[155-157] The reasons for this are not clear.

Laboratory diagnosis

A diagnosis of HDV is not tenable unless the patient tests positive for HBsAg. HDV should be suspected when there is a history of percutaneous or sexual exposure in a patient with chronic HDV infection, especially an IV drug user.[147,151,158,159] It should also be suspected in a patient with acute HBV who has a second rise in ALT level or a patient with chronic HBV who develops an acute exacerbation of hepatitis.[147,151,158,159]
The diagnosis of HDV can be made by PCR, IgG anti-HDV, or IgM anti-HDV. The first test should be anti-HDV IgG. Co-infection of HBV and HDV is suggested by the simultaneous finding of a positive test for IgM anti-HBc.[147,151,158,159] The anti-HDV IgG is short-lived in co-infection and is not protective. It may remain elevated as a "serologic scar" in superinfection patients who have cleared their HDV infection. A positive anti-HDV IgG should be followed up with HDV PCR to evaluate for evidence of active infection.[147,151,158,159]

Treatment

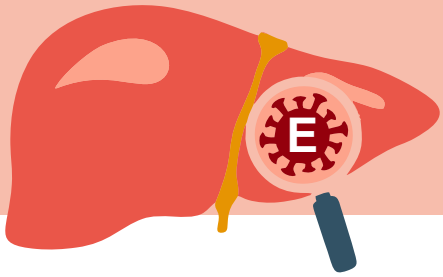
In acute HDV, supportive care is given. For chronic HDV, high-dose interferon alfa (IFN-a) may induce remission of disease in 40 to 50 percent of selected patients with histologic and biochemical response as well as viral

suppression.[160-162] However, relapse viremia is common, and effects are unlikely to last once therapy is stopped. The side effects of interferon therapy may be a severe limitation to its use. Regarding antiviral medications, lamivudine has been shown to be ineffective, but tenofovir has been shown in a small study to decrease HDV viral loads, particularly when used with interferon. In acute fulminant HDV or end-stage hepatic failure or cirrhosis, liver transplantation is often necessary.[160-162]

Prevention

General preventive measures for HDV, as for HBV, include modification of high-risk behaviours by individuals. Standard Precautions are used in healthcare setting.[147,149,151,160] Post-exposure passive immunization with HBIG with HBV vaccine can prevent infection with HBV. By eliminating HBV, co-infection with HDV will not occur. Preexposure active immunization with HBV vaccine will prevent co-infection with HDV.[147,149,151,160] No vaccine to prevent HDV super-infection is yet available. Patients with chronic HDV infection should be candidates for HAV vaccine. Needle exchange programs may be effective in preventing the spread of HDV among injection drug users.[147,149,151,160]

HEPATITIS E



Key facts

- Hepatitis E is a liver disease caused by infection with a virus known as hepatitis E virus.
- Every year, there are an estimated 20 million HEV infections worldwide, leading to an estimated 3.3 million symptomatic cases of hepatitis E.[163]
- WHO estimates that hepatitis E caused approximately 44,000 deaths in 2015 (accounting for 3.3% of the mortality due to viral hepatitis).
- The virus is transmitted via the faecal-oral route, principally via contaminated water.
- Hepatitis E is found worldwide, but the prevalence is highest in East and South Asia.

Epidemiology

Hepatitis E is unique among the hepatic viruses as it carries a particularly high mortality rate among pregnant women.[164] HEV is a positive-stranded RNA virus belonging to the family hepeviridae. HEV has 4 genotypes of which genotypes 1 and 2 exclusively infect humans whereas genotypes 3 and 4 also infect several other mammalian species.[165] HEV is primarily spread via the faecal – oral route and is an enterically transmitted pathogen like HAV.[2] The incubation period of HEV infection is estimated to be around 2–9 weeks and during an epidemic of HEV, anicteric hepatitis is more common than icteric hepatitis and clinical hepatitis is seemingly more frequent in adults than in children aged less than 15 years.2 Usually the infection is self-limiting and resolves within 2–6 weeks. Occasionally a serious disease, known as fulminant hepatitis (acute liver failure) develops, and a proportion of people with this disease can die.[166]

HEV infection can also cause, albeit rarely, a chronic hepatitis which occurs when HEV replication persists for at least 6 months. Chronic HEV infection is classically described with HEV genotype 3 and can lead to cirrhosis in immunosuppressed patients and in patients undergoing a solid organ transplantation.[2]

Hepatitis E infection is found worldwide. The disease is common in resource-limited countries with limited access to essential water, sanitation, hygiene and health services.[167] In these areas, the disease occurs both as outbreaks and as sporadic cases.[167] The outbreaks usually follow periods of faecal contamination of drinking water supplies and may affect several hundred to several thousand persons.[167] Some of these outbreaks have occurred in areas of conflict and humanitarian emergencies, such as war zones, and in camps for refugees or internally displaced populations (IDP), situations where sanitation and safe water supply pose special challenges.[168]

Indian scenario

HEV is responsible for majority of the sporadic and epidemic cases of AVH in India.2 During an HEV epidemic, the secondary attack rate among the household contacts is estimated to be about 0.7–2% when compared to 50–75% for HAV. During an outbreak, it is observed that pregnant women have a higher likelihood to get infected (12–20%) with HEV and have a higher propensity to develop acute liver failure (10–22%) when compared to non-pregnant females and males (1–2%).2 Hepatitis E infection during pregnancy, especially in the third trimester, is characterized by a more severe infection that sometimes results in fulminant hepatitis,

increasing maternal and fetal mortality and morbidity.[169]

Transmission

The hepatitis E virus is transmitted mainly through the faecal-oral route due to faecal contamination of drinking water.[170] This route accounts for a very large proportion of clinical cases with this disease. The risk factors for hepatitis E are related to poor sanitation, allowing virus excreted in the faeces of infected people to reach drinking water supplies.

Other routes of transmission have been identified but appear to account for a much smaller number of clinical cases. These routes of transmission include:[170]

- Ingestion of undercooked meat or meat products derived from infected animals;
- Transfusion of infected blood products; and via allograft.
- Vertical transmission from a pregnant woman to her foetus.
- Ingestion of raw or uncooked shellfish
- Zoonotic transmission[171-173]

Table 13: Difference between routes of transmission for hepatitis A and E

	Hepatitis A	Hepatitis E
MODES OF TRANSMISSION	**Faecal oral route:** faeces, serum, contaminated food, water, infected food handlers, utensils, water vegetable grown on contaminated water, Raw shellfish, poor sanitation, over crowding	**Faecal oral route:** Faecal-Oral route: Faeces, serum, contaminated food, water, hands, utensils, poor sanitation, over crowding
	Close personal contact • Household contact • Homosexual in men • Child day care centers	Rarely from person to person
	Rarely by blood exposure • Intravenous drug use • Blood transfusion	Possible zoonotic transmission (Fig 3)

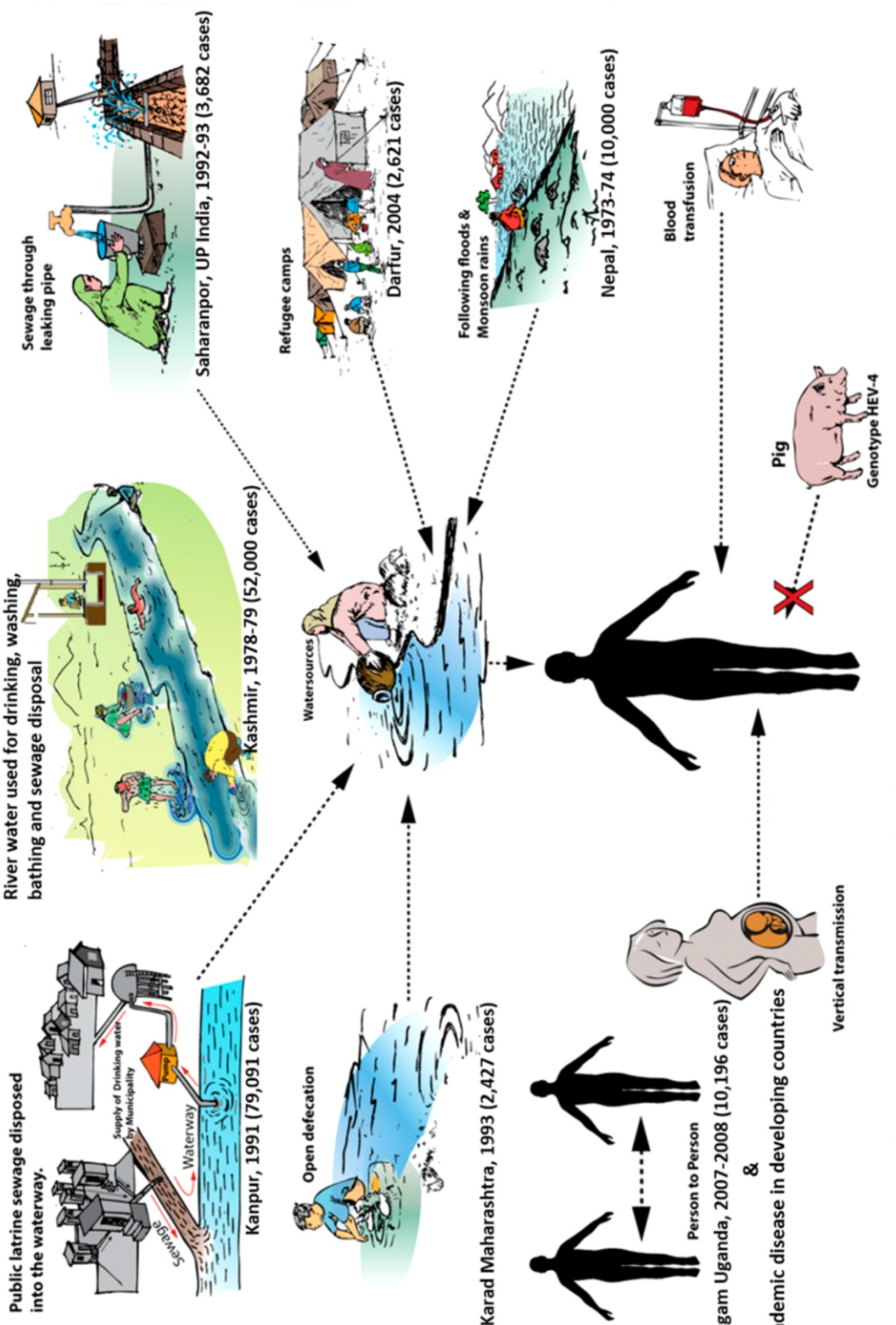
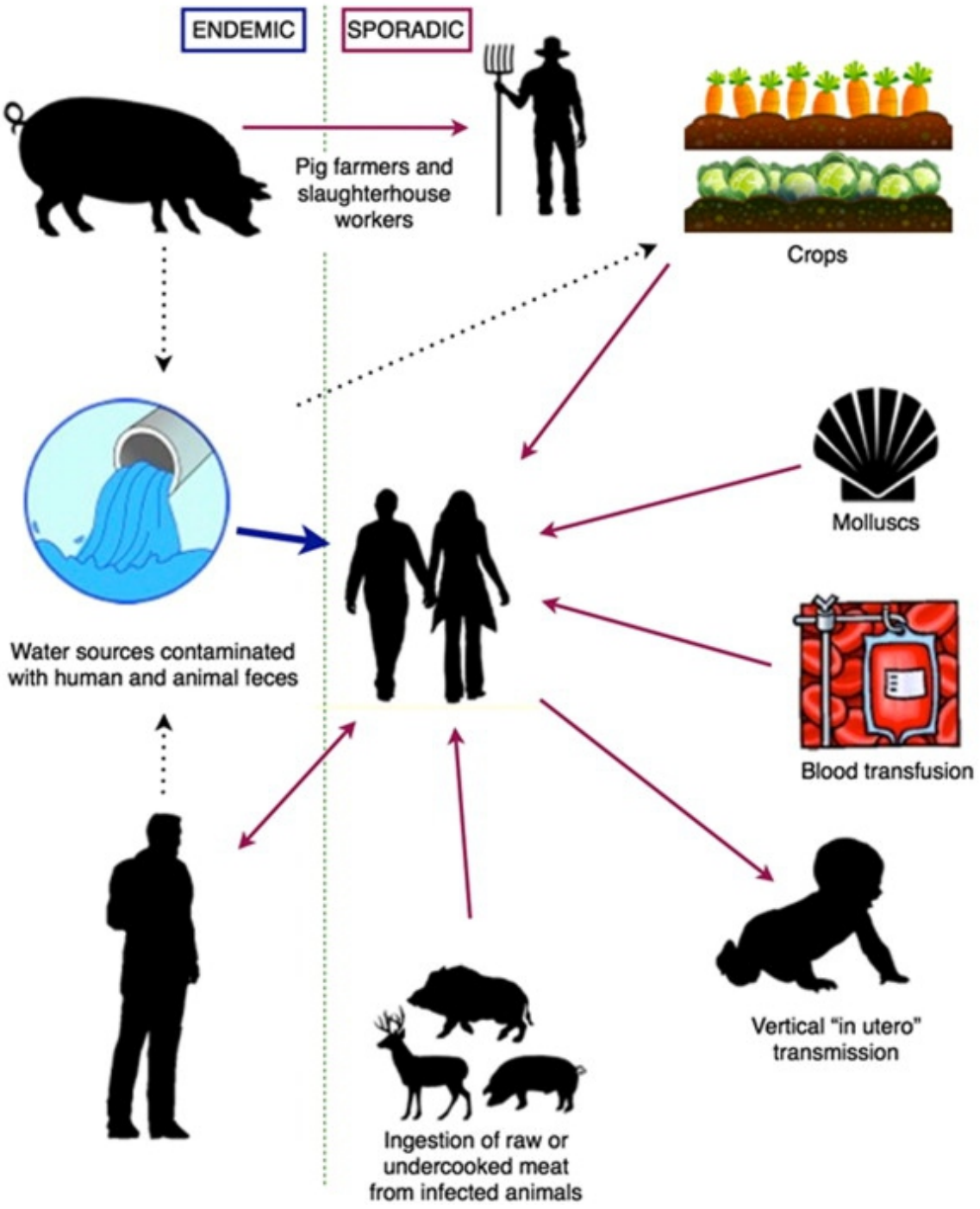


Figure 14: Modes of transmission of hepatitis E in India and it's major outbreaks174

Figure 15: Zoonotic transmission of hepatitis E



Source: Hepatitis E: An emerging disease; https://www.sciencedirect.com/science/article/abs/pii/S1567134814000057

Pathogenesis

Animal studies show replication of HEV in liver, blood cells, and other organs. Early liver damage may result from direct cytopathic effect of HEV, but later pathologic effects are immune mediated.[175] HEV is transiently present in serum during prodrome, and at the onset of clinical disease it is found in faeces.[176] Faecal shedding of HEV persists for 1 week to 2 months. Appearance of anti-HEV roughly correlates with cessation of viral replication and beginning resolution of disease.[176]

Clinical features

The incubation period of HEV is between 2 and 9 weeks (45 days), and it is generally a self-limiting disease that is relatively severe compared with HAV.[170] There is a prodromal (pre-icteric) phase of nonspecific constitutional symptoms followed by an icteric phase that lasts several weeks.[177] Fulminant HEV is rare (0.5 to 4 percent) except in pregnant women, in whom HEV occurring in the third trimester carriers a 20 percent maternal fatality rate and a 50 percent rate of fetal loss.[178] Mortality rate of those infected during the third trimester was 100 percent in one study.[178]

Symptoms

In areas with high disease endemicity, symptomatic infection is most common in young adults aged 15–40 years.[179] In these areas, although infection does occur in children, they often have either no symptoms or only a mild illness without jaundice that goes undiagnosed.[179]

Typical signs and symptoms of hepatitis E include:

- An initial phase of mild fever, reduced appetite (anorexia), nausea and vomiting, lasting for a few days; some persons may also have abdominal pain, itching (without skin lesions), skin rash, or joint pain.[166-168]
- Jaundice (yellow discolouration of the skin and sclera of the eyes), with dark urine and pale stools; and a slightly swollen and painful liver (hepatomegaly).
- These symptoms are often indistinguishable from those experienced during other liver illnesses and typically last between 1–6 weeks. In rare cases, acute hepatitis E can be severe, and results in fulminant hepatitis (acute liver failure).[180] Fulminant hepatitis occurs more frequently when hepatitis E occurs during pregnancy. Pregnant women with hepatitis E, particularly those in the second or third trimester, are at an increased risk of acute liver failure, fetal loss and mortality.[180] Cases of chronic hepatitis E infection have been reported in immunosuppressed people, particularly organ transplant recipients on immunosuppressive drugs.[166]

Diagnosis

- Cases of hepatitis E are not clinically distinguishable from other types of acute viral hepatitis. Diagnosis can often be strongly suspected in appropriate epidemiologic settings.[181]
- Definitive diagnosis of hepatitis E infection is usually based on the detection of antibodies to the virus in a person's blood.[170] The commonly used tests for HEV infection include detection of IgM and IgG anti-HEV antibodies and detection of HEV RNA. IgM anti-HEV antibodies can be detected during the first few months after HEV infection, whereas IgG anti-HEV antibodies represent either recent or remote exposure. The presence of HEV RNA indicates current infection, whether acute or chronic.[169] However, recently developed tests (includes the HEV IgM ELISA and the rapid point of care test) have been shown to be highly sensitive and specific and particularly useful in endemic regions, and does not require advanced laboratory equipment.[166,170,181]
- Additional confirmatory tests include tests to detect the presence of virus by PCR/molecular methods in

blood and/or stool.[166,170,181]

Treatment

- Supportive care should be provided, as for any acute hepatitis. With fulminant HEV, hospitalization and liver transplantation is indicated.[181,182] Ribavirin and interferon-α has been used to treat cases of HEV infection. Most of these cases where antivirals have been used are in the setting of chronic HEV infection in immunosuppressed host. There are anecdotal reports of use of ribavirin in the setting of severe acute HEV infection with worsening liver function and acute on chronic liver failure (ACLF). In vitro experiments have demonstrated activity of sofosbuvir against HEV replication, but there have been no reports of its use in humans.[183]

Prevention

- At the population level, transmission of HEV and hepatitis E disease can be reduced by:[184]
  - Maintaining quality standards for public water supplies;
  - establishing proper disposal systems for human faeces.
- On an individual level, infection risk can be reduced by:
  - Maintaining hygienic practices such as hand-washing with safe water, particularly before handling food;
  - Avoiding consumption of water and/or ice of unknown purity
  - During outbreaks where sanitation has eroded, efforts such as water chlorination may be inadequate. Boiling or other disinfection of the water supply should still be attempted, and avoidance of uncooked fruits, vegetables, and shellfish in these settings is also prudent.
  - Pregnant women should be cautious about travel to endemic regions due to elevated mortality risk.

Unlike with HAV, passive immunization with IG has not been shown to protect against HEV transmission or disease. Several potentially effective prototype HEV vaccines are being studied but none is yet available.[185] Two recombinant hepatitis E vaccines developed from HEV genotype 1, by GlaxoSmithKline and Xiamen Innovax Biotech, have had short-term efficacy in clinical trials. The latter vaccine, with the commercial name of Hecolin, has been in use in China since 2012. However, the long-term efficacy of this hepatitis E vaccine has not yet been determined.[186] Standard precautions are adequate to prevent HEV transmission in healthcare settings.[187] The finding of asymptomatic carriage of HEV in swine raises concern of xenotransplantation from pigs to humans.[188]

NUTRITIONAL NEEDS

Everything we eat and drink passes through our liver. A patient suffering from acute infectious hepatitis will experience severe loss of appetite or anorexia, nausea, vomiting, abdominal pain, taste changes, fever and jaundice.[195-197] All these symptoms complicate food intake and make it difficult to ensure that the patient is well nourished at a time when it is essential to provide the patient with a highly nutritious diet to prevent liver damage.

General dietary advice

- Eat regular, balanced meals
- Maintain healthy calorie intake
- Eat whole-grain cereals, breads, and grains
- Eat lots of fruits and vegetables
- Get adequate protein
- Go easy on fatty, salty, and sugary foods
- Drink enough fluids
- Reach and maintain a healthy weight
- **Eat regular, balanced meals**: Eating regularly means eating at least 3 meals a day. One way to keep your energy level up is to eat small meals or snacks at least every 3 to 4 hours.
- **Eat lots of fruits and vegetables**: Fruits and vegetables are important sources of many nutrients, including potassium, fiber, vitamin C, beta-carotene (a form of vitamin A), and folic acid. Some of these substances are antioxidants that can fight cell damage. As a bonus, most fruits and vegetables are naturally low in fat, sodium, and calories.
- **Get enough protein**: Protein is needed to fight infection and to heal damaged liver cells. Protein helps rebuild and maintain muscle mass and it aids in healing and repair of body tissues.
- **Dairy products**: Besides providing protein, dairy products are the richest source of calcium and one of the few sources in the diet of vitamin D. Choose dairy products that are low-fat or fat-free.
- Go easy on fatty, salty, and sugary foods
- **Drink plenty of fluids**: Drink at least 6 to 8 glasses of fluid a day.
- **Reach and stay at a healthy weight**: Weighing either too much or too little can allow hepatitis C to progress more quickly in your body. Being overweight also can make your hepatitis C treatment less effective. But people who lose weight slowly can reverse these changes. Keeping off extra weight can improve the liver enzymes and fibrosis, even though the hepatitis C virus is still in the body. Avoid fad diets, because losing weight too fast can put strain on the liver.
- **Avoid alcohol**: Alcohol is a strong toxin to the liver, even in people without hepatitis
- **Be careful with dietary supplements**: Some supplements in high amounts can be dangerous. Here are some special concerns:
  - **Caution about iron**: Some people with hepatitis C have above-average iron levels in their body. Hepatitis C progression occurs in such patients as a result of accelerated hepatic iron uptake and the oxidative stress caused by iron-catalysed free radical production.199 If you have too much iron, your doctor may ask you to eat fewer iron-rich foods, such as red meats, liver, and iron-fortified cereals. Avoid cooking with iron-coated cookware because the iron from the pots gets absorbed into food.

- Fatty salad dressings, mayonnaise, sour cream
  - Avocado
  - Fatty, fried meats, fatty fish, poultry skin, all processed meats and sausages, bacon, fatty gravies, fish canned in oil (buy tuna or pilchards canned in water or tomato sauce)
  - Nuts, peanut butter, nut spreads
  - Potato chips, vegetables smothered in butter or white/cheese sauces
  - Fatty snacks or very spicy snacks
  - All food preparation that increases the amount of fat contained in meals, such as frying in butter, margarine or oil. Rather boil, poach, grill, cook in a non-stick pan with Spray and Cook, and cook stews and soups the day before, chill and skim off all the coagulated fat before serving.

- **Vitamin, mineral and electrolyte supplements**:
  - Patients suffering from dehydration because of repeated vomiting need to drink an electrolyte mixture.
  - In serious cases the patient may have to be put on a drip to replenish body water and electrolytes.
  - Monitor the patients' liquid intake and if you suspect dehydration, contact the doctor immediately.

Note: Safe hygiene and sanitation practices are utmost important to prevent hepatitis A & E. Boiling or cooking food and water for ≥ 1 minute to 85°C (185°F) is necessary to inactivate HAV.[198]

Diet for special cases

- If you have hepatitis, you usually don't need a special diet. Just trying to eat healthy and not being overweight and avoid alcohol is all that is needed. There are special cases, however, when hepatitis can affect the diet:[195-197]
- **Patients being treated with interferon**: Hepatitis C treatment can cause side effects that make it difficult to eat. Side effects include loss of appetite, sore mouth and throat, metallic tastes, nausea, and vomiting.
- **Patients with cirrhosis**: As liver disease progresses, patients may lose their appetite and become so tired they have a hard time eating. They may become very thin and poorly nourished and be less able to fight off disease. They may need to limit salt in their diet to prevent their body from putting fluid into their legs and abdomen.
- **Other medical conditions and diet**: Conditions that warrant specific dietary restrictions include high blood pressure, heart disease, diabetes mellitus, high cholesterol, celiac sprue or chronic kidney disease.

Coffee consumption and chronic hepatitis C: Coffee consumption may be helpful, reducing oxidative DNA damage, increasing death of virus-infected cells, stabilizing chromosomes, and reducing fibrosis.[200] Moderate daily unsweetened coffee ingestion is a reasonable adjunct to therapy for NAFLD patients.[201]

Summary

Providing adequate nutrition is a major concern in patients with viral hepatitis. Ensure that patient gets protein rich diet with sufficient calories to prevent sarcopenia. Eating a healthy and regular diet should be the goal for patient. Patients must abstain from alcohol intake. Dietary recommendations also depend on individual needs as well as the stage of viral hepatitis.

MENTAL HEALTH

Mental health is a state of well-being in which every individual realizes his or her own potential, can cope with the normal stress of life, can work productively and fruitfully, and is able to contribute to her or his community. (WHO)[352]
Mental wellbeing describes your mental state, how you are feeling and how well you can cope with day today life.

Mental health in viral hepatitis – key facts

Living with the hepatitis virus doesn't just take a toll on your liver. It can also affect your mental health.

- Mental illness and hepatitis frequently co-occur (Rosenberg et al., 2001; Rosenberg et al., 2003). People who have mental illness are at greater risk than the general public for exposure to infectious diseases, including chronic hepatitis.
- It is completely normal to have strong reactions when a person finds out they have hepatitis, including feelings such as fear, anger, and a sense of being overwhelmed.
- Depression and anxiety are common in people who have hepatitis. But seeking social support and treating the disease with new medications can improve mental health and quality of life.
- Hepatitis viruses are linked with psychiatric conditions in both adults and children, according to study data presented at The American Association for the Study of Liver Diseases. 353

The link between certain mental illness conditions with hepatitis are explained below:

Depression and hepatitis

- There can be an unfortunate stigma attached to a viral hepatitis diagnosis, especially from people who don't understand the condition. Globally, stigma has identified as a significant barrier for screening, diagnosis and treatment of viral hepatitis. Stigma is associated with lack of knowledge surrounding transmission of viral hepatitis. Fear of infection and lack of information about the disease often leads to breakdown of intimate relationships.
- The stigma associated with viral hepatitis can influence everyday life as well as willingness of the patient to engage with medical professionals or disclose disease status.
- As a result, people with viral hepatitis may become isolated, which can pave the way to depression, and if the sadness becomes overwhelming, it may be the time to seek medical help.

Anxiety, mood changes, and hepatitis

Mood changes, including anxiety and irritability, is common with a person living with viral hepatitis. They may feel anxious about the diagnosis and long term continuity of the treatment. HCP can support patients by educating them about hepatitis in detail, emphasizing the importance of family screening & vaccination. One must be encouraged to adopt healthy lifestyle. All these can help in coping with the anxiety and mood swings.

Sleep problems and hepatitis

Sleep disturbances affect about 50 percent of people living with hepatitis, according to a study published in

November 2014 in the Journal of Circadian Rhythms. Some sleep issues may be due to psychiatric problems, substance abuse issues, or advanced liver disease. If a person is not getting appropriate sleep it increases the risk for depression, anxiety, and feeling unwell in general. Sleep disturbances can also be a side effect of viral hepatitis.

Substance abuse, mental illness, and hepatitis

Drug users often involves in sharing of needles and other equipment's, which is one of the major causes of hepatitis B & C infection. Such patients are already dealing with substance use and hepatitis, which can lead to increased mental health issues.[354]"Pre-existing mental health issues can increase risk for substance use and viral hepatitis in a patient.

Common signs & symptoms that indicate mental health problem:

- Feeling sad or hopeless
- Thoughts of death
- Fatigue
- Weight loss
- Trouble with focus
- Sleeping problems[355]

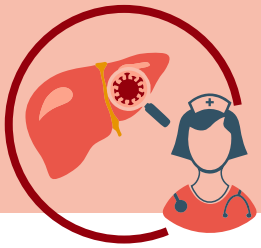
Getting mental health support[356]

- Mental health is a critical component for a person's recovery to achieve overall wellness. If a person is experiencing mental health challenges, it is important that the patient communicate with their health care professional and appropriate support and guidance can be provided. Some people may also benefit from therapy, support groups, or a combination of both.
- Patient must ensure healthy lifestyle choices, such as exercising regularly, can also help treat the depression and anxiety associated with viral hepatitis as healthy choices can improve overall mood and general feelings of well-being."

A HCP must ensure to discuss the following techniques with patients to deal with mental health in general:

- **Discontinue consumption of alcohol & drugs**: Substance use such as alcohol consumption will cause serious damage to the liver. It can also worsen depression and anxiety in the patients. Encourage patients to practice ways to say no, and to stay away from people who pressure them to partake.
- **Practice safe sex**: Patients must be encouraged to disclose their medical condition to their partners and necessary precautions must be practiced during intimacy. Partners should be screened and vaccinated for HBV.
- **Managing worries**: Guide patients to get enough sleep, eat healthy food & exercise regularly. Managing stress can be difficult as it can consume a lot of energy.
- **Be patient**: Hepatitis B & C and mental health problems require long term treatment and support. Patients and families must be counselled to keep patience and adherence to the treatment.
- **Talking about Hepatitis**: Hepatitis is a disease that infects all sort of people, but many struggles to admit due to social stigma attached to it. Encourage patients to disclose their illness among family and friends. Telling others about having hepatitis isn't only for their benefit. It's for self-benefit too. Person living with hepatitis need the support of family and possibly some close friends to help them better cope with the illness.[357]

NURSING INTERVENTIONS



Viral Hepatitis Nurses work with patients in the community or in hospital settings. They provide a link between public hospital specialist services and general practice, and give specialised support to general practitioner to assist in the management of patients with hepatitis B & C.[32,34,35,107,112] With advanced knowledge and skills in testing, management and treatment of viral hepatitis, they assist with the management of patients on antiviral medications, and work in shared care arrangements with the physicians.

Hepatology Nursing

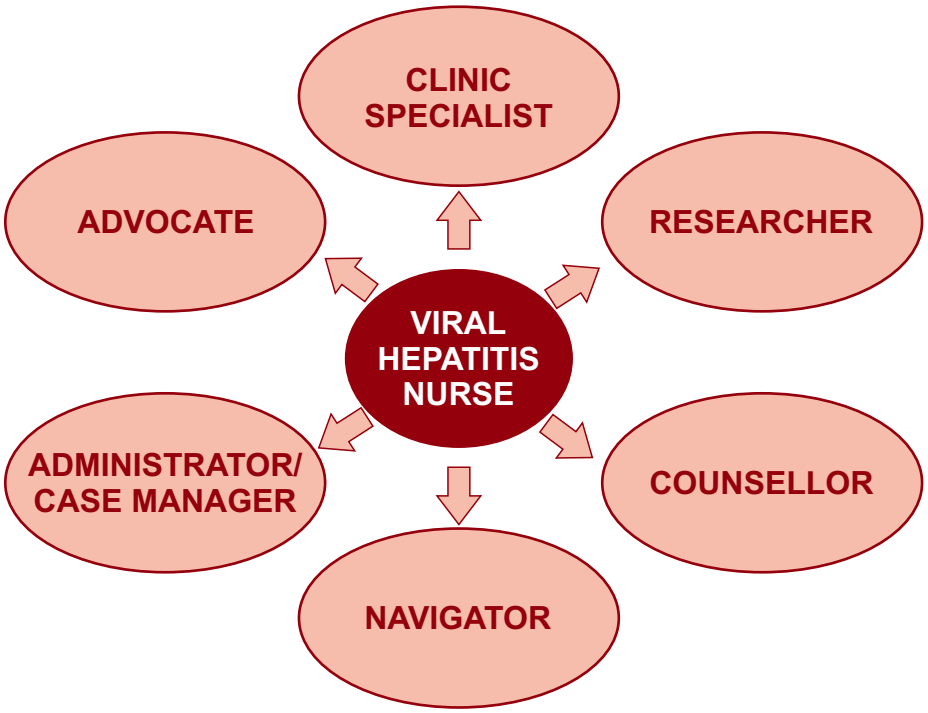
- Hepatology nursing is a recognized specialized area of nursing that focuses on the promotion of health, prevention of illness, care and support of patients experiencing liver-related diseases, and research. Key components include:
  - **Promotion of health**: hepatology nurses perform activities that include providing educational sessions for the general public, marginalized populations and other health care professionals, as well as promoting harm-reduction initiatives such as safe needle disposal.
  - **Prevention of illness**: this include immunization, education regarding prevention of the spread of disease and needle exchange program.
  - **Care, support and treatment:** nurses educate patients and their families; provide emotional support and advocacy; counsel before, during and after treatment on benefits, risks, side effects, coping strategies and adherence to treatment; interpret results; and liaison with the family, support groups and other health professionals (i.e., psychiatrist, ophthalmologist, social worker, etc).
  - **Research**: nurses are active in clinical trials (industry and/or pharmaceutical), monitoring adherence to treatment, their own nurse-initiated studies, quality of life and continually incorporate new research- and evidence-based findings into their practice.

Viral Hepatitis specialist nurse

This role involves:[202,203]

- Screening patients and family at risk of hepatitis infection.
- Educating patients and partners/relatives/friends about hepatitis after a positive diagnosis.
- Taking a thorough medical history, including assessing pre-existing conditions and looking for signs of extra-hepatic manifestations of viruses and cirrhosis or decompensated liver disease.
- Liasoning with other health professionals involved in patient care, which is particularly important for managing side effects.
- Closely monitoring treatment efficacy and side-effects according to the treatment protocol.
- Providing education to other health professionals (such as general physicians, general nurses and midwives) to increase awareness of the disease.
- She acts as a direct care provider, collaborator, team leader, educator, primary care practitioner, and referral service provider.

Figure 25: Roles of a viral hepatitis specialist nurse



Nurse as a patient advocate

Role of a nurse as a patient advocate includes:[204,205]

- **Maintain records** such as copy of medical chart if the patient moves or changes doctor. When hospitalized, keep a daily log of who did what, when, where, how and why.
- **Know the medication(s)** and learn both brand and generic names. Advice for the drug's actions, side effects, adverse reactions, contraindications, proper dosing and what to avoid - such as alcohol, other drugs, certain foods or sunlight.
- **Keep a paper trail** of billing slips, insurance forms, encounter slips (those papers left with the doctor's office), pharmacy receipts and the insurance company's EOBs (explanation of benefits).
- **Get educated** if the patient has a serious or chronic disease or disorder. Research the condition thoroughly to work as a team.
- **Use information wisely** and don't stop or change medications or treatments, no matter how compelling.
- **Be assertive** and be the best health advocate possible. Become an educator, make informed decisions and play an active role in protecting the patient's health.

Nurse as a patient counsellor

Role of nurse as a patient counsellor includes:[205,208,209]

- Counselling patients with hepatitis infections is often the most difficult aspect of patient management for a number of reasons. Despite the limitations, important, useful, and relevant information can be transmitted to most patients within the final three to five minutes of the patient visit for consistency.

- **Key counselling goals**:
  - Ensuring the safety of patients.
  - Providing reliable information to patients and their families.
  - Building the therapeutic relationship with patients.
  - Helping patients understand their diagnosis.
  - Incorporating patient needs in substance abuse treatment planning.
  - Developing a prevention plan.
  - Using motivational interviewing.
  - Confronting the social ramifications of hepatitis.
  - Addressing relapse issues.
  - Building support.
  - Providing case management.
- **Patient counselling topics**:
  - Disease itself: prevalence, natural history, treatment
  - Impact of disease on patient: daily activities, exercise/rest, food, alcohol, further investigations required if any
  - Transmission: general, sexual/intimate, children, blood/organ donation
  - Family screening: indications, explanations.
- **Specific advices**: Patients are advised
  - Not to share any injecting equipment such as needles and syringes
  - Not to donate blood nor carry a donor card
  - Not to share razors, toothbrushes or anything else that may possibly be contaminated with blood
  - To use condoms when having sex. The risk of passing on the hepatitis C virus during sex is small but is reduced even further by using condoms. However, partners in regular monogamous relationships may accept the small risk of having sex without condoms.

Hepatitis nursing care plan

Hepatitis nursing care plan (NCP) includes:[210-212]

- **Nursing priorities:**
  - Reduce demands on liver while promoting physical well-being.
  - Prevent complications.
  - Enhance self-concept, acceptance of situation.
  - Provide information about disease process, prognosis, and treatment needs.
- **Discharge goals:**
  - Meeting basic self-care needs.
  - Complications prevented/minimized.
  - Dealing with reality of current situation.
  - Disease process, prognosis, and therapeutic regimen understood.
  - Plan in place to meet needs after discharge.

Nursing Diagnosis

The nursing diagnosis has several components explained below:

Imbalanced Nutrition

- **Risk factors** include less than body requirements may be related to
  - Insufficient intake to meet metabolic demands: anorexia, nausea/vomiting

- Altered absorption and metabolism of ingested foods: reduced peristalsis (visceral reflexes), bile stasis
  - Increased calorie needs/hyper metabolic state: Possibly evidenced by aversion to eating/lack of interest in food; altered taste sensation, abdominal pain/cramping, Loss of weight; poor muscle tone
- **Desired outcomes**
  - Initiate behaviours, lifestyle changes to regain/maintain appropriate weight.
  - Demonstrate progressive weight gain toward goal with normalization of laboratory values and no signs of malnutrition.
- **Nursing interventions**:
  - Monitor dietary intake and caloric count.
  - Suggest several small feedings and offer "largest" meal at breakfast.
  - Encourage mouth care before meals.
  - Recommend eating in upright position.
  - Encourage intake of fruit juices, carbonated beverages, and hard candy throughout the day.
  - Consult with dietitian, nutritional support team to provide diet according to patient's needs, with fat and protein intake as tolerated.
  - Monitor serum glucose as indicated.
  - **Administer medications as indicated**: Antiemetics, Antacids, Vitamin Supplements Etc.
  - Provide supplemental feedings and TPN if needed.
  - Deficient fluid volume

Risk for deficient fluid volume

- **Risk factors may include**: Excessive losses through vomiting and diarrhoea, third-space shift, Altered clotting process
- **Possibly evidenced by**: Not applicable. A risk diagnosis is not evidenced by signs and symptoms, as the problem has not occurred, and nursing interventions are directed at prevention.
- **Desired outcomes**
  - Maintain adequate hydration, as evidenced by stable vital signs, good skin turgor, capillary refill, strong peripheral pulses, and individually appropriate urinary output.
  - Be free of signs of haemorrhage with clotting times within normal limits.
- **Nursing interventions**:
  - Monitor intake & output, compare with periodic weight. Note enteric losses: vomiting and diarrhoea.
  - Assess vital signs, peripheral pulses, capillary refill, skin turgor, and mucous membranes.
  - Check for ascites or oedema formation. Measure abdominal girth as indicated.
  - Use small-gauge needles for injections, applying pressure for longer than usual after venepuncture.
  - Have patient use cotton or sponge swabs and mouthwash instead of toothbrush or use soft bristled toothbrush.
  - **Observe for signs of bleeding**: haematuria, melena, ecchymosis, oozing from gums, puncture sites
  - **Monitor periodic laboratory values**: Hb/Hct, Na, albumin, and clotting times.
  - Provide IV fluids (usually glucose), electrolytes. Protein hydrolysates.
  - **Administer medications as indicated**: Vitamin K, Antacids or H2-receptor antagonists.
  - Infuse fresh frozen plasma, as indicated.

Fatigue

- **May be related to**:
  - Decreased metabolic energy production
  - States of discomfort

- Altered body chemistry (e.g., changes in liver function, effect on target organs)
  - **Possibly evidenced by**:
    - Reports of lack of energy/inability to maintain usual routines.
    - Decreased performance
    - Increase in physical complaints
- **Desired outcomes**:
  - Report improved sense of energy.
  - Perform activities for daily living and participate in desired activities at level of ability.
- **Nursing interventions**:
  - Institute bed red or chair rest during toxic state. Provide quiet environment; limit visitors as needed.
  - Recommend changing position frequently. Provide and instruct caregiver in good skin care.
  - Do necessary tasks quickly and at one time as tolerated.
  - Determine and prioritize role responsibilities and alternative providers and possible community resources available
  - Identify energy-conserving techniques: sitting to shower and brush teeth, planning steps of activity so that all needed materials are at hand, scheduling rest periods.
  - Increase activity as tolerated, demonstrate passive or active range of motions exercises.
  - Encourage use of stress management techniques: progressive relaxation, visualization, guided imagery. Discuss appropriate diversional activities: radio, TV, reading.
  - Monitor for recurrence of anorexia and liver tenderness or enlargement.
  - Administer medications as indicated: sedatives, antianxiety agents
- Monitor serial liver enzyme levels.

Risk for Impaired Skin Integrity

- **Risk factors may include**:
  - Chemical substance: bile salt accumulation in the tissues
- **Possibly evidenced by**:
  - Not applicable. A risk diagnosis is not evidenced by signs and symptoms, as the problem has not occurred, and nursing interventions are directed at prevention.
- **Desired outcomes**:
  - Display intact skin/tissues, free of excoriation.
  - Report absence/decrease of pruritus/scratching.
- **Nursing interventions**:
  - Encourage use of cool showers and baking soda or starch baths. Avoid use of alkaline soaps. Apply calamine lotion as indicated.
  - Provide diversional activities
  - Suggest use of knuckles if desire to scratch is uncontrollable. Keep fingernails cut short, apply gloves on comatose patient or during hours of sleep. Recommend loose-fitting clothing. Provide soft cotton linens.
  - Provide a soothing massage at bedtime.
  - Observe skin for areas of redness, breakdown.
  - Avoid comments regarding patient's appearance
  - **Administer medications as indicated: Antihistamines, Antilipemic**: cholestyramine
  - Knowledge deficit

Knowledge Deficit

- **May be related to**:

- Lack of exposure/recall; information misinterpretation
  - Unfamiliarity with resources
- **Possibly evidenced by**:
  - Questions or statements of misconception; request for information
  - Inaccurate follow-through of instructions; development of preventable complications
- **Desired outcomes**:
  - Verbalize understanding of disease process, prognosis, and potential complications.
  - Identify relationship of signs/symptoms to the disease and correlate symptoms with causative factors.
  - Verbalize understanding of therapeutic needs.
  - Initiate necessary lifestyle changes and participate in treatment regimen.
- **Nursing interventions**:
  - Assess level of understanding of the disease process, expectations and prognosis, possible treatment options.
  - Provide specific information regarding prevention and transmission of disease: contacts may require gamma-globulin; personal items should not be shared; observe strict hand washing and sanitizing of clothes, dishes, and toilet facilities while liver enzymes are elevated. Avoid intimate contact, such as kissing and sexual contact, and exposure to infections, especially URI.
  - Plan resumption of activity as tolerated with adequate periods of rest. Discuss restriction of heavy lifting, strenuous exercise and/or contact sport.
  - Help patient identify appropriate diversional activities.
  - Identify ways to maintain usual bowel function: adequate intake of fluids and dietary roughage, moderate activity and exercise to tolerance.
  - Discuss the side effects and dangers of taking OTC and prescribed drugs (acetaminophen, aspirin, sulphonamides, some anaesthetics) and necessity of notifying future healthcare providers of diagnosis.
  - Discuss restrictions on donating blood.
  - Emphasize importance of follow-up physical examination and laboratory evaluation
  - Review necessity of avoidance of alcohol
  - Refer to community resources, drug/alcohol treatment program as indicated.
  - Low self-esteem

Situational Low Self-Esteem

- **May be related to**:
  - Annoying/debilitating symptoms, confinement/isolation, length of illness/recovery period
- **Possibly evidenced by**:
  - Verbalization of change in lifestyle; fear of rejection/reaction of others, negative feelings about body; feelings of helplessness
  - Depression, lack of follow-through, self-destructive behaviour
- **Desired outcomes**:
  - Verbalize feelings.
  - Identify feelings and methods for coping with negative perception of self.
  - Verbalize acceptance of self in situation, including length of recovery/need for isolation.
  - Acknowledge self as worthwhile; be responsible for self.

Risk for Infection

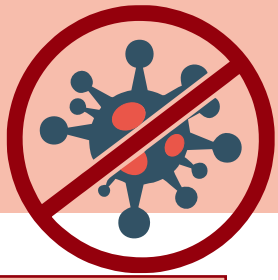
- **Risk factors may include**:

- Inadequate secondary defences (e.g., leukopenia, suppressed inflammatory response) and immunosuppression
  - Malnutrition
  - Insufficient knowledge to avoid exposure to pathogens
- **Desired outcomes**:
  - Verbalize understanding of individual causative/risk factor(s).
  - Demonstrate techniques; initiate lifestyle changes to avoid reinfection/transmission to others.

Other possible nursing diagnosis

- Home Maintenance, impaired—prolonged recovery/chronic condition, insufficient finances, inadequate support systems, unfamiliarity with neighbourhood resources.
- Nutrition: imbalanced, less than body requirements—insufficient intake to meet metabolic demands: anorexia, nausea/vomiting; altered absorption and metabolism of ingested foods; increased calorie needs/hypermetabolic state.

STANDARD PRECAUTIONS



Infection prevention and control measures aim to ensure the protection of those who might be vulnerable to acquiring an infection both in the general community and while receiving care due to health problems, in a range of settings. The basic principle of infection prevention and control is hygiene.[11,62,65,189]

Standard precautions

Figure 16: Standard Precautions

Standard Precautions are guidelines that outline the minimum set of interventions that are required for preventing the transmission of microorganisms. [11,62,65,189] They provide a foundation for infection prevention measures that are to be used for all patients in every healthcare setting.

There are many factors that contribute to the consistent use of Standard Precautions within healthcare facilities.

Administrative support is necessary to ensure infection prevention is an integral component of the organizational structure. Healthcare personnel must be educated and empowered to be accountable for providing safe care to all patients by incorporating Standard Precautions into the interventions and education they provide.

There are several key components that the Healthcare Infection Control Practices Advisory Committee identifies that constitute the Standard Precautions guidelines. Hand hygiene, respiratory hygiene and cough etiquette, appropriate use of personal protective equipment, safe work and injection practices, and environmental cleaning, as well as patient placement, are all elements essential in breaking the cycle of microorganism transmission.

In today's global society, it is imperative that all facilities and settings that provide healthcare meticulously practice Standard Precautions to prevent transmission of known, as well as unknown threats of emerging pathogens protecting all persons including healthcare personnel, patients, and the community at large.

Key concepts

- Transmission of infection requires a source of infection, a mode of transmission, and a vulnerable host.
- Application of Standard Precautions is the first step in breaking the cycle and preventing the transmission of microorganisms between healthcare personnel, patients, and the environment.
- Standard Precautions are intended to be utilized for the care of all patients, in all settings in which healthcare services are rendered, even in the absence of a suspected or confirmed infectious process.
- Standard Precautions are utilized to protect both healthcare personnel and patient(s) from infection preventing the spread of microorganisms between hosts (person-to-person, person to environment to person).

Figure 17: WHO recommended 5 moments of hand hygiene

1 BEFORE PATIENT CONTACT	WHEN? Clean your hands before touching a patient when approaching him or her WHY? To protect the patient against harmful germs carried on your hands
2 BEFORE AN ASEPTIC TASK	WHEN? Clean your hands immediately before any aseptic task WHY? To protect the patient against harmful germs, including the patient's own germs, entering his or her body
3 AFTER BODY FLUID EXPOSURE RISK	WHEN? Clean your hands immediately after an exposure risk to body fluids (and after glove removal) WHY? To protect yourself and the health-care environment from harmful patient germs
4 AFTER PATIENT CONTACT	WHEN? Clean your hands after touching a patient and his or her immediate surroundings when leaving WHY? To protect yourself and the health-care environment from harmful patient germs
5 AFTER CONTACT WITH PATIENT SURROUNDINGS	WHEN? Clean your hands after touching any object or furniture in the patient's immediate surroundings, when leaving - even without touching the patient WHY? To protect yourself and the health-care environment from harmful patient germs

Hand hygiene

- Perform hand hygiene by means of hand rubbing or hand washing. [11,62,65,189]
- Hands should always be washed with soap and water if hands are visibly soiled, or exposure to spore-forming organisms is proven or strongly suspected, or after using the restroom. For other indications, if resources permit, perform hand rubbing with an alcohol-based preparation.
- Ensure availability of hand-washing facilities with clean running water.
- Ensure availability of hand hygiene products (clean water, soap, single use clean towels, alcohol-based hand rub). Alcohol-based hand rubs should ideally be available at the point of care.
- Hand washing (40–60 sec): wet hands and apply soap; rub all surfaces; rinse hands and dry thoroughly with a single use towel; use towel to turn off faucet.
- Hand rubbing (20–30 sec): apply enough product to cover all areas of the hands; rub hands until dry.
- Healthcare personnel need to be educated about when and how to perform hand hygiene.
- The WHO recognized that the multiple indications for hand hygiene were difficult to remember and sought to simplify the message with the "My 5 Moments for Hand Hygiene," which has become widely adopted. The five moments include:[11,62,65,189]
  - Before patient care
  - Before an aseptic procedure
  - After any contact with blood or other body fluids—even if gloves are worn
  - After patient care
  - After contact with the patient's environment

Hand hygiene technique

- **When using an alcohol-based hand rub**, it is important to check the manufacturer's recommendation for volume of product and ensure that the appropriate amount is dispensed. [10,62,65,189] If not, enough product is dispensed or if the product is not applied to all parts of the hands, antimicrobial efficacy may be limited. After dispensing the product, personnel should rub all areas of hand surfaces together until they are dry. HCP with larger hands may need to dispense two dollops of product when performing hand hygiene. A good rule is that it should take 15 to 20 seconds of rubbing for the hand sanitizer to dry.

- **When using soap and water**, hands should be wet with water that is not too hot, then product should be applied per manufacturer's recommendations, and hands should be rubbed together vigorously, covering all skin surfaces and under rings, for at least 15 seconds. Hands should be rinsed thoroughly, so that no product is left, and then dried with a disposable towel. A dry towel is then used to turn off the water faucet.

Figure 18: How to handrub as recommended by WHO

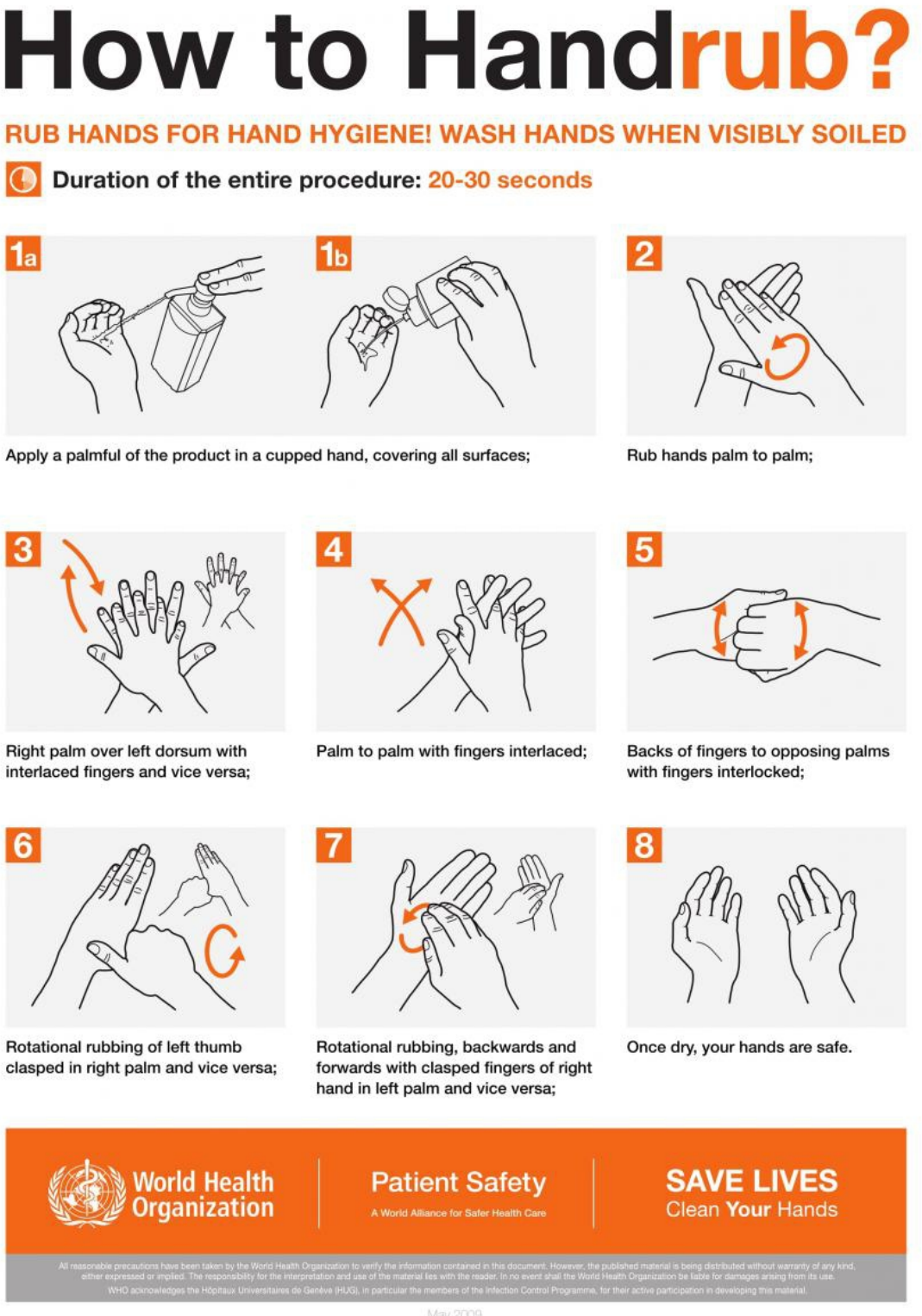
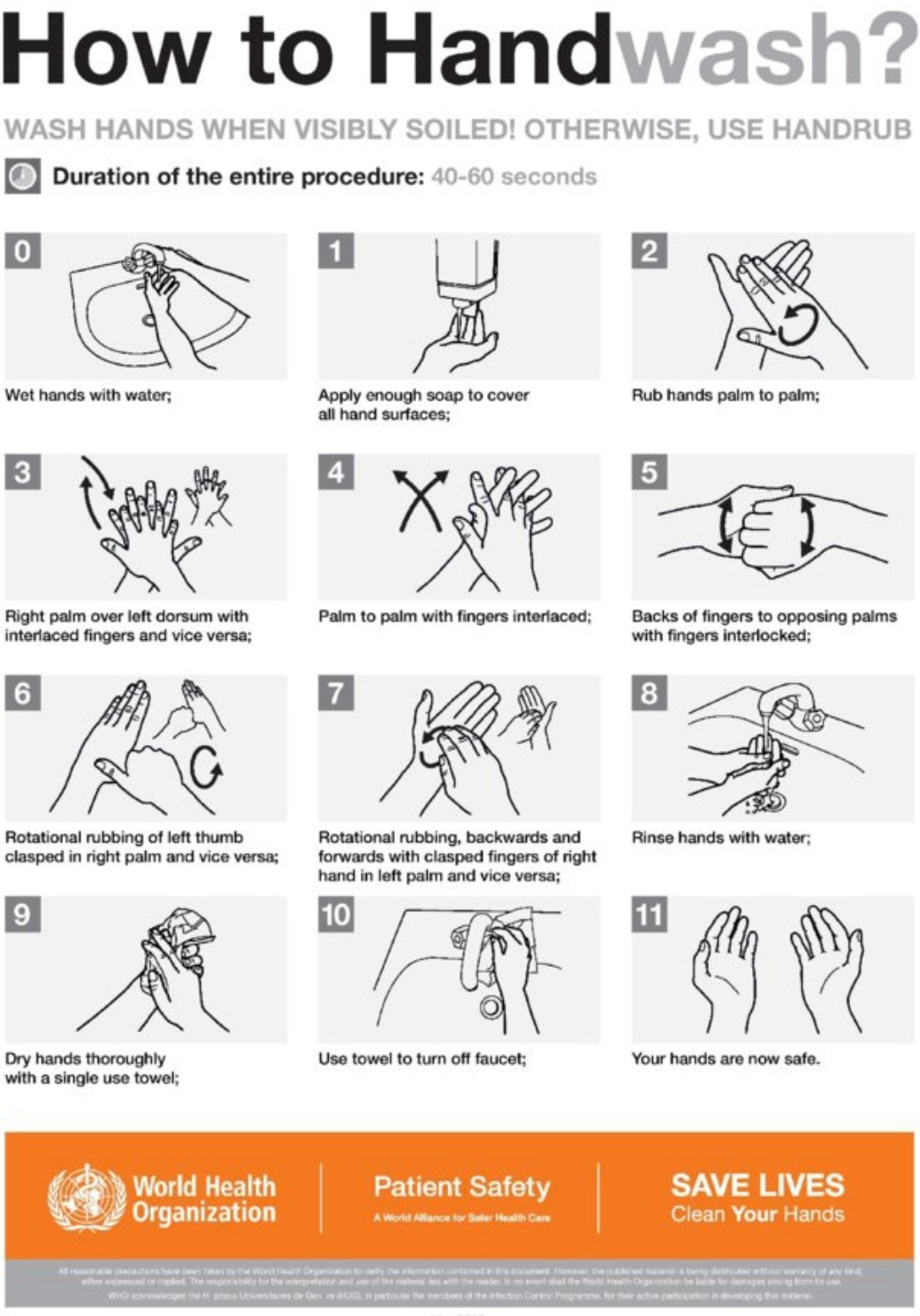


Figure 19: How to handwash as recommended by WHO

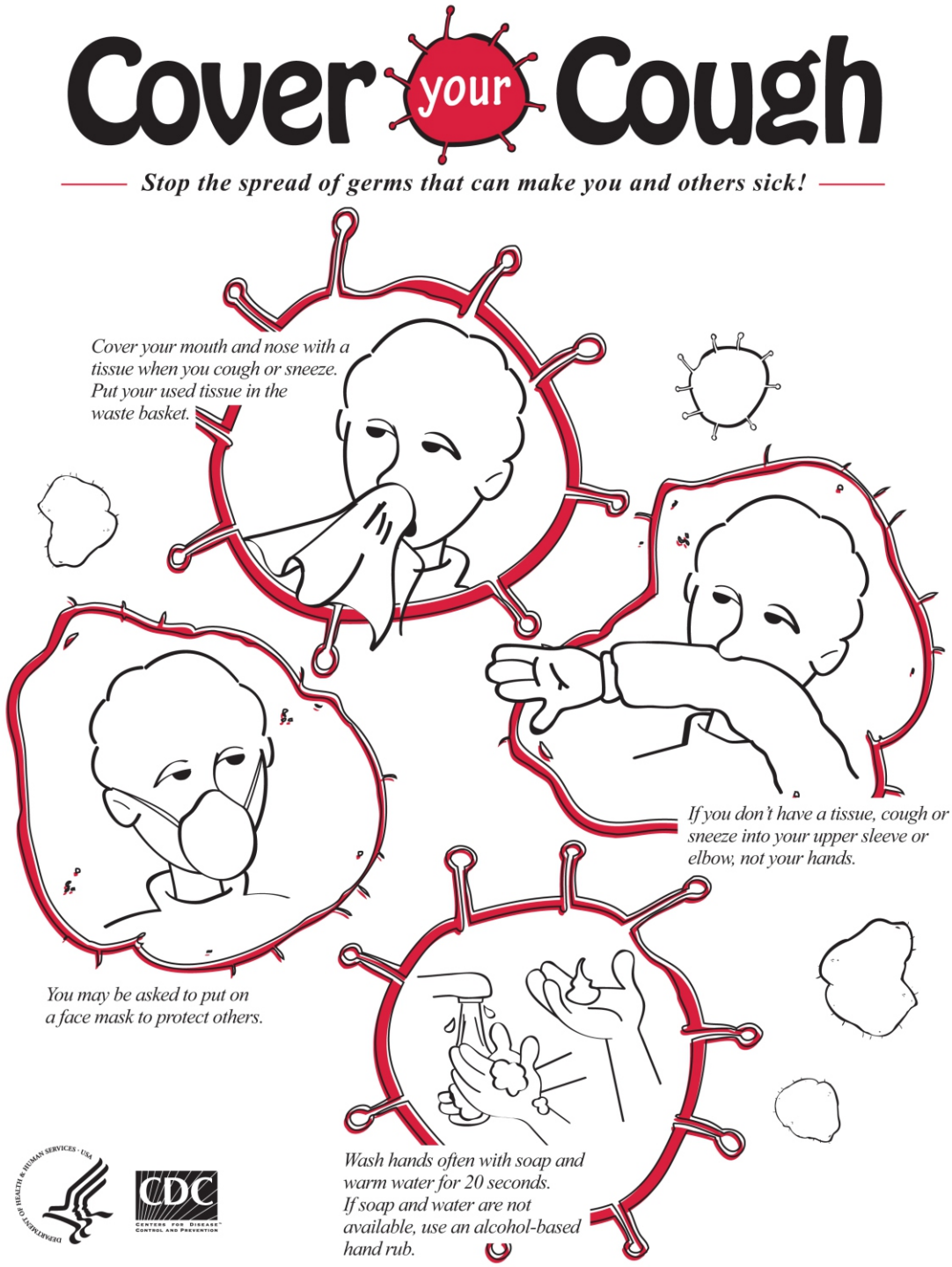


Respiratory hygiene

- Respiratory hygiene and cough etiquette interventions are intended to limit the spread of infectious organisms from persons with potentially undiagnosed respiratory infections.
- In order for respiratory hygiene interventions to be effective, early implementation of infection control measures needs to occur at the first point of entry within a healthcare setting and maintained throughout the duration of the visit. The effort of respiratory hygiene interventions are targeted at patients and accompanying significant others with respiratory symptoms and applies to any person entering a healthcare setting with signs of respiratory illness including cough, congestion, rhinorrhoea, or increased production of respiratory secretions.[11,62,65,189]
- The five main elements of an effective respiratory hygiene program include:
- Education of HCP, patients, and visitors on the signs and symptoms of respiratory illness
  - Posted signs at facility entries with instructions for prevention of transmission of respiratory illness in languages of the local population
  - Easy availability of source control measures (tissues, surgical masks) to enable patient and visitors to cover sneezes and coughs and mask persons with a cough
  - Use in the nearest waste receptacle to dispose of the tissue after use
  - Easy and frequent availability of hand hygiene located close to other source control supplies including the facility entrance and waiting rooms
  - Encourage patients or visitors with respiratory symptoms to sit apart from other people in the waiting room, more than 3 feet apart, or place in a separate area when feasible.
- HCP with respiratory illness should avoid providing direct patient contact. A barrier mask should be worn by HCP who demonstrate signs and symptoms of respiratory illness but need to provide direct patient contact. Barrier masks are also indicated in some instances where the HCP may be infectious prior to the onset of symptoms such as with exposure to varicella or measles.

Note: Respiratory hygiene and cough etiquette are very important components to minimise risk of cross transmission of respiratory illness.

Figure 20: CDC guidelines on cough etiquettes



Personal Protective Equipment (PPE)

- Personal protective equipment (PPE) is designed to protect the wearer's skin, eyes, mucous membranes, airways, and clothing from coming into contact with infectious agents. The selection of PPE is made based on the tasks being performed and anticipated level of exposure the employee expects to encounter.[11,62,65,189]
- Components of PPE can be used alone or in combination to provide the desired level of protection. Mucous membranes and skin with compromised integrity are portals of entry that are highly susceptible to infectious agents; therefore, it is important that appropriate protective measures be taken.[11,62,65,189]
  - Assess the risk of exposure to body substances or contaminated surfaces before any health-care activity. Make this a routine!
  - Select PPE based on the assessment of risk: Clean non-sterile gloves, Clean, non-sterile fluid-resistant gown, Mask and eye protection or a face shield.

Gloves

- Wear when touching blood, body fluids, secretions, excretions, mucous membranes, nonintact skin.
- Change between tasks and procedures on the same patient after contact with potentially infectious material.
- Remove after use, before touching non-contaminated items and surfaces, and before going to another patient.
- Perform hand hygiene immediately after removal.

Facial protection (Eyes, Nose, and Mouth)

- **Barrier masks or barrier masks with shields** worn when HCP anticipate sprays of blood or body fluids, particularly respiratory secretions. HCP, patients, or visitors in healthcare settings also wear barrier masks to limit the spread of potentially infectious respiratory secretions.[11,62,189] In some cases, HCP should consider wearing barrier masks when providing direct patient care if at risk of spreading respiratory illness after unprotected exposure prior to becoming symptomatic such as in the case of influenza.[11,62,184]
- **Surgical masks**: worn by HCP to protect the patient from infectious agents in the HCP's nose or mouth during sterile procedures such as insertion of catheters or injections into spinal or epidural spaces during lumbar puncture procedures.
- **Goggles/face shields** worn by HCP to protect the eyes and face of the wearer from sprays of respiratory secretions, blood, or body fluids. They should be worn when the HCP anticipate participating in a procedure that has the potential to generate splashes or sprays of blood, body fluids, secretions, or excretions. Personal eyeglasses or contact lenses do not provide adequate protection and are not considered acceptable eye protection. The use of face shields allows HCP to wear their own personal eyeglasses and increase protection to other areas of the face, including the eyes.

Gown

- Wear to protect skin and prevent soiling of clothing during activities that are likely to generate splashes or sprays of blood, body fluids, secretions, or excretions.
- Remove soiled gown as soon as possible and perform hand hygiene.
- Fluid-resistant gowns worn when HCP anticipate performing patient care activities or procedures in which exposed skin or clothing are likely to be exposed to any patient blood, body fluids, secretions, or excretions.

Note: Rationale use of PPE is crucial to avoid shortage of PPE without jeopardizing the health of HCPs.

Figure 21: Personal protective equipements for healthcare workers

Safe work practices

- In an effort to limit exposure to potentially infectious microorganisms, HCP must take care to keep gloved and ungloved hands from touching their own mucous membranes.[11,62,65,189]
- Patients should be positioned to direct any splatters or sprays of patient blood, body fluids, secretions, or excretions away from the face of the HCP. Prior to providing patient care, HCP need to ensure that their PPE is positioned properly and secured to avoid potential contamination during repositioning of PPE.
- HCP should always use a barrier for resuscitation such as a mouthpiece, resuscitation bag, or other ventilation device to prevent direct contact with secretions from the patient.

Environmental cleaning

- Cleaning and disinfection of all surfaces, equipment, and devices in patient care areas are an integral part of Standard Precautions. Cleaning of all medical equipment and devices, including computers and technological devices that enter patient care areas is important to prevent transmission of infectious organisms.[11,62,65,189]
- Use adequate procedures for the routine cleaning and disinfection of environmental and other frequently touched surfaces.
- Noncritical patient care equipment should be cleaned and disinfected after each patient use.
- All soiled medical equipment and devices should be handled in a manner that prevents the transfer of microorganisms to others and the environment. Contaminated equipment that must be cleaned and disinfected and must be stored in an area that is separate from clean supplies and equipment.
- HCP should wear gloves when handling equipment that is contaminated or visibly soiled and perform hand hygiene immediately after removal of gloves.
- Soiled linen should be handled utilizing a method that prevents microorganisms from being transmitted to other people and the environment.
- Commonly used disinfectants in hospitals:
  - Formaldehyde
  - Glutaraldehyde
  - Hydrogen peroxide
  - Sodium hypochlorite
  - Iodophors
  - Quaternary ammonium compounds

Note: Always follow manufacturer's recommendations for use of any disinfectants.

Waste disposal

- Ensure safe waste management.
- Treat waste contaminated with blood, body fluids, secretions and excretions as clinical waste, in accordance with local regulations.
- Human tissues and laboratory waste that is directly associated with specimen processing should also be treated as clinical waste.
- Always follow biomedical waste management protocol.
- Person who generates waste must dispose the waste in appropriate bins.

Note: Segregation of waste at the point of generation is utmost important.

Patient care equipment

- Handle equipment soiled with blood, body fluids, secretions, and excretions in a manner that prevents skin and mucous membrane exposures, contamination of clothing, and transfer of pathogens to other patients or the environment.
- Clean, disinfect, and reprocess reusable equipment appropriately before use with another patient.
- An organization's culture may need to shift from thinking that only infection preventionists are accountable for infection prevention and must present all healthcare workers with an infection prevention opportunity. All caregivers are accountable and to encourage infection prevention protocols, healthcare professionals should show appreciation for all the people who help keep infections at bay.

Patient placement

- In the event that a patient is determined to be at increased risk for transmission of microorganisms, the patient should be placed in a single-patient room when available.[11,62,65,189]
- Those patients that are likely to contaminate the environment, do not maintain appropriate hygiene, or are at increased risk for acquiring infections or developing adverse outcomes following infection should be considered for single room placement.
- When single patient room is not available, patient spacing should be maintained at a minimum of 3 feet or more. Privacy curtains may be pulled and used as an environmental barrier.[11,62,65,189]

Instrument / equipment safety

As part of standard infection-control practice, instruments and other reusable equipment used in performing invasive procedures should be appropriately disinfected and sterilized as follows:

- Critical equipment and devices such as surgical instruments, intravascular catheters, needles that enter the patient's vascular system or other normally sterile areas of the body should be sterilized before being used for each patient.
- Semi eritical equipment and devices such as ET tube, suction tube, endoscopes that touch intact mucous membranes but do not penetrate the patient's body surfaces should be sterilized when possible or undergo high-level disinfection if they cannot be sterilized before being used for each patient.
- Non critical equipment and devices such as bedpans, linens, food utensils, stethoscopes that do not touch the patient or that only touch intact skin of the patient need only be cleaned with a detergent or as indicated by the manufacturer.
- All health care personnel should adhere to Standard Precautions. Depending on the medical procedure involved,
- Standard Precautions may include the appropriate use of personal protective equipment (e.g., gloves, masks, and protective eyewear).
- Compliance with infection control protocols by healthcare professionals, performing viral serological tests periodically, and continuing training courses for personnel.
- The main practical points to be considered are cleaning the rooms and patients' area, disinfection of instruments, correct drug preparation, and regular hand hygiene.
- Appropriate staff training and regular monitoring for hepatitis viruses are also mandatory.

Conclusion

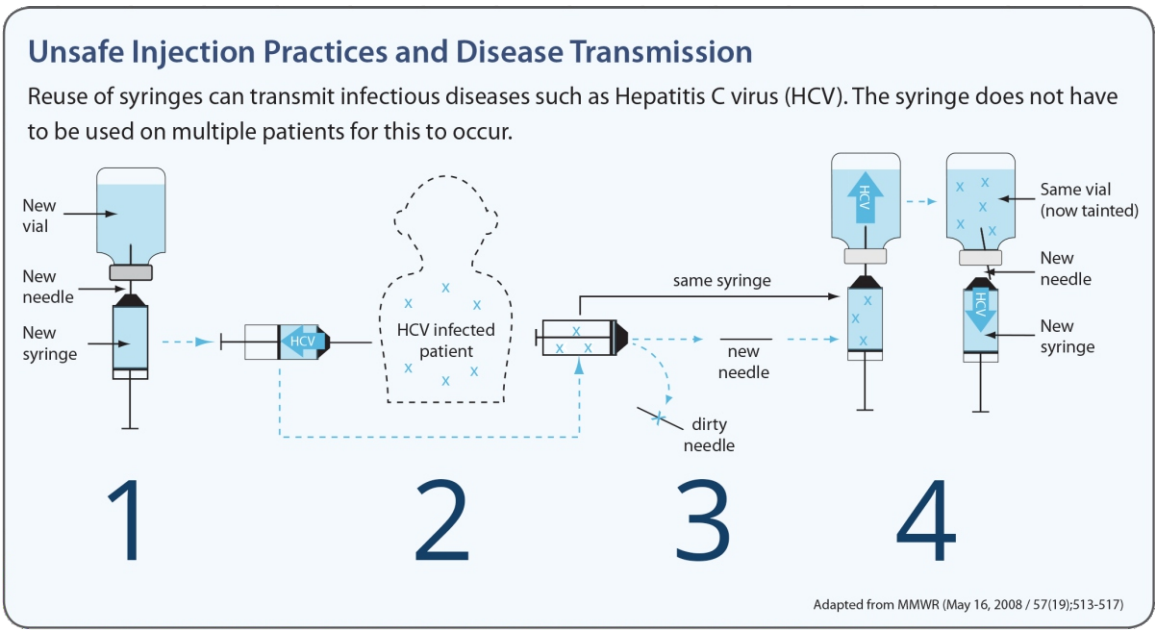
- Standard Precautions are the primary defence in preventing the transmission of microorganisms between HCP, patients, and the environment. The components of Standard Precautions are aimed at breaking the cycle of infection by interrupting the method in which transmission occurs. While it is the role of the

healthcare administration to ensure infection, prevention is an important component of the organizational structure, the value of the interventions remains the responsibility of HCP and their accountability for adhering to these essential guidelines. When Standard Precautions are correctly implemented, the spread of infectious diseases can be prevented, leading to improved health of both HCP and patients.

- Training of HCPs in proper infection-control technique should begin in professional schools and continue as an ongoing process. Institutions should provide all HCPs with appropriate in-service education regarding infection control and safety and should establish procedures for monitoring compliance with infection-control policies. Avoiding occupational exposure to blood is the primary way to prevent transmission of blood-borne illnesses among health care personnel. All health care personnel should adhere to Standard Precautions.[9,11]

INJECTION SAFETY

Figure 22: Unsafe infection practices and disease transmission



Key Facts

- Injections are one of the most common health-care procedures. Every year at least 16 billion injections are administered worldwide. The vast majority – around 90% – are given in curative care. Immunization injections account for around 5% of all injections, with the remaining covering other indications, including transfusion of blood and blood products, intravenous administration of drugs and fluids and the administration of injectable contraceptives.[192,193]
- Injection practices worldwide and especially in low- and middle-income countries (LMICs) include multiple, avoidable unsafe practices that ultimately lead to large scale transmission of blood-borne viruses among patients, health-care providers and the community at large.
- Recent investigations undertaken by state and local health departments and the Centre for Disease Control and Prevention have identified improper use of syringes, needles, and medication vials during routine healthcare procedures, such as administering injections. These practices have resulted in one or more of the following:
  - Transmission of blood borne viruses, including hepatitis C virus to patients
  - Notification of thousands of patients of possible exposure to blood-borne pathogens and recommendation that they be tested for HCV, HBV, and HIV
  - Referral of providers to licensing boards for disciplinary action
  - Malpractice suits filed by patients
- Unsafe practices include, but are not limited to the following prevalent and high-risk practices:
- Reuse of injection equipment to administer injections on more than one patient including

reintroduction of injection equipment into multi-dose vials, reuse of syringes barrels or of the whole syringe, informal cleaning with reuse and other practices.
- Accidental needle-stick injuries (NSIs) in health-care workers which occur while giving an injection or after the injection, including handling infected sharps before and after disposal.
- Overuse of injections for health conditions where oral formulations are available and recommended as the first line treatment. Demand for and prescriptions of injectable medicines that are inappropriate include overuse of antibiotics, use of unnecessary injectable products such as certain vitamins, moving directly to second line injectable treatments and others.
- Unsafe sharps waste management putting health-care workers, waste management workers and the community at large at risk of needle-stick injuries and subsequent blood-borne infections. Unsafe management of sharps waste includes incomplete incineration, disposal in open pits or dumping sites, leaving used injection equipment in hospital laundry and other practices that fail to secure infected sharps waste.

Safe injection practices

- Safe injection practices are essential to ensuring both patient and HCP safety.[192,193]
- Injection safety, or safe injection practices, is a set of measures taken to perform injections in an optimally safe manner for patients, healthcare personnel, and others. A safe injection does not harm the recipient, does not expose the provider to any avoidable risks, and does not result in waste that is dangerous for the community (e.g., through inappropriate disposal of injection equipment).
- HCP should always use a sterile, single-use disposable syringe and needle for each injection given.
- Care needs to be taken to ensure that all injection equipment and medication vials remain free from contamination.
- Sterile packaging should only be opened immediately prior to use and the vial access diaphragm should be disinfected with an approved antiseptic immediately prior to accessing.
- It is highly recommended that single dose vials be used over multiple dose vials, especially when the medications will be administered to multiple patients. This decreases the risk of the solution becoming contaminated from multiple accesses to the vial.
- Used needles should never be recapped, bent, or broken and any safety device present should be engaged immediately after use. If recapping is necessary, only a one-handed scoop technique should be used.
- All used sharps should be placed immediately in an approved puncture-resistant container that is designated for sharps disposal. Injection safety includes practices intended to prevent transmission of infectious diseases between one patient and
- another, or between a patient and healthcare provider, and also to prevent harms such as needle stick injuries.

Safety measures during medication preparation

- Parenteral medications should be accessed in an aseptic manner. This includes using a new sterile syringe and sterile needle to draw up medications while preventing contact between the injection materials and the non-sterile environment. [192,193]
- Proper hand hygiene should be performed before handling medications and the rubber septum should be disinfected with alcohol prior to piercing it.
- Medications should be drawn up in a designated clean medication area that is not adjacent to areas where potentially contaminated items are placed. Examples of contaminated items that should not be placed in or near the medication preparation area include: used equipment such as syringes, needles, IV tubing, blood collection tubes, needle holders (e.g., vacutainer holder), or other soiled equipment or materials that have been used in a procedure.

- Any item that could have come in contact with blood or body fluids should not be in the medication preparation area.
- A needle should never be left inserted into a medication vial septum for multiple uses. This provides a direct route for microorganisms to enter the vial and contaminate the fluid.
- The safest practice is to always enter a medication vial with a sterile needle and sterile syringe. In multiple multi-dose vials for the purpose of combining their contents into a single syringe, if one vial becomes contaminated, this practice can spread contamination to the others, prolonging presence of the pathogen and increasing the potential for disease transmission.

Safety measures during medication administration

- Once used, the syringe and needle are both contaminated and must be discarded. Use a new sterile syringe and needle for each patient.[192,193]
- A small amount of blood can flow into the needle and syringe even when only positive pressure is applied outward. The syringe and needle are both contaminated and must be discarded.
- All of the components are directly or indirectly exposed to the patient's blood and cannot be used for another patient. A syringe that intersects through ports in the IV tubing or bags also becomes contaminated and cannot be used for another patient. Separation from the patient's IV by distance, gravity and/or positive infusion pressure does not ensure that small amounts of blood are not present in these items.
- The safest practice is to always enter a medication vial with a sterile needle and sterile syringe, even when obtaining additional doses of medication for the same patient.
- This adds an extra layer of safety in case, for some reason, the medication vial is not discarded at the end of the procedure as it should be and is inadvertently used on a subsequent patient.

Single-dose/use vials

- A single-dose or single-use vial is a vial of liquid medication intended for parenteral administration (injection or infusion) that is meant for use in a single patient for a single case/procedure/injection. [192,193]
- Even if a single-dose or single-use vial appears to contain multiple doses or contains more medication than is needed for a single patient, that vial should not be used for more than one patient nor stored for future use on the same patient.
- Medication vials should always be discarded whenever sterility is compromised or questionable. In addition, the following recommendations are made for handling of single-dose or single-use vials:
- If a single-dose or single-use vial has been opened or accessed (e.g., needle-punctured) the vial should be discarded according to the time the manufacturer specifies for the opened vial or at the end of the case/procedure for which it is being used, whichever comes first. It should not be stored for future use.
- If a single-dose or single-use vial has not been opened or accessed (e.g., needle-punctured), it should be discarded according to the manufacturer's expiration date.

Multi-dose Vials

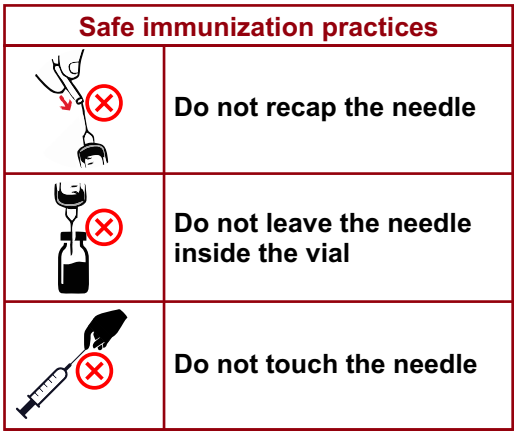
- A multi-dose vial is a vial of liquid medication intended for parenteral administration (injection or infusion) that contains more than one dose of medication.[192,193]
- Multi-dose vials should be dedicated to a single patient whenever possible.
- If multi-dose vials must be used for more than one patient, they should not be kept or accessed in the immediate patient treatment area. This is to prevent inadvertent contamination of the vial through direct or indirect contact with potentially contaminated surfaces or equipment that could then lead to infections in subsequent patients.
- If a multi-dose has been opened or accessed (e.g., needle-punctured) the vial should be dated and

discarded within 28 days unless the manufacturer specifies a different (shorter or longer) date for that opened vial.
- If a multi-dose vial has not been opened or accessed, it should be discarded according to the manufacturer's expiration date.

Preparation for vaccine administration

- Do not open a single-dose vial until ready to use.[192,193]
- Once the protective cap is removed the vaccine should be used or discarded at the end of the workday.[192,193]
- Multidose vials can be used until the expiration date printed on the vial unless contaminated, compromised, or there is a "beyond use date" (BUD) noted in the package insert.[192,193]
- Never use partial doses from two or more vials to obtain a full dose of vaccine.[192,193]
- Once a manufacturer-filled syringe is activated (i.e., syringe cap removed or needle attached), the vaccine should be used or discarded at the end of the workday.
- Diluents are not interchangeable unless specified by manufacturer. (e.g., diluent for MMR).
- If vaccine must be reconstituted, use only diluent supplied by manufacturer for that vaccine. Never use a stock vial of sterile water or normal saline to reconstitute vaccines.
- Always check expiration dates on both diluent and vaccines to make sure neither has expired.
- Refer to manufacturer's product information/package insert for instructions on reconstituting specific vaccines. CDC recommends that providers draw up vaccines only at time of administration.
- If not used by the end of the workday, vaccines should be discarded.
- You should only administer vaccines that you have prepared.

Figure 23: Safe immunization practices for healthcare workers



Infection prevention during blood glucose monitoring and insulin administration

Unsafe practices during assisted monitoring of blood glucose and insulin administration have put persons at risk for infection includes:[192,193]

- Using finger stick devices for more than one person.
- Using a blood glucose meter for more than one person without cleaning and disinfecting it in between uses.
- Using insulin pens for more than one person.
- Failing to change gloves and perform hand hygiene between fingerstick procedures.
- Finger stick devices should never be used for more than one person.
- Whenever possible, blood glucose meters should not be shared. If they must be shared, the device should be cleaned and disinfected after every use, per manufacturer's instructions. If the manufacturer does not specify how the device should be cleaned and disinfected, then it should not be shared.
- Insulin pens and other medication cartridges and syringes are for single-patient-use only and should never be used for more than one person.
- **Single-use, auto-disabling finger stick devices**: These are devices that are disposable and prevent reuse through an auto-disabling feature. In settings where assisted monitoring of blood glucose is performed, single-use, auto-disabling fingerstick devices should be used.

Blood glucose meters

- Blood glucose meters are devices that measure blood glucose levels.[192,193]
- Whenever possible, blood glucose meters should be assigned to an individual person and not be shared.
- If blood glucose meters must be shared, the device should be cleaned and disinfected after every use, per manufacturer's instructions, to prevent carry-over of blood and infectious agents. If the manufacturer does not specify how the device should be cleaned and disinfected, then it should not be shared.

Insulin administration

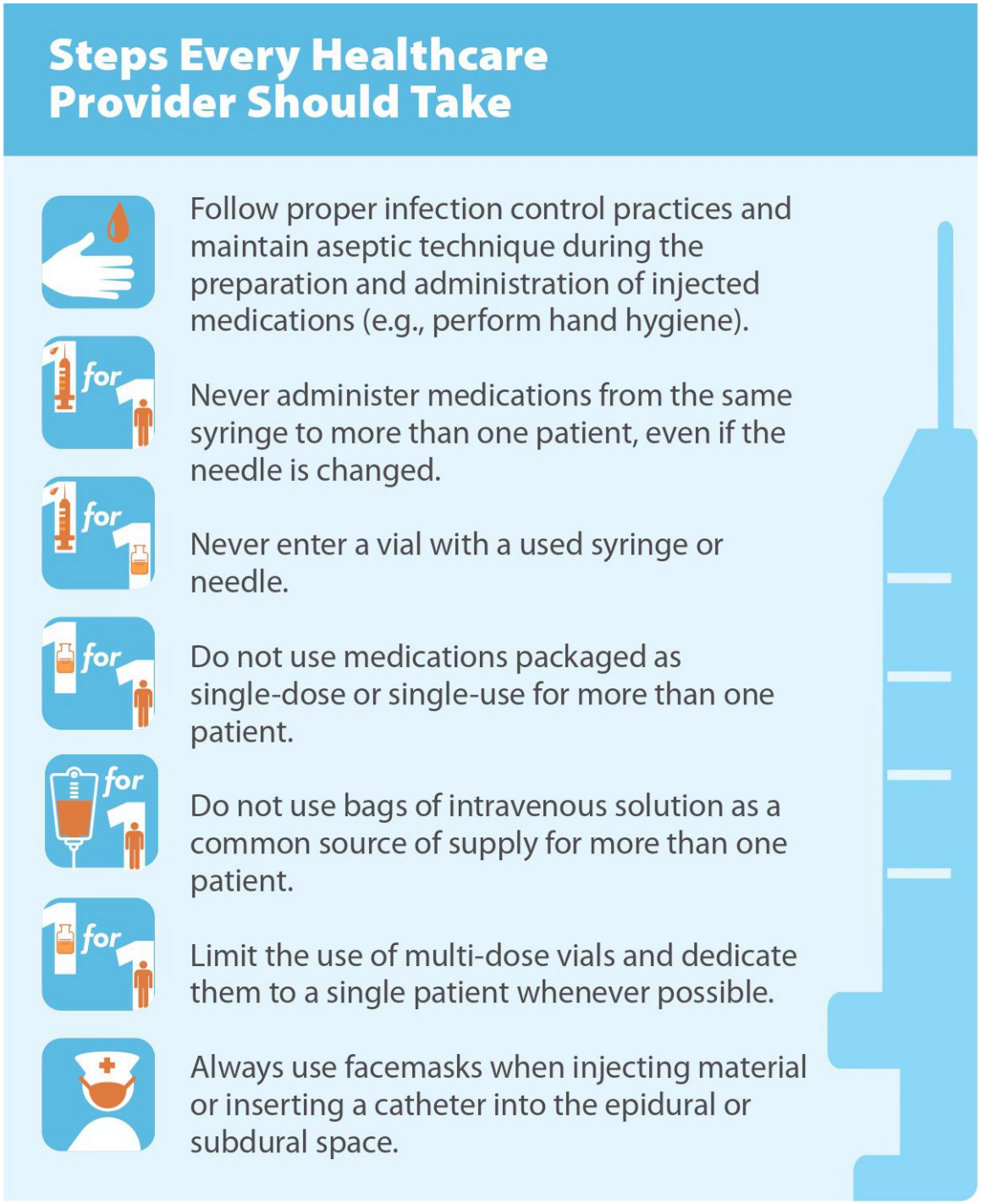
- Insulin can be administered using an insulin pen that is designed for reuse on a single patient. It can also be administered using a needle and syringe after drawing up contents from an insulin vial.[192,193]
- Insulin pens are designed to be safe for a single person to use a single pen multiple times, with a new needle for each injection.
- Insulin pens should be assigned to individual persons and labelled appropriately. They should never be used for more than one person.
- Multi-dose vials of insulin should be dedicated to a single person whenever possible.
- If the vial must be used for more than one person, it should be stored and prepared in a dedicated medication preparation area outside of the patient care environment and away from potentially contaminated equipment.
- Insulin vials should always be entered with a new needle and new syringe.
- Needles and syringes should never be used to administer insulin to more than one person and should be disposed of immediately after use in an approved sharps container.

Summary

Injection safety and other basic infection control practices are central to patient safety. All healthcare providers are urged to carefully review their infection control practices and the practices of all staff under their supervision. In particular, providers should ensure that staff:

- Never administer medications from the same syringe to more than one patient, even if the needle is changed.
- Do not enter a vial with a used syringe or needle.
- Never administer medications from the same syringe to more than one patient, even if the needle is changed or you are injecting through an intervening length of IV tubing.
- Do not enter a medication vial, bag, or bottle with a used syringe or needle.
- Never use medications packaged as single-dose or single-use for more than one patient. This includes ampoules, bags, and bottles of intravenous solutions.
- Always use aseptic technique when preparing and administering injections.
- **1 needle + 1 syringe + 1 time = 0 infections**

Figure 24: Injection safety guidelines for healthcare workers by CDC



NSI & PEP

Needle stick injuries are puncture wounds, cuts, or scratches inflicted by medical instruments intended for cutting or puncturing (cannulae, lancets, scalpels, etc.) that may be contaminated with a patient's blood or other body fluids. Contact of blood with non intact skin and contact with mucous membranes (eye, mouth, nose) are also subsumed under the term "needlestick injury."

Post exposure prophylaxis

PEP refers to the comprehensive management given to minimize the risk of infection following potential exposure to blood-borne pathogens (HIV, HBV, HCV). The ultimate goal of PEP is to maximally suppress any limited viral replication that may occur, and to shift the biological advantage to the host cellular immune system to prevent or abort early infection.

Every HCP who sustains a NSI should have access to post-exposure prophylaxis (PEP), as appropriate, within hours of the injury, along with counseling, confidential testing, and follow-up.

Table 14: First aid to be taken in case of a needle stick injury

Contaminated Wound	Contaminated Intact Skin
Encourage bleeding from the skin wound and wash injured area with soap and water. DO NOT squeeze.	Wash the area with soap and water.
Contaminated Eyes	**Contaminated Mouth**
Gently rinse the eyes wide open with distilled water	Spit out any fluid - rinse the mouth with water and spit it out again.

Table 15: Do's & Don'ts in case of a needle stick injury

Do's	Don'ts
• Remove gloves, if appropriate. • Wash site thoroughly with running water. • Irrigate thoroughly with running water or distill water if splashes have gone into the eye or mouth.	• Do not panic! • Do not reflexively place pricked finger into mouth. • Do not squeeze blood from wound, this cause trauma and inflammation, increasing risk of infection transmission. • Do not use bleach, alcohol, betadine, or iodine, on the wound surface as this may further increase trauma.

Testing of the source patient for HBsAg, Anti-HCV and HIV1 and 2 (after consent) should be done. Depending on the source serostatus PEP may be started.

PEP for HIV: If the source is HIV positive or unknown source, antiretroviral prophylaxis should be started ideally within 2 hours of exposure, or within 72 hours. The health care worker should also be tested for HIV at baseline and then 6 to 8 weeks later.

Table 16: PEP for HBV

Treatment when source is found to be			
Exposed person	**HBsAg Reactive**	**HBsAg Non reactive**	**Unknown/not tested**
Not Vaccinated	Hep B Immunoglobulin, initiate vaccination	Initiate vaccination	Initiate vaccination
Previously vaccinated, known responder*	Test for anti-HBs If >10mIU/ml: nothing If < 10mIU/ml: booster dose vaccine	No treatment	No treatment
Previously vaccinated, known non responder*	Hep B Immunoglobulin Vaccination	No treatment	If known high risk, may treat as if source were HbsAg positive
Response unknown	Test for anti-HBs If >10mIU/ml: nothing If < 10mIU/ml: Hep B immunoglobulin + booster dose vaccine	No treatment	Test for anti-HBs If >10mIU/ml: nothing If < 10mIU/ml: booster dose vaccine

*Responder- Anti-HBs titre >10 mlu/ml after completion of vaccination series.
*Non- responder- Anti-HBs titre <10 mlu/ml after completion of 2 vaccination series.

PEP for HCV: In case source is anti HCV reactive, the HCP should be checked for baseline anti HCV and liver function test and followed up periodically with the same. If the HCP becomes anti HCV positive, he should be referred for appropriate management.

Prevention of needle stick injuries

- Safe handling of needles and other sharp devices are components of standard precautions that are implemented to prevent health care workers exposure to blood borne pathogens.[190,191]
- Use care when:
  - handling needles, scalpels, and other sharp instruments or devices
  - cleaning used instruments
  - Disposing of used needles.
- The safety devices on needles and other sharps should be activated immediately after use.
- Used needles should be discarded immediately after use and not recapped, bent, cut, removed from the syringe or tube holder, or otherwise manipulated.
- Any used needles, lancets, or other contaminated sharps should be placed in a leak-proof, puncture-resistant sharps container that is either red in colour or labelled with a biohazard label.
- Do not overfill sharps containers. Discard after 2/3 full or when contents are at the 'full' line indicated on the containers.
- Used sharps containers may be taken to a collection facility such as an area pharmacy, hospital, or clinic that provides this service.

BMW MANAGEMENT

Bio-medical waste means any waste, which is generated during the diagnosis, treatment or immunization of human beings or animals or research activities pertaining thereto or in the production or testing of biological or in health camps. Bio-Medical waste includes all the waste generated from the Health Care Facility which can have any adverse effect to the health of a person or to the environment in general if not disposed properly. All such waste which can adversely harm the environment or health of a person is considered as infectious and such waste has to be managed as per BMWM Rules, 2016.[351]

Figure 26: Categorization & classification of wastes in health care facilities

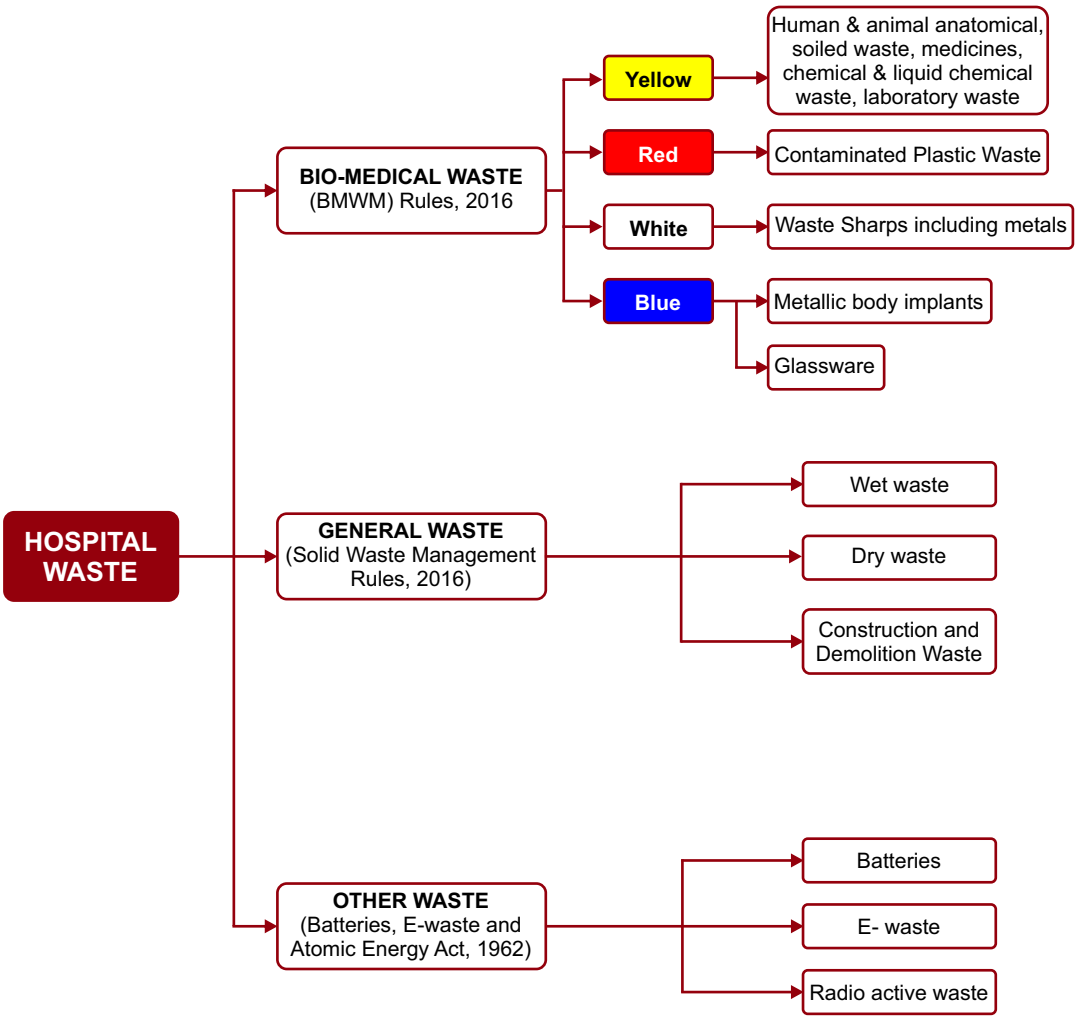


Table 17: Bio-medical waste management: its categories, segrigation, treatment & disposal[351]

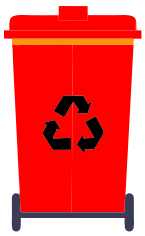
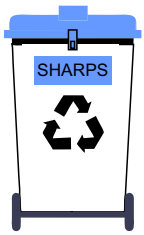
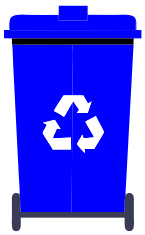
Bin category	Type of waste
 **Yellow (a-e)** coloured & coded, non-chlorinated plastic bags or containers.	a. Human Anatomical Waste b. Animal Anatomical Waste c. Soiled waste: dressings, plaster casts, cotton swabs and bags containing residual or discarded blood and blood components. d. Discarded or Expired Medicine e. Chemical Waste f. Chemical Liquid Waste g. Discarded Linen, Mattresses, beddings contaminated with blood, body fluids, routine mask and gown. h. Microbiology, Biotechnology and other clinical laboratory waste
 **Red** coloured non-chlorinated plastic bags (having thickness equal to more than 50 µ) and containers.	**Contaminated plastic waste (recyclable)**: Wastes generated from disposable items such as tubing, bottles, intravenous tubes and sets, catheters, urine bags, syringes without needles, fixed needle syringes with their needles cut, vacutainers and gloves.
 **White** coloured translucent, puncture proof, leak proof, temper proof containers.	**Waste Sharps** including metals Needles, syringes with fixed needles, needles from needle tip cutter or burner, scalpels, blades, or any other contaminated sharp object that may cause puncture and cuts. This includes both used, discarded and contaminated metal sharps.
 **Blue (a-b)** Puncture proof and leak proof boxes or containers or card board boxes with blue colored marking	a. Broken or discarded and contaminated glass including medicine vials and ampoules except those contaminated with cytotoxic wastes. b. Metallic Body Implants.

Table 17: Bio-medical waste management: its categories, segrigation, treatment & disposal[351]

Treatment & disposal if HCF having tie-up with CBWTF	Treatment & disposal if HCF having its own treatment and disposal facility
Yellow category waste along with pre-treated waste (if treated) should be stored in central storage point and must be handed over to CBWTF.	Incineration or plasma pyrosis disposal in case of no linkage to CBWTF. Disposal of the waste in the deep burial pit should not be practiced unless the hospitals is located in rural or remote isolated place.
No onsite treatment of Red category waste is required. All such waste is needed to be sent to CBWTF for final treatment and disposal	All the recyclable waste generated from the HCF having its own treatment and disposal facility must be sterilised using autoclaving / microwaving / hydro-calving followed by shredding or mutilation or combination of sterilisation and shredding.
Handover the waste to CBWTF without any alteration or onsite treatment.	Sharps waste should be disinfected either with autoclaving or dry-heat sterilization or a combination of autoclaving cum shredding.
Dispose of the empty glass bottles by handing over to CBWTF without any onsite treatment. The residual chemicals in glass bottle should be collected as chemical waste in yellow coloured container / bags and over to CBWTF as yellow(e) waste.	The waste has to be sterilized or disinfected (either by autoclaving or microwaving or hydroclaving or by Sodium Hypochlorite Solution) followed by soaking & washing with detergent prior to sending it for recycling.

Spill management

Blood or plasma spill:

Healthcare workers must follow proper guidelines in case of a blood or plasma spill in hospitals/laboratories. Below are the step wise guidelines of a blood or a plasma spill management:

- Clean the area taking all precautions (gloves, mask, protective gown etc.)
- Mark the area using demarcation tape.
- Cover the spillage with a filter paper sheet or absorbent material.
- After soaking of spillage discard the filter paper in yellow bin.
- After this mop the area with water, then wipe it with 1% sodium hypochlorite solution (at least three times and finally dry the area).
- Broken glass/plastic should be swept with a brush and dustpan (Do not use hands).
- Pour 1% sodium hypochlorite over the area and leave for 15-20 minutes.
- All spills and accidents are to be reported to the lab supervisor.

Mercury spill:[351]

Healthcare facilities have to ensure environmentally sound management of mercury or other chemical spills as per steps as given in CPCB guidelines explained below:

- **Evacuate area**: As far as possible, keep people who are not involved in the clean-up away from spill area to limit exposures and to prevent the spread of contamination.
- **Put on face mask**: In order to prevent breathing of mercury vapour, wear a protective face mask.
- Remove jewellery so that the mercury cannot combine (amalgamate) with the precious metals.
- **Put on rubber or latex gloves**. If there are any broken pieces of glass or sharp objects, pick them up with care using brush and a dustpan. Place all broken objects on a paper towel, fold the paper towel and place in a secure puncture proof yellow bag or container and label it as items contaminated with mercury.
- **Check a wide area beyond the spill**: Locate all mercury beads and look for mercury in any surface cracks or in hard-to reach areas of the floor using flashlights.
- **A syringe (without a needle)** shall be used to suck the beads of mercury. Collected mercury should be placed into an unbreakable plastic container/glass bottle with an airtight lid half filled with water. After removing larger beads, use sticky tape to collect smaller hard-to-see beads.
- **Place all the materials (used & collected)** from the spill area into a yellow plastic bag or container with lid and seal properly and label it as mercury containing waste.
- **Sprinkle sulphur or zinc powder over the area**. Either powder will quickly bind any remaining mercury. Use the cardboard and then dampened paper towels to pick up the powder and bound mercury. Place all towels and cardboard in a yellow plastic bag and seal all the bags that were used and store in a designated area.
- All the mercury spill surfaces should be **decontaminated with 10 % sodium thiosulfate** solution. Keep a window open to ventilate after the clean-up.

Waste collected from chemical spills has to be categorized as yellow-e waste, which shall be collected in separate yellow bag and handed over to operator of CBWTF or Hazardous Waste TSDF.

Figure 27: Spill management guidelines for healthcare workers

Role of nurses in handling BMW[351]

- Adhere to BMW rule 2016 and any special guidelines released for the management of biomedical waste.
- Ensure display of bio hazard symbol and labels, and the types of waste to be put in as per BMW rules.
- Do regular check and supervise.
- Use Personal Protective equipment while handling BMW.
- Emphasise the importance of hand hygiene and refrain from touching face, mouth, nose and eyes.
- Maintain a separate BMW record/ register.

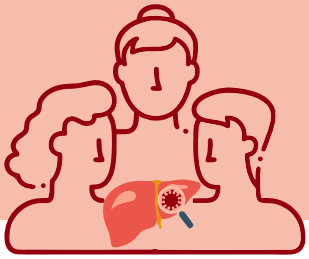
Safety of staff handling BMW[351]

As per the BMWM rules 2016, it is the responsibility of the in charge of the healthcare facility to ensure the occupational safety of the healthcare workers and other staff involved in handling of Bio medical waste in the facility.

Occupational safety of the staff has to be ensured in following methods:

- Providing adequate and appropriate Personal Protective Equipment (PPE) to the staff handling Bio Medical Waste. Use of PPE must be checked and encouraged at all times.
- Annual health check-up of all the employees must be ensured.
- Staff handling BMW must be immunized at least against the hepatitis B and tetanus.
- Ensuring remedial steps during occurrence of an accident which can lead to any harm to the employee.

OUTBREAK & PREVENTION



Key Concepts

- The official definition of the word outbreak from the World Health Organization (WHO) is:[213,214]
- The occurrence of cases of disease in excess of what would normally be expected in a defined community, geographical area or season. It may last for a few days or weeks, or for several years. A single case of a communicable disease long absent from a population or caused by an agent (e.g. bacterium or virus) not previously recognised in that community or area, or the emergence of a previously unknown disease, may also constitute an outbreak and should be reported. (WHO, 2013)
- In healthcare settings, the general definition of an outbreak is 'an incident in which two or more people experiencing a similar illness are linked in time or place' (HPA, 2012). Nursing or medical staff may be the first to spot signs of illness or infections amongst their patients, such as rashes, chest infections, diarrhoea and/or vomiting, and signs of post-operative surgical site infection. These can all be an early indication of an impending outbreak, and if the Infection Prevention and Control Team (IP&CT) are alerted swiftly enough, control measures can be implemented more or less immediately and outbreak investigations initiated, and a full-blown outbreak may be avoided. Laboratory-based surveillance of microbiology results or notifications of infectious diseases may also indicate an outbreak.
- Outbreaks should be suspected when healthcare-associated infections, recovery of specific pathogens, or other adverse events occur above the background rate or when an unusual microbe or adverse event is recognized.[213,214]
- Outbreaks in healthcare settings may be due to a variety of factors, including lapses in infection prevention or clinical practices, contaminated or defective products or devices, and colonized or infected healthcare personnel.
- Outbreaks in healthcare are often multifactorial.
- Epidemiological investigations of a possible outbreak must be conducted in a standardized way that assesses the possible contributing factors.
- Ending an outbreak involves modifying one or more of the contributing factors.
- The goals of an outbreak investigation are to identify contributing factors to control the outbreak and prevent similar outbreaks in the future.

Outbreak investigation

- Recognition of a 'Potential Outbreak'
- Epidemics or outbreaks are defined as an increase over the expected occurrence of an event.[213,214] Given that definition, it is important to note that a single case of an unusual disease may constitute an outbreak. In some instances, small outbreaks are referred to as "clusters," but both outbreaks and clusters require prompt investigation. The term "pseudo-outbreak" is generally applied to situations in which there is a rise in test results (e.g., positive microbiology cultures) without actual clinical disease.
- Surveillance for HAIs and adverse events can be a great aid in the recognition of outbreaks in healthcare settings because it provides both a baseline rate and ongoing monitoring. However, because outbreaks often occur in areas that are not under surveillance, most healthcare-associated outbreaks are recognized by observant HCP and infection preventionists.
- Although local and state health department requirements may differ, most require reporting of possible

healthcare-associated outbreaks as soon as they are suspected. Public health officials may also be able to assist in arranging or providing epidemiological and/or laboratory support. When a contaminated or defective product (including blood and human tissues), device, or medication is suspected as the cause of an outbreak, it should be notified.

Conducting an outbreak investigation

Although outbreaks are generally divided into steps for the purposes of teaching and explanation, it is important to remember that outbreaks generally do not unfold in a linear or orderly manner. Thus, it is possible that not all of the steps described in the following discussion will be applicable in all settings and it is possible, if not likely, that many steps might have to occur simultaneously and be repeated multiple times in the course of the investigation. In general, outbreak investigations can be divided into two major sections, the initial investigation and the follow-up investigation, each with multiple components.

Primary prevention

- Advocate and raise awareness of all types of viral hepatitis infections to reduce transmission in the community.
- Ensure vaccines are available for the prevention of HBV infections through the health system.
- Ensure Implementation of blood safety strategies, including blood supplies based on voluntary non-remunerated blood donations, effective public education on blood donation, donor selection, and screening (Quality-assured screening of all donated blood and blood components used for transfusion can prevent transmission of HBV and HCV).
- Implement necessary infection control precautions in health care and community settings to prevent transmission of viral hepatitis as well as many other diseases.
- Ensure safe injection practices and safer sex practices, including minimizing the number of partners and using barrier protective measures (condoms), to protect against HBV and HCV transmission.
- Introduce harm reduction practices for injecting drug users prevent HBV and HCV transmission such as needle exchange program.
- Strictly follow the occupational safety measures prevent transmission of viral hepatitis to health care workers.
- Supervise and ensure safe food handling, water and sanitation facilities to protect against HAV and HEV infections.

Secondary and tertiary prevention

- Early diagnosis provides the best opportunity for effective medical support and prevention of further spread. It also allows the infected persons to take steps to prevent transmission of the disease to others. Early diagnosis of those with chronic infection also allows people to take precautions to protect the liver from additional harm, specifically by abstaining from alcohol and tobacco consumption and avoiding certain drugs that are known to be toxic to the liver.
- Both the introduction of confirmatory testing and the notification and counselling of blood donors who have reactive results detected during screening of donated blood provide unique opportunities for early diagnosis and medical support to asymptomatic individuals who come to donate blood.
- Antiviral agents against HBV and HCV exist. However, drugs active against HBV or HCV are not widely accessible.
- Although HCV can be treated, access to treatment remains an issue in many countries. Therapeutic advances and intense research have led to the development of many new oral antiviral drugs for HCV infection. A number of HCV-specific oral drugs have been recently registered.

Health education and behavioural change

- Behaviour is the way in which a person behaves and responds to a particular situation or living environment. This is determined by several factors, among them pre-emptive perception of the situation and the sense of experience are much influential. If we wanted to make aware of viral hepatitis and the mode of spread of the diseases; we have to spread the knowledge of preventive measures through simple and culturally acceptable mode or media.
- This can be made through child hood or community education or dramas, songs or posters and media programs and announcements from respectable sources like community leaders.
- Once the knowledge is repeatedly spread through appropriate medias among the community it will process into attitude change in the community.
- If the environment is conducive for practising the knowledge it would make a change in their practice and behaviour. (E.g. outbreaks of diseases and adequate availability of clean water supply and sanitation facilities, adequate syringe needle and condom supply might improve appropriate personal protective habits).
- Children, women and sensible community members will follow the practice first, and ultimately majority will adopt the healthy habits .
- To encourage the community on water sanitation, safe sex and universal precaution of patient care; we have selected some very important messages regarding the above primary preventive steps and formulate them into attractive messages/posters/songs/dramas and publish among right people at right time.
- Right message through right media at right place among right people at right time will make a reasonable behavioural change.

ASSESSMENT SCORES

Introduction

- Assessment scales and scores normally used in critical care patients are to assess the prognosis and severity of the illness. It is a mathematical analysis of multiple parameters like, laboratory reports, physiological condition, and psychological response of the patients.
- The scales/score are used for assessing prognosis, pain status, level of organ function, required strength of treatment, modification of treatment, and the necessity of liver transplantation, and mortality etc., in critically ill patients.

Various tools and scores

The various types of tools and scores used in critical areas are explained below:

- **Pain scale**[215,216]
  - A pain scale measures the patient's pain intensity. Self-report is considered primary and should be obtained if possible. Pain measurements help determine the severity, type, duration of the pain, and are used to make an accurate diagnosis, determine a treatment plan, and evaluate the effectiveness of treatment. The pain is considered as the 5th vital signs.
  - Types of pain scales -
    - Wong- backer/facial grimace scale (children)
    - Numerical pain scale
    - Verbal descriptor scale
    - Activity tolerance scale

UNIVERSAL PAIN ASSESSMENT TOOL

This pain assessment tool is intended to help patient care providers assess pain according to individual patient need. Explain and use 0-10 Scale for patient self-assessment. Use the faces or behavioral observations to interpret expressed pain when patient cannot communicate his/her pain intensity.

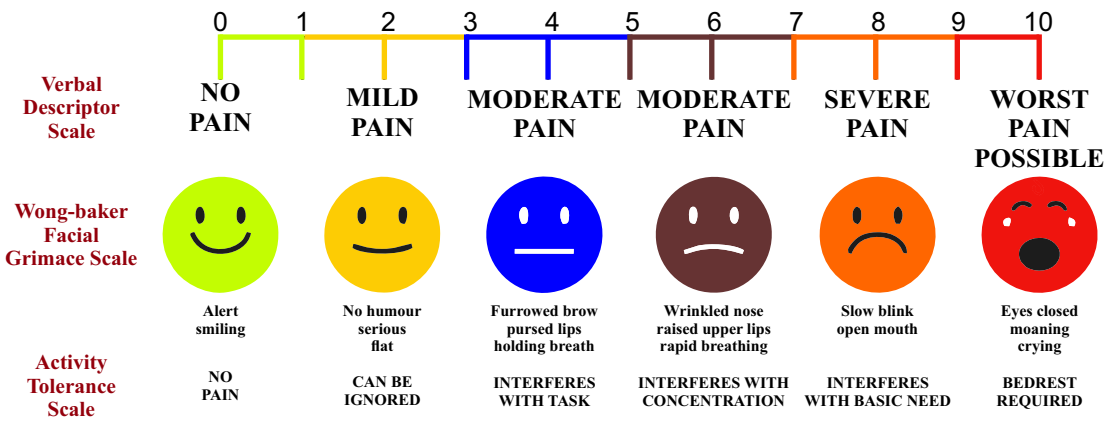


Figure 28: Universal pain assessment tool

- **Glasgow coma scale**[217]
  - The Glasgow Coma Scale (GCS) is a neurological scale which aims to give a reliable and objective way of recording the conscious state of a person for initial as well as subsequent assessment. A patient is assessed against the criteria of the scale, and the resulting points give a score between 3-15
  - A score of 3 indicates deep unconsciousness.
  - Maximum score is 15 indicates best prognosis.
  - Less than 8 is considered poor prognosis

Table 18: Glassgow coma scale

Behavior	Score	Response
Eye opening response	**4**	Spontaneous
	3	Speech
	2	Pain
	1	Nil
Verbal response	**5**	Oriented
	4	Confused
	3	In appropriate
	2	In comprehensible
	1	No power
Motor response	**6**	Obeys
	5	Localized
	4	Withdrawal
	3	Abnormal flexion
	2	Extension
	1	None
Total Score	**15**	*Best response*
	8 or less	*Comatose client*
	3	*Totally unresponsive*

- Limitations in GCS
  - Tracheal intubation and severe facial/eye swelling or damage make it impossible to test the verbal and eye responses.
  - Psychological issue
  - Sedation
  - Paralysis
  - Intubation
  - Neurological issues

- **Fibro scan**

  Transient elastography (Fibro scan) is a new, non-invasive, rapid, and reproducible method allowing evaluation of liver fibrosis by measurement of liver stiffness. The elasticity is directly correlated with the

degree of hepatic fibrosis. Fibro scan result ranges from 2.5 kPa to 75 kPa.[227]

- **MELD/PELD Score218**
  - The MELD (Mayo End-stage Liver Disease), is a scoring system for assessing the severity of chronic liver disease and was subsequently found to be useful in determining prognosis and prioritizing for liver transplant. The original MELD score included renal function, bilirubin and INR, while the revised MELD (MELD-Na) also includes serum sodium level also.
  - It is calculated according to the following formula: MELD = 3.78×ln [serum bilirubin (mg/dL)] + 11.2×ln [INR] + 9.57×ln [serum creatinine (mg/dL)] + 6.43.
  - MELD– Na = MELD Na [0.025 MELD (140 Na)] +140
  - The MELD score ranges from 6 to 40 with higher values indicating more severe disease
  - Mortality reduction with MELD219
    - Fewer deaths on transplant list
    - Shorter time to transplant
    - Fewer removals from transplant waiting list
    - No changes in survival
  - Pediatric end-stage liver disease (PELD) is a disease severity scoring system for children under 12 years of age.220 It is calculated from the patient's albumin, bilirubin, and international normalized ratio (INR) together with the patient's age and degree of growth failure. This score is also used for prioritizing allocation of liver transplants.

- **Child-Pugh Score[211]**
  - Child–Pugh score is used to assess the prognosis of chronic liver disease, mainly cirrhosis. It is used to determine the prognosis, as well as the required strength of treatment and the necessity of liver transplantation.
  - In cases of cirrhosis, CTP is useful for doctors to know the likelihood of patient survival in the short- and medium-term so that interventions can be prioritized. CTP considers cirrhosis-related symptoms and certain lab test results. The following clinical variables are considered to calculate CTP score:

Table 19: Child-Turcotte-Pugh Score

Clinical parameters	Points		
	1	2	3
Encephalopathy213	None	Grade 1 or 2	Grade 3 or 4
Ascites214	Absent	Slight	Moderate
Bilirubin (mg/dL)	<2	2-3	>3
Albumin (g/dL)	>3.5	2.8-3.5	<2.8
Prothrombin time prolongation	<4 second	4-6 second	>6 second
or Prolonged INR	<1.7	1.7-2.3	2.3

Source

- **Encephalopathy Grading**[223]
  - None
  - Grade 1: Altered mood/confusion
  - Grade 2: Inappropriate behavior, impending stupor, somnolence
  - Grade 3: Markedly confused, stuporous but arousable
  - Grade 4: Comatose/unresponsive
- **Classification of CTP**[222]: Entering these into an equation or calculator produces a score that has a relatively high predictive value. child score has been classified into-
  - 5 to 6 points Child class A
  - 7 to 9 points: Child class B
  - 10 to 15 points: Child class C
- The more severe the symptoms and the greater the abnormality in lab test results, the greater the CTP score.

- **SOFA score**[225]
  - Sequential organ failure assessment score (SOFA score), is used to assess a person's status during the stay in an intensive care unit (ICU) to determine the extent of a person's organ function or rate of failure. The score is based on six different scores.
  - Each representing an organ system. Each organ system is assigned a point value from 0 (normal) to 4 (high degree of dysfunction/failure) The worst physiological variables were collected serially every 24 hours of a patient's ICU admission. ... The SOFA score ranges from 0 to 24.
  - Components of SOFA
    - Neurological - GCS
    - Cardiovascular - MAP/vasopresser use
    - Renal - Serum creatinine/urine output
    - Respiratory - PaO_2/FiO_2 ratio
    - Hematological - Platelet count
    - Hepatic - Serum bilirubin

Table 20: SOFA calculator

Points	0	1	2	3	4
Respiratory PaO_2/FiO_2, mmHg	>400	<400	<300	<200	<100
Coagulation Platelets	>150	<150	<100	<50	<20
Serum bilirubin mg/dl	<1.2	1.2-1.9	2.0-5.9	6.0-11.9	12
Cardiovascular hypotension	No hypo	MAP<70 s	Hypotension dopa>5	Dopa>15 Norepi<0.1	Dopa>15 Norepi>0.1
Central nervous system Glasgow coma score	15	13-14	10-12	6-9	<6
Renal creatnine mg/dl or urine output	1-2	1.2-1.9	2.0-3.4	3.5-49	>5

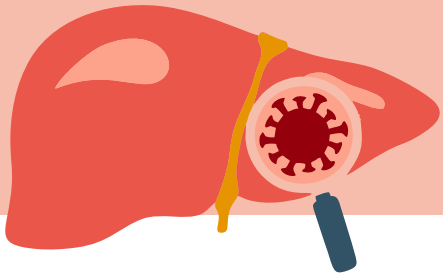
*dop - dopamine; hypo - hypotesnion; MAP - Mean arterial pressure; Norepi - Norepinephrine

- **West Haven Criteria**[226]
  - It is the assessment tool for encephalopathy.
  - Hepatic encephalopathy (HE) is an altered level of consciousness as a result of liver failure. Onset may be gradual or sudden. Other symptoms may include movement problems, changes in mood, or changes in personality. In the advanced stages it can result in a coma
  - Hepatic encephalopathy is a syndrome observed in some patients with cirrhosis. It is defined as a spectrum of neuropsychiatric abnormalities in patients with liver dysfunction, when other known brain disease has been excluded. Signs and symptoms may be debilitating, and they can begin mildly and gradually, or occur suddenly and severely. They may include personality or mood changes, intellectual impairment, abnormal movements, a depressed level of consciousness, and other symptoms. There are several theories regarding the exact cause, but development of the condition is probably at least partially due to the effect of substances that are toxic to nerve tissue (neuro-toxic), which are typically present with liver damage and/or liver disease. Treatment depends upon the severity of mental status changes and upon the certainty of the diagnosis.

Table 21: West Haven Criteria

Stage	Conciousness	Intellect and behaviour	Neurological findings
0	Normal	Normal	Normal
1	Mild lack of awareness	Shortened attention span	Mild flaps/tremor
2	lethargic	Disoriented, inappropriate behavior	Slurred speech
3	Somnolent but arousable	Gross disoriented	Muscular rigidity
4	Coma	Coma	Comatose, unarousable in pain

COMPLICATIONS



Burden of liver disease

- Liver disease falls into two main categories: hepatocellular, such as viral hepatitis or alcohol- or drug-related liver disease, and cholestatic, or obstructive disease, such as that caused by gallstones, malignancy, or primary biliary cirrhosis.
- Liver disease accounts for approximately 2 million deaths per year worldwide, 1 million due to complications of cirrhosis and 1 million due to viral hepatitis and hepatocellular carcinoma.[228]
- Cirrhosis is the end result of many chronic liver diseases, such as viral hepatitis, alcoholic liver disease, autoimmune hepatitis, and hemochromatosis. It occurs when repeated hepatocyte damage results in the formation of fibrous tissue and the development of regenerative nodules. Globally, cirrhosis currently causes 1.16 million deaths, and liver cancer 788,000 deaths, making them the 11th and 16th most common causes of death, respectively, each year (Table 1).[229] Combined, they account for 3.5% of all deaths worldwide.[229] Cirrhosis is within the top 20 causes of disability-adjusted life years and years of life lost, accounting for 1.6% and 2.1% of the worldwide burden.[230,231]

- **Classification of cirrhosis**: These clinical types of cirrhosis reflect its diverse aetiology:
  - **Laennec's cirrhosis**: The most common type, this occurs in 30% to 50% of cirrhotic patients, up to 90% of whom have a history of alcoholism. The most common, Laennec's cirrhosis, occurs in 30% to 50% of cirrhotic patients.
  - **Biliary cirrhosis**: Biliary cirrhosis results in injury or prolonged obstruction. Biliary cirrhosis occurs in 15% to 20% of patients.
  - **Post necrotic cirrhosis**: Post necrotic cirrhosis stems from various types of hepatitis. Post necrotic cirrhosis occurs in 10% to 30% of patients.
  - **Pigment cirrhosis**: Pigment cirrhosis may result from disorders such as hemochromatosis. Pigment cirrhosis occurs in 5% to 10% of patients.
  - **Cardiac cirrhosis**: Cardiac cirrhosis refers to cirrhosis caused by right-sided heart failure.
  - **Idiopathic cirrhosis**: Idiopathic cirrhosis has no known cause. Idiopathic cirrhosis occurs in about 10% of patients.

- **Causes of cirrhosis**:
  - **Excessive alcohol consumption**: Too much alcohol intake is the most common cause of cirrhosis as liver damage is associated with chronic alcohol consumption.
  - **Injury**: Injury or prolonged obstruction causes biliary cirrhosis.
  - **Hepatitis**: The different types of hepatitis can cause post necrotic cirrhosis.
  - **Other diseases**: Diseases such as hemochromatosis causes pigment cirrhosis.
  - **Right-sided heart failure**: Cardiac cirrhosis, a rare kind of cirrhosis, is caused by right-sided heart failure.

- **Clinical manifestations**

Clinical manifestations in all types of cirrhosis remains similar, regardless of the cause.

  - **GI system**: Early indicators usually involve gastrointestinal signs and symptoms such as anorexia,

indigestion, nausea, vomiting constipation, or diarrhoea.

- **Respiratory system**: Respiratory symptoms occur late as a result of hepatic insufficiency and portal hypertension, such as pleural effusion and limited thoracic expansion due to abdominal ascites, interfering with efficient gas exchange leading to hypoxia.
- **Central nervous system**: Signs of hepatic encephalopathy also occur as a late sign, and these are lethargy, mental changes, slurred speech, asterixis (flapping tremor), peripheral neuritis, paranoia, hallucinations, extreme obtundation, and ultimately, coma.
- **Hematologic**: The patient experiences bleeding tendencies and anaemia.
- **Endocrine**: The male patient experiences testicular atrophies, while the female patient may have menstrual irregularities, and gynecomastia and loss of chest and axillary hair.
- **Skin**: There is severe pruritus, extreme dryness, poor tissue turgor, abnormal pigmentation, spider angiomas, palmar erythema, and possibly jaundice.
- **Hepatic**: Cirrhosis causes jaundice, ascites, hepatomegaly, oedema of the legs, hepatic encephalopathy, and hepatic renal syndrome.

Compensated cirrhosis and its management

- Cirrhosis can remain compensated for years before development of decompensating events like jaundice, ascites, encephalopathy and/or variceal haemorrhage. The median survival of patients with compensated cirrhosis is much longer than in patients with evidence of decompensation and is about 9 years.[264]
- The main goals of management of compensated cirrhosis are
  - treatment of underlying aetiology
  - early recognition and treatment of complications; and
  - preventing superimposed insults.
- Specific therapy directed against underlying aetiology has shown to improve survival, long-term outcomes and regression of fibrosis.[265-269]
- Evidence favouring regression of cirrhosis has now been documented in entire spectrum of chronic liver diseases including viral hepatitis, autoimmune hepatitis, primary biliary cirrhosis, biliary obstruction, NASH and hemochromatosis.[270-275]
- The last few years have seen significant improvement in cure rates for chronic liver disease especially viral hepatitis though the use of more effective anti-viral therapy for hepatitis B virus, Hepatitis C.[276,277] More importantly regression of fibrosis associated with ant-viral therapy is associated with improved liver function.[278]

Chronic liver diseases

- **Alcohol-associated liver disease (AALD)**, is a major cause of liver disease worldwide.[232] Further, alcohol use often exacerbates liver injury, as it coexists with other factors (e.g. viral hepatitis). According to the World Health Organization, about 2 billion people consume alcohol worldwide and upwards of 75 million are diagnosed with alcohol-associated liver disease.[233]

- **NAFLD** encompasses 2 distinct conditions
  - NAFL which includes steatosis or steatosis with mild lobular inflammation and
  - Non-alcoholic steatohepatitis (NASH) that includes varying degrees of fibrosis, cirrhosis and HCC[233].

  There has been a palpable increase in NAFLD across the world. The true incidence and prevalence globally are hard to characterise given variations in assessment and definitions. Analogous to alcohol use and AALD, approximately 2 billion adults are obese or overweight and over 400 million have diabetes; both of which are risk factors for non-alcoholic fatty liver disease and hepatocellular carcinoma.[234-238]

- Although **viral hepatitis** affects individuals in all geographic regions, those from low and middle-income countries are disproportionately affected.[239] In 2010, deaths from viral hepatitis accounted for 0.3 million deaths per year, an increase of 46% from1990.7 During 1990–2013, the absolute number of deaths attributable to viral hepatitis-related deaths (from acute infection, cirrhosis and cancer) increased by 63% and DALY by 34%.[240] Viral hepatitis increased from the 10th leading cause (1990) to the 7th leading cause of mortality in 2013.4, 5In 2015, viral hepatitis-related disease led to 1.34 million deaths[241],similar to the number caused by tuberculosis (1.37 million) and higher than the number caused by HIV (1.06 million deaths) or malaria (0.44 million deaths).[239] Hepatitis B virus (66%) and hepatitis C virus (30%) accounted for 96% of mortality and were predominantly a burden in Asia and sub-Saharan Africa,[241] whereas hepatitis A virus and hepatitis E virus accounted for 0.8% (11,000 deaths) and 3.3%(44,000) deaths, respectively.[239] Cirrhosis, and viral hepatitis, specifically B and C are independent risk factors for the development of HCC and cholangiocarcinoma (CCA).

- **Autoimmune hepatitis (AIH)** is a rare disease occurring in all races, ethnic groups and ages. Females are affected more commonly than males by a ratio of 4:1. Incidence studies are few and are mainly reported from Europe where the dis-ease is more common and increasing. AIH is rare in Asia where the disease is detected at an advanced stage with higher mortality[242]. Two subtypes (AIH-1 and AIH-2) are recognised with characteristic serologic and phenotypic char-acteristics.[243] AIH type 1 (AIH-1) is defined by the presence of antinuclear antibody and/or anti-smooth muscle antibody, whereas AIH type 2(AIH-2) is characterised by the presence of anti-liver kidney microsomal type 1 antibody or anti-liver cytosol type 1 antibody. Further, AIH-1commonly affects adolescents and young adults whereas AIH-2 affects children and adolescents. At presentation the disease is mild to moderate in AIH-1 and moderate to severe in AIH-2.[244]

- **Wilson's disease** is a rare autosomal recessive genetic disorder characterised by excess accumulation of copper in various body tissues, such as the liver, brain, and eyes. Wilson's disease is caused by mutations of theATP7Bgene, which plays an important role in the movement of copper from the hepatocytes to biliary canaliculi for eventual excretion. More than 600 different mutations of the ATP7Bgene have been identified with-out clear genotype-phenotype correlates, although the disease appears at a younger age with increased severity in Egyptians and Indians.[245] Wilson's disease is estimated to occur in approximately one in 30,000–40,000 people worldwide, with approximately 1 in 90 people carrying the disease mutation gene,[246] however, the burden may be higher based on recent data.

- **Drug induced liver injury** is a common reason to withdraw drugs during development, preclinical studies and following marketing. From 1953 to 2013, drug-induced liver injury (DILI) was a leading cause of withdrawal (18%) followed by immune reactions (17%) and cardiotoxicity (14%).[247] The estimated incidence of DILI varies between 1 in10,000 and 1 in 1,000,000 patients. Incidence is dependent on the definition used, frequency of testing, population characteristics, diseases prevalence, type of drugs ingested, sociocultural factors and reporting mechanisms. The reported incidence of DILI in 2 prospective population studies varied between 13.9 per 100,000 and 19 cases per 100,000 individuals.[248,249] These rates were 6 to 8 times higher than previous estimates; yet the real magnitude may be even higher as adverse drug reaction reporting is heavily dependent on spontaneous reporting. Although over a thousand drugs are speculated to cause liver injury, only 353 drugs have convincingly been linked to liver injury.[250] Many of these drugs were approved before 1999. Antimicrobials (27%) were the leading cause followed by central nervous system agents including anti-epileptic drugs (17%), cardiovascular drugs (15%) and anti-neoplastic agents (14%)250. The advent of drugs that undergo minimal or no liver metabolism will likely result in a decreased incidence of DILI.[251] The type of drugs producing liver injury has varied over time. Epidemiologic studies before the turn of the century found chlorpromazine, isoniazid, amoxicillin and

cimetidine as the top 4 drugs that cause DILI.[252] Presently, antimicrobial agents continue to be the leading cause of idiosyncratic DILI worldwide, with amoxicillin/clavulanic acid-induced DILI in the West253 and combination anti-tuberculosis DILI in the East.[254] DILI due to amoxicillin/clavulanate occurs in 1 in 2,350 individuals.[249]It is unsurprising that DILI related to anti-tuberculosis treatments occurs in Eastern countries, considering that India and Nigeria have the highest burden of tuberculosis in the world.[255] Herbal and alternative medicines are the most common cause of DILI in China and South Korea, where a large proportion of the population are exposed to these agents for various dis-eases.[256,257] Herbal and dietary supplements are an increasingly frequent cause of DILI globally.[247] The herbal and dietary supplements that contribute to DILI in the western countries are mainly those used for bodybuilding (in men) and weight loss (in women), whereas in Asia it is from drugs used for a variety of diseases.[258] Weight loss agents produce hepatocellular injury that can progress to liver failure, requiring liver transplantation, while body building agents produce mixed or cholestatic injury.[259,260] Despite receiving a higher dose of drugs based on body weight, children are less prone to develop DILI and constitute less than 10% of all cases in most registries.[246,249,261,263] Older age is a risk factor for DILI for unclear reasons; polypharmacy leading to drug-drug interactions, together with multi system involvement may be contributing factors.[246,249,261,263] Women are disproportionately more at risk of DILI than men.[246,249,261,263] Severe DILI requiring hospitalisation and leading to liver failure and death is more common in women across all populations.

Complications of Liver disease

- **Liver failure**, also known as end-stage liver disease, can be caused by an acute injury (also called fulminant liver failure) or result from a chronic disease. Fulminant liver failure might follow an infection (hepatitis) or an acetaminophen overdose, or it could result from hepatic vein obstruction (Budd-Chiari syndrome).
- **Fulminant liver failure** is characterized by coagulopathy and encephalopathy that develop within 8 weeks of the injury or start of an illness. Prompt treatment based on the underlying problem is key.
- Symptoms of liver failure occur later in patients with chronic liver disease. Alcohol abuse and viral hepatitis are among the diseases that can lead to cirrhosis, a nonuniform scarring and fibrosis of the liver that can lead to liver failure.
- Some patients with well-compensated chronic liver disease may experience an acute decline in liver function after an infection or gastrointestinal (GI) bleeding. This is referred to as acute-on-chronic liver failure. These patients may return to baseline liver function with supportive treatment and not need an emergency liver transplant.
- Complications that occur in patients with liver disease are seen most often in those with chronic liver damage. However, some complications, such as hepatic encephalopathy and clotting disorders, can also occur in acute liver failure. The management of the following complications remains the same regardless of the cause of liver disease.

Coagulopathy and bleeding diathesis

- Because the liver is the principal site for the synthesis of coagulation factors, clotting abnormalities are likely to develop in patients with liver disease. Various factors contribute to coagulation abnormalities in patients with advanced liver disease. Cirrhotic patients are at risk of bleeding as well as venous thromboembolism. Disease management must be tailored based on the individual patient's presentation. Commonly used indicators of coagulopathy, like INR, cannot precisely predict risk of bleeding in patients with cirrhosis.[279] As a result, there have been attempts to develop a liver specific INR, the "INR liver" in patients with cirrhosis.[279,280]
- Vitamin K deficiency is commonly seen in cases of decompensated liver cirrhosis. Vitamin K 10 mg injections administered for three days are considered adequate to correct the vitamin K deficiency and

should be given to patients with decompensated liver cirrhosis.[281]

- In cases with acute bleeding, transfusion of platelets and fresh frozen plasma can be considered for patients with thrombocytopenia and coagulopathy.[282]
- An oral, water soluble preparation of vitamin K is an alternative, but it may not be as effective for patients with impaired liver function since it requires activation by the liver. Patients with severe liver disease may have a metabolic inability to use the vitamin K in the formation of clotting factors and will therefore not respond to treatment.
- Cirrhotic patients undergoing surgeries should have platelet levels maintained at a minimum of 50000/cc3 for moderate-risk procedures like liver biopsies, and close to 100000/cc3 before high risk procedures.[283,284]
- Recent evidence suggests that daily low dose LMWH can prevent PVT inpatients with cirrhosis without significant increase in risk of bleeding. In addition, prophylactic use of LMWH decreased the incidence of hepatic decompensation.[285-287]
- Thrombopoietin-mimetic agents, in particular, eltrombopag and romiplostim, have been shown to increase platelet count without eliciting any immunogenicity.[288-290]
- Romiplostin is a peptibody composed of four TPO mimetic peptides attached by glycine bridges to the heavy chain portion of immunoglobulin G. It acts by dimerizing the TPO receptor via its paired peptides, which stimulates platelet production.[291] It is given by weekly subcutaneous injections. Various clinical trials in patients with chronic immune thrombocytopenic purpura have shown romiplostin to cause a dose dependent increase in platelet count, resulting in lower rates of treatment failure, decreased the need for splenectomy and improved quality of life.[292-294] Lee et al. described romiplostim use in a case of resistant ITP after DAA therapy.295 A study by Moussa et al. in 35 patients with chronic liver disease and thrombocytopenia secondary to HCV infection showed more than three-fold increase in mean platelet count from the baseline after 3 weeks of therapy and the mean platelet count remained 1.5 times above the baseline even after 2 months of stopping the drug.296 Similarly, Voican et al. reported two cases where romiplostin was used to control severe thrombocytopenia; this allowed anti-HCV treatment with pegylated-IFN and ribavirin to be completed successfully without any dose reduction or discontinuation.[297]
- Eltrombopag, an orally active TPO agonist, interacts with the trans-membrane domain of the thrombopoietin receptor, activating JAK2/STAT signalling pathways and increasing proliferation and differentiation of human bone marrow progenitor cells into megakaryocytes298. Preclinical studies have shown the binding site on the receptor and the signal transduction mechanism to be different for eltrombopag as compared to thrombopoietin, causing the two to have an additive effect on platelet production.[299] Eltrombopag has been found to be safe and effective in the management of HCV-related thrombocytopenia.[300,301]

Hepatic Encephalopathy

Hepatic (portosystemic) encephalopathy represents a potentially reversible decrease in neuropsychiatric function caused by acute and chronic liver disease, occurring predominantly in patients with portal hypertension. The onset often is insidious and is characterized by subtle and sometimes intermittent changes in memory, personality, concentration, and reaction times. Hepatic encephalopathy is a diagnosis of exclusion; therefore, all other aetiologies of altered mental status must be effectively ruled out.

- Treatment options for hepatic encephalopathy are currently limited. Treatment goals for hepatic encephalopathy include provision of supportive care, identification and removal of precipitating factors (e.g., limiting dietary protein intake), reduction in the nitrogenous load from the gut, and optimization of long-term therapy[302], and administration of various ammonia lowering therapies.[303]
- Increases in the ratio of plasma aromatic amino acids to branched-chain amino acids as a consequence of

hepatic insufficiency also may contribute to encephalopathy.

- Evidence suggested that mental recovery was consistently more rapid in patients whose treatment included a branched-chain amino acid infusion; three studies found lower mortality rates in patients who received this treatment, and two others suggested that the treatment increased mortality.[304]
- Laxative therapy is used to increase the throughput of bowel contents. The drug of choice is lactulose. It is broken down by bacteria in the gut to lactic acid, resulting in acidification of the gut, which in turn leads to a reduction in bacterial conversion of protein to ammonia. The usual adult starting dose of lactulose is 20–30ml, increasing as tolerated. Generally, the aim will be for patients to have two to three loose stool motions a day; the dose is reduced in the event of diarrhoea, abdominal cramping or bloating. For patients unable to take medicines orally, or for whom rapid bowl evacuation is needed, phosphate enemas can be administered.
- Antibiotics have been used in the past to kill bacteria present in the bowel, thereby reducing the amount of ammonia generated. Neomycin has been reported to be as effective as lactulose for the management of HE, and similar efficacy has been reported with vancomycin and metronidazole. However, the adverse effects frequently associated with these antimicrobials (eg, ototoxicity with neomycin) mean they are no longer recommended as treatment options for HE.[303]
- Rifaximin is a novel antimicrobial agent with a broad spectrum of activity. High rifaximin concentrations are achieved in the faeces and the drug has low systemic absorption (so has a better side effect profile than other antibiotics traditionally prescribed for HE).
- Other treatment options include a preparation of L-ornithine L-aspartate (LOLA), which forms part of the urea cycle — a metabolic pathway that removes ammonia by turning it into the neutral substance urea. However, the evidence for its use is limited.

Ascites

Ascites is defined as the pathologic accumulation of fluid in the peritoneal cavity. Approximately 85 percent of patients with ascites have cirrhosis, and the remaining 15 percent have a non-hepatic cause of fluid retention.[305,306]

- Initial management of uncomplicated ascites is with salt restriction and generally patients are restricted to 90mmol/day of sodium.
- In terms of pharmacological interventions, the mainstay of treatment has been with diuretics. Aldosterone is one of the hormones that acts to increase sodium retention; spironolactone is the drug of choice for the management of ascites since it blocks the aldosterone receptor in the distal tubule.
- Aldosterone antagonists are more effective than loop diuretics for managing ascites. Generally, oral spironolactone is started at a dose of 100mg/day for adults and increased every three to five days up to 400mg/day to achieve adequate natriuresis. There is a lag of three to five days between the beginning of spironolactone treatment and the onset of the natriuretic effect.[307]
- Spironolactone's side effects are mostly related to its antiandrogenic activity and include libido loss, impotence and gynaecomastia in men and menstrual irregularities in women. Hyperkalaemia is a side effect that often limits the use of spironolactone in the treatment of ascites.[307]
- A long-standing debate in the management of ascites is whether an aldosterone antagonist should be given alone or in combination with a loop diuretic (e.g., furosemide). Evidence suggests that a diuretic regimen based on combination of an aldosterone antagonist and furosemide is the most appropriate for patients with recurrent ascites but not for those with a first episode of ascites.[308] The latter patients should be treated initially with an aldosterone antagonist as monotherapy; for patients who do not respond to spironolactone, and those who develop hyperkalaemia, furosemide should be added in a step-wise approach from 40mg/day to a maximum adult dose of 160mg/day (in 40mg increments).
- To prevent diuretic-induced renal failure or hyponatraemia, diuretic doses should be adjusted to achieve a

rate of weight loss of 1.0kg/day or less for patients with both ascites and peripheral oedema and 0.5kg/day or less for patients with ascites alone.

- The goal of long-term therapy is to keep patients free of ascites with the minimum doses of diuretic, so once ascites has resolved the doses should be reduced.
- For patients with severe ascites a large volume paracentesis (needle drainage of fluid) is the treatment of choice. The removal of large volumes of ascitic fluid can cause post-paracentesis circulatory dysfunction (PPCD) — and associated electrolyte disturbances and renal impairment — due to the reduction in effective blood volume.
- The most effective method to prevent PPCD is with the administration of albumin. The British Society of Gastroenterology recommends that when more than 5L of fluid is removed by paracentesis, albumin should be administered in a volume proportional to the amount of ascitic fluid removed. The BSG recommends using 8g albumin per litre of ascitic fluid removed (approximately 100ml of human serum albumin 20% should be administered for every 3L drained).[307]

Hyponatremia

Hyponatremia is commonly seen in patients with cirrhosis but symptoms are uncommon unless the levels are < 110 mmol/L or there is a rapid decline in sodium levels.[309]

- Severe hyponatremia warrants fluid restriction. Although there is no data supporting specific threshold and level of restriction; a serum sodium level < 120 mmol/L is reasonable.
- The efficacy of vaptans (vasopressin receptor antagonist) in treating hyponatremia and fluid overload has been studied mainly in heart failure but also in cirrhosis.[310,311]
- These drugs have shown to correct mild hyponatremia and the intravenous agent conuvaptan is approved for the treatment of Euvolemic and hypervolemic hyponatremia in inpatient setting311. Tolvaptan orally has shown to correct serum sodium in patients who have pre-treatment levels < 130 mmol/L but discontinuation of drug leads to recurrence.[310-312]
- Rapid correction of hyponatremia can lead to central pontine myelinolysis and requires caution with their use.[313] More studies are needed to prove the safety, efficacy and cost effectiveness of these drugs in patients with less urgent need to correct hyponatremia (levels > 120 mmol/L, chronic, asymptomatic).

Bacterial infections

The world-wide prevalence of bacterial infection in hospitalized patients with cirrhosis ranges between 33% and 47%.[314,315] Infections are a leading cause of death in patients with cirrhosis and mortality has been reported as high as 19%.[316]

- Prevalence of infection is related to severity of liver disease and is more common in patients with Child C cirrhosis compared to Child A/ B cirrhosis.
- Other risk factors include previous infection, gastrointestinal bleeding and history of alcohol abuse.[317]
- Medical procedures that can trigger bacterial infection include placement of intravenous catheters and urinary catheters, endoscopic sclerotherapy, variceal ligation, TIPS and paracentesis.
- Spontaneous bacterial peritonitis (SBP) is the most common infection in cirrhosis and is described in detail below.[318]
- Urinary tract infections, pneumonia and bacteraemia are responsible for 20%, 15% and 12% respectively of the remaining infections in this patient population.[315]
- The factors that predisposes cirrhotic to infections are not well defined but following mechanism have been suggested
  - portal hypertension results in creation of Porto-systemic anastomosis, diverting blood that would normally go to the liver and thus impairing detoxification;
  - dysfunction of reticuloendothelial system;

  - impaired neutrophil phagocytosis; and
- bacterial translocation resulting from bacterial overgrowth and intestinal barrier dysfunction.[319,320]
- As expected bacteria of intestinal origin especially E. coli are the most commonly recognized pathogens.[321]
- In hospitalized patients especially, those receiving quinolones prophylaxis multiple drug resistant (MDR) gram positive cocci are being increasingly identified.[316]
- Commonly used diagnostic parameters like C-reactive protein and Systemic inflammatory Response (SIRS) criteria have limited value secondary to decreased number of baselines polymorphonuclear leucocytes, elevated heart rate at baseline, baseline hyperventilation and blunted elevation of body temperature.[322-324] This can delay diagnosis and worsen outcomes thus a high level of suspicion is warranted.
- Prompt and appropriate empirical antibiotic treatment should be instituted. When possible, cultures should be obtained prior to starting antibiotics and therapy should be adjusted according to results.
- A careful strategy of limiting prophylactic antibiotics to high-risk population and selection of antibiotics based on culture results can help reduce the incidence of MDR infections.

Spontaneous bacterial peritonitis

Spontaneous bacterial peritonitis is a frequent and serious complication in cirrhotic patients with ascites. Patients are often asymptomatic on presentation and have normal white cell counts and C-reactive protein levels. However, many patients present with symptoms such as fever, nausea, vomiting and mild confusion.[307] Patients may also have abdominal pain and worsening ascites.

- Diagnosis of SBP is based on diagnostic paracentesis, which involves extracting a sample of ascitic fluid to look at the types and number of cells. An ascitic neutrophil count of greater than 250/mm3 confirms the diagnosis of SBP.
- Initial management involves the use of empirical antibiotic therapy. Since the most common causative organisms of SBP are Gram-negative aerobic bacteria, such as Escherichia coli, the first-line antibiotic treatments are third-generation cephalosporins such as cefotaxime; alternatives include co-amoxiclav.
- Renal impairment develops in 30% of patients with SBP and this is closely associated with mortality.[307] The administration of albumin (1.5g/kg in the first six hours of SBP diagnosis followed by 1g/kg on day 3) reduces the risk of the patient developing hepatorenal syndrome (HRS) and improves survival. Therefore, it is recommended that all patients with SBP and signs of developing renal impairment should be given albumin.[307,308]
- We can use oral norfloxacin 400mg/day or oral ciprofloxacin 500mg/day as SBP prophylaxis. There are concerns around the long-term use of antibiotic prophylaxis and the emergence of Gram-negative bacteria resistant to quinolones. In addition, there is an increased likelihood of infection from Gram-positive bacteria in patients who have received long-term SBP prophylaxis. Therefore, it should be restricted to patients with the greatest risk of SBP, for example, those with: acute gastrointestinal haemorrhage; low protein content in ascitic fluid and no prior history of SBP; or a previous history of SBP.

Hepatorenal syndrome

Hepatorenal syndrome is defined as functional renal failure in cirrhotic patients in the absence of intrinsic renal disease.[20] It is characterized by sodium and water retention in patients with renal vasoconstriction, resulting in decreased renal blood flow, glomerular filtration rate, and urinary output, which contribute to azotaemia.[325]

- The pathogenesis of hepatorenal syndrome is not completely understood, but it is likely the result of an extreme underfilling of the arterial circulation secondary to arterial vasodilation in the splanchnic circulation.[326]
- Although hepatorenal syndrome can occur with most forms of severe hepatic disease, patients with primary biliary cirrhosis appear to be relatively protected.[327]

- There are two types of HRS:
  - Type 1 hepatorenal syndrome is defined as a rapid deterioration of renal function indicated by a two-fold increase of serum creatinine to values above 2.5 mg per dL (221 µmol per L), or a decrease of creatinine clearance to values below 20 mL per minute (0.33 mL per second). This form of hepatorenal syndrome usually is precipitated by spontaneous bacterial peritonitis and occurs in approximately 25 percent of patients with spontaneous bacterial peritonitis, even with the clearance of infection. The median survival duration of these patients is less than two weeks without treatment, and almost all patients die within 10 weeks after the onset of renal failure.[328]
  - Patients with type 2 hepatorenal syndrome exhibit moderately increased serum creatinine levels above 1.5 mg per dL (133 µmol per L) that remain stable over a longer period, and ascites that generally is resistant to diuretics. The median survival duration in these patients is three to six months.[328]
- If type 1 HRS develops, diuretic therapy should be stopped. Spironolactone should be avoided to prevent hyperkalaemia and excessive intravenous fluids should be avoided to prevent fluid overload.
- Haemodialysis often is used to control azotaemia in hepatorenal syndrome and to correct electrolyte imbalances. Nonsteroidal anti-inflammatory drugs and potentially nephrotoxic medications should be avoided.
- Terlipressin, a synthetic analogue of vasopressin, should be given with albumin as the first-line treatment for type 1 HRS. It causes vasoconstriction of the gut circulation, which is thought to reverse some of the circulatory changes associated with HRS. The usual adult dose is 1mg IV every four to six hours. The aim of therapy is to improve renal function; if serum creatinine does not reduce by at least 25% after three days, the dose of terlipressin should be increased in steps up to a maximum of 2mg administered every four hours. For patients with partial or no response, treatment should be discontinued after 14 days.308 Ischemic cardiovascular disease is a contraindication to terlipressin therapy, and patients receiving terlipressin should be monitored for the development of cardiac arrhythmias.
- Octreotide is another potential therapy for HRS; however, there are few data to support its use. Nonpharmacological therapy can involve the insertion of a trans jugular intrahepatic portosystemic shunt (TIPS), and dialysis may be useful for patients who do not respond to vasoconstrictor therapy.
- Terlipressin has also been used with albumin for the management of type 2 HRS, although there are limited data on the impact of this treatment on clinical outcomes.[308]
- One controlled trial demonstrated a substantial improvement in renal plasma flow, glomerular filtration rate, and urinary sodium excretion in patients with type 1 hepatorenal syndrome after 20 days of treatment with oral midodrine and parenteral octreotide compared with the use of non-pressor dose dopamine.[302,305,329,331] These therapies also appear to improve survival rates and may serve as a bridge to liver transplantation.
- In the future, endothelin's, adenosine antagonists, long-acting vasoconstrictors, and anti-leukotriene, antagonists may play a role in preventing and treating hepatorenal syndrome.[332]
- Liver transplantation is the best treatment option for both type 1 and type 2 HRS. Both conditions should be treated before liver transplantation to improve posttransplant outcomes.

Hepatopulmonary syndrome

Hepatopulmonary syndrome (HPS) is defined as the triad of liver disease, pulmonary gas exchange abnormalities leading to arterial deoxygenation, and evidence of intrapulmonary vascular dilatations.[333]

- The hallmark of HPS is microvascular dilatation within the pulmonary arterial circulation. Microvascular dilatation impairs ventilation-perfusion matching and can produce anatomical and functional shunt physiology, leading to hypoxemia. The potent vasodilator nitric oxide was identified as a leading agent.
- Management include: Nitric oxide antagonists, selective pulmonary vasoconstrictor Long-term

supplementary oxygenation, orthotopic liver transplantation.[333]

Portal Hypertension and Variceal Bleeding

Regardless of the aetiology of cirrhosis, the development of portal hypertension is nearly universal and results from an increased resistance to portal flow secondary to scarring, narrowing, and compression of the hepatic sinusoids. When the portal pressure exceeds a certain threshold, it results in the development of varices. Approximately 50 percent of patients with cirrhosis develop varices, most commonly in the distal 2 to 5 cm of the oesophagus[334].

- Variceal haemorrhage is defined as bleeding from an oesophageal or gastric varix at the time of endoscopy, or the presence of large oesophageal varices with blood in the stomach and no other recognizable source of bleeding[331]. The rate of variceal bleeding is approximately 10 to 30 percent per year.[334]
- Patients with cirrhosis who present with evidence of upper gastrointestinal bleeding undergo an urgent upper endoscopic evaluation[331]. If no varices are observed, these patients should have repeat endoscopy at three-year intervals. If small varices are diagnosed, patients should have repeat surveillance at one-year intervals.
- Primary prophylaxis of variceal bleeding is aimed at reducing the portal pressure gradient, azygous blood flow, and variceal pressure.
- Portal hypertension is managed with non-selective beta-blockers (e.g., propranolol), which lower portal blood pressure by reducing splanchnic blood flow. Assuming there are no contraindications, the beta-blocker dose should be started low and titrated aiming for a 25% reduction in resting heart rate. If propranolol is contraindicated or not tolerated, isosorbide mononitrate at a dosage of 20 mg twice daily is the treatment of choice.[331]
- A TIPS procedure can be performed to control portal hypertension. This involves the creation of a shunt between the portal vein and the hepatic venous system, which helps to relieve the portal venous pressure.
- Variceal bleeds are a serious complication of portal hypertension and one of the leading causes of death in patients with liver cirrhosis. Patients who survive an initial episode have a one-year risk of rebleeding of around 80%.[335]
- The goals of treatment in acute variceal bleeding include hemodynamic resuscitation, treatment of active bleeding, and prevention of rebleeding. Band ligation is the standard for the control of variceal bleeding.[331] If banding is difficult because of continued variceal bleeding, endoscopic sclerotherapy with vasoconstrictors (e.g., octreotide) or a Sengstaken-Blakemore tube insertion (with adequate airway protection) may be used until TIPS or surgical treatment can be arranged.[331]
- TIPS has been shown to improve outcomes and is more cost-effective than endoscopic band ligation in reducing variceal bleeding, but it is associated with a higher risk of encephalopathy.[331] This treatment option should be performed in medical centers with particular expertise. TIPS has been shown to reduce portal hypertension and can be effective in converting patients with diuretic-resistant ascites to diuretic-sensitive ascites, as well as reducing gastrointestinal bleeding in patients with refractory variceal haemorrhage. Compared with large-volume paracentesis plus albumin, TIPS improve survival without liver transplantation in patients with refractory or recidivant ascites.[336]
- After the cessation of active variceal haemorrhage, the subsequent six weeks carry a high risk of recurrent haemorrhage. The greatest risk of rebleeding is within the first 48 to 72 hours, with more than 50 percent of episodes occurring within the first 10 days.[337]
- Risk factors for early rebleeding include age older than 60 years, renal failure, large varices, and severe initial bleeding (i.e., haemoglobin less than 8 g per dL [80 g per L] at admission).[337] A retrospective study showed that in-hospital mortality of patients with cirrhosis and variceal bleeding decreased from 43 percent in 1980 to 15 percent in 2000, in concurrence with an early and combined use of pharmacologic

and endoscopic therapies and short-term antibiotic prophylaxis.[338]

- Terlipressin is the drug of choice. It causes vasoconstriction of the varices to reduce bleeding. Octreotide is an alternative for this indication.
- Once the bleeding is under control, it is important also to consider the prevention of rebleeding using approaches such as variceal banding, TIPS and other strategies to reduce portal hypertension.

Pruritus

Pruritus can be a distressing symptom for patients with liver disease, especially those with cholestatic conditions. It is thought to be due to a build-up of bile salts, which are irritating to the skin in high concentrations.

- Aside from having a sedative effect, antihistamines are relatively ineffective for treating pruritus, and are not used as first-line treatment.
- Cholestyramine is an anion exchange resin that acts by binding to bile acids thereby preventing their reabsorption. The dose is titrated to give adequate relief without causing diarrhoea.
- Ursodeoxycholic acid is frequently used for pruritus associated with cholestatic liver disease and long-term use may improve symptoms.
- Other drugs used include rifampicin (which improves bile flow by inducing hepatic microsomal enzymes) and naloxone.
- Local application of coconut oil and aloe Vera gel has been found to be effective in relieving pruritus.

Malnutrition

Malnutrition is highly prevalent and associated with adverse outcomes in patients with cirrhosis. The presence of malnutrition is estimated to be as high as 80% in patients with cirrhosis and is related to the degree of liver disease.[339,340]

- Malnutrition is often underdiagnosed because liver disease can affect the results of many of the traditional techniques currently used to evaluate nutritional status.[339,340]
- Malnutrition is often associated with vitamin and mineral deficiency. Deficiencies in water-soluble vitamins are common in alcoholic cirrhosis, while deficiencies in fat-soluble vitamins are more common in cholestatic liver disease.
- In more advanced stages, both fat-soluble and water-soluble vitamin deficiencies occur. Additionally, zinc, selenium, and magnesium deficiencies are common.[340]
- To minimize malnutrition, patients should be encouraged to eat 4 to 7 small meals per day, including a late-evening snack. Oral nutritional supplements should be added when patients are not able to maintain adequate dietary intake.

Acute Liver Failure

Acute liver failure is an uncommon condition in which rapid deterioration of liver function results in coagulopathy, usually with an international normalized ratio of greater than 1.5, and alteration in the mental status (encephalopathy) of a previously healthy individual. Acute liver failure often affects young people and carries a very high mortality.

- Acute liver failure is a broad term that encompasses both fulminant hepatic failure and sub fulminant hepatic failure (or late-onset hepatic failure). Fulminant hepatic failure is generally used to describe the development of encephalopathy within 8 weeks of the onset of symptoms in a patient with a previously healthy liver. Sub fulminant hepatic failure is reserved for patients with liver disease for up to 26 weeks before the development of hepatic encephalopathy.
- Signs and symptoms of acute failure may include the following:

- Encephalopathy
- **Cerebral edema**: May lead to signs of increased intracranial pressure (ICP) (eg, papilledema, hypertension, bradycardia)
- **Jaundice**: Often present but not always
- **Ascites**: Potential for hepatic vein thrombosis with rapid development in the presence of fulminant hepatic failure accompanied by abdominal pain
- **Right upper quadrant tenderness**: Variably present
- **Change in liver span**: May be small due to hepatic necrosis or may be enlarged due to heart failure, viral hepatitis, or Budd-Chiari syndrome
- **Hematemesis or melena**: Due to upper gastrointestinal (GI) bleeding
- **Hypotension and tachycardia**: Due to reduced systemic vascular resistance

- There are important differences between FHF in children and FHF in adults. For example, in children with FHF, encephalopathy may be absent, late, or unrecognized.
- Some patients with previously unrecognized chronic liver disease decompensate and present with liver failure; although this is not technically FHF, discriminating such at the time of presentation may not be possible. Patients with Wilson disease, vertically acquired hepatitis B, or autoimmune hepatitis may be included in spite of the possibility of cirrhosis, if their disease has been manifested for less than 26 weeks.
- The most important step in the assessment of patients with acute liver failure is to identify the cause, as certain causes demand immediate and specific treatment.
- The most important aspect of treatment is to provide good intensive care support.[341-347] Careful attention should be paid to fluid management and hemodynamic.[341-347] Monitoring of metabolic parameters, surveillance for infection, maintenance of nutrition, and prompt recognition of gastrointestinal bleeding are crucial. Bed rest is recommended.[341-347]
- Patients with grade II encephalopathy should be transferred to the intensive care unit (ICU) for monitoring. As encephalopathy progresses, protection of the airway becomes increasingly important. Most patients with acute liver failure tend to develop some degree of circulatory dysfunction.[341-347]
- Monitoring of metabolic parameters, surveillance for infection, maintenance of nutrition, and prompt recognition of gastrointestinal bleeding are crucial. Coagulation parameters, complete blood cell count, and metabolic panel should be checked frequently. Serum aminotransferases and bilirubin are generally measured daily to follow the course of the disease.[341-347]
- Multiple medications may be necessary in patients with acute liver failure because of the wide variety of complications that may develop from fulminant hepatic failure. Decreased hepatic metabolism and the potential for hepatotoxicity become central issues. In patients with liver failure from Amanita phalloides or acetaminophen toxicity, antidotes that effectively bind or eliminate the relevant toxins are essential.[341-347]
- The development of liver support systems provides some promise for patients with FHF, although the systems remain a temporary measure and, to date, have had no impact on survival. Other investigational therapeutic modalities, including hypothermia, have been proposed but remain unproven.[341-347]

Nursing Management

Nursing management for the patient with cirrhosis of the liver should focus on promoting rest, improving nutritional status, providing skin care, reducing risk of injury, and monitoring and managing complications.

Nursing Assessment

Assessment of the patient with cirrhosis should include assessing for:

- **Bleeding**: Check the patient's skin, gums, stools, and vomitus for bleeding.
- **Fluid retention**: To assess for fluid retention, weigh the patient and measure abdominal girth at least once

daily.
- **Mentation**: Assess the patient's level of consciousness often and observe closely for changes in behaviour or personality.

Nursing Diagnosis

Based on the assessment data, the major nursing diagnosis for the patient are:
- **Activity intolerance** related to fatigue, lethargy, and malaise.
- **Imbalanced nutrition**: less than body requirements related to abdominal distention and discomfort and anorexia.
- **Impaired skin integrity** related to pruritus from jaundice and edema.
- **High risk for injury** related to altered clotting mechanisms and altered level of consciousness.
- **Disturbed body image** related to changes in appearance, sexual dysfunction, and role function.
- **Chronic pain** and discomfort related to enlarged liver and ascites.
- **Fluid volume excess** related ascites and oedema formation.
- **Disturbed thought processes** and potential for mental deterioration related to abnormal liver function and increased serum ammonia level.
- **Ineffective breathing pattern** related to ascites and restriction of thoracic excursion secondary to ascites, abdominal distention, and fluid in the thoracic cavity.

Nursing Care Planning & Goals

The major goals for a patient with cirrhosis are:
- Report decrease in fatigue and increased ability to participate in activities.
- Maintain a positive nitrogen balance, no further loss of muscle mass, and meet nutritional requirements.
- Decrease potential for pressure ulcer development and breaks in skin integrity.
- Reduce the risk of injury.
- Verbalize feelings consistent with improvement of body image and self-esteem.
- Increase level of comfort.
- Restore normal fluid volume.
- Improve mental status, maintain safety, and ability to cope with cognitive and behavioural changes.
- Improve respiratory status.

Nursing Interventions

The patient with cirrhosis needs close observation, first-class supportive care, and sound nutrition counselling.
- **Promoting rest**
  - Position bed for maximal respiratory efficiency; provide oxygen if needed.
  - Initiate efforts to prevent respiratory, circulatory, and vascular disturbances.
  - Encourage patient to increase activity gradually and plan rest with activity and mild exercise.
- **Improving nutritional status**
  - Provide a nutritious, high-protein diet supplemented by B-complex vitamins and others, including A, C, and K.
  - Encourage patient to eat: Provide small, frequent meals, consider patient preferences, and provide protein supplements, if indicated.
  - Provide nutrients by feeding tube or total parenteral nutrition if needed.
  - Provide patients who have fatty stools (steatorrhea) with water-soluble forms of fat-soluble vitamins A, D, and E, and give folic acid and iron to prevent anaemia.
  - Provide a low-protein diet temporarily if patient shows signs of impending or advancing coma; restrict

sodium if needed.

- **Providing skin care**
  - Change patient's position frequently.
  - Avoid using irritating soaps and adhesive tape.
  - Provide lotion to soothe irritated skin; take measures to prevent patient from scratching the skin.
- **Reducing risk of injury**
  - Use padded side rails if patient becomes agitated or restless.
  - Orient to time, place, and procedures to minimize agitation.
  - Instruct patient to ask for assistance to get out of bed.
  - Carefully evaluate any injury because of the possibility of internal bleeding.
  - Provide safety measures to prevent injury or cuts (electric razor, soft toothbrush).
  - Apply pressure to venepuncture sites to minimize bleeding.
- **Monitoring and managing complications**
  - Monitor for bleeding and haemorrhage.
  - Monitor the patient's mental status closely and report changes so that treatment of encephalopathy can be initiated promptly.
  - Carefully monitor serum electrolyte levels are and correct if abnormal.
  - Administer oxygen if oxygen desaturation occurs; monitor for fever or abdominal pain, which may signal the onset of bacterial peritonitis or other infection.
  - Assess cardiovascular and respiratory status; administer diuretics, implement fluid restrictions, and enhance patient positioning, if needed.
  - Monitor intake and output, daily weight changes, changes in abdominal girth, and oedema formation.
  - Monitor for nocturia and, later, for oliguria, because these states indicate increasing severity of liver dysfunction.
- **Home management**
  - Prepare for discharge by providing dietary instruction, including exclusion of alcohol.
  - Refer to Alcoholics Anonymous, psychiatric care, counselling, or spiritual advisor if indicated.
  - Continue sodium restriction; stress avoidance of raw shellfish.
  - Provide written instructions, teaching, support, and reinforcement to patient and family.
  - Encourage rest and probably a change in lifestyle (adequate, well-balanced diet and elimination of alcohol).
  - Instruct family about symptoms of impending encephalopathy and possibility of bleeding tendencies and infection.
  - Offer support and encouragement to the patient and provide positive feedback when the patient experiences successes.
  - Refer patient to home care nurse, and assist in transition from hospital to home.

Evaluation

Expected patient outcomes include:

- Reported decrease in fatigue and increased ability to participate in activities.
- Maintained a positive nitrogen balance, no further loss of muscle mass, and meet nutritional requirements.
- Decreased potential for pressure ulcer development and breaks in skin integrity.
- Reduced the risk of injury.
- Verbalized feelings consistent with improvement of body image and self-esteem.
- Increased level of comfort.
- Restored normal fluid volume.

- Improved mental status, maintain safety, and ability to cope with cognitive and behavioural changes.
- Improved respiratory status.

Discharge and Home Care Guidelines

The focus of discharge education is dietary instructions.

- **Alcohol restriction**: Alcohol restriction of greatest importance is the exclusion of alcohol from the diet, so the patient may need referral to Alcoholics Anonymous, psychiatric care, or counselling.
- **Sodium restriction**: Sodium restriction will continue for considerable time, if not permanently.
- **Complication education**: The nurse also instructs the patient and family about symptoms of impending encephalopathy, possible bleeding tendencies, and susceptibility to infection.

Documentation Guidelines

The focus of documentation may include:

- Level of activity.
- Causative or precipitating factors.
- Vital signs before, during, and following activity.
- Plan of care.
- Response to interventions, teaching, and actions performed.
- Teaching plan.
- Changes to plan of care.
- Attainment or progress toward desired outcome.
- Caloric intake.
- Individual cultural or religious restrictions, personal preferences.
- Availability and use of resources.
- Duration of the problem.
- Perception of pain, effects on lifestyle, and expectations of therapeutic regimen.
- Results of laboratory tests, diagnostic studies, and mental status and cognitive evaluation.

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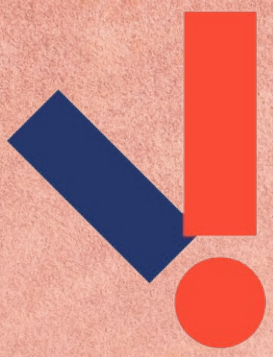
Patient Security & Copyright Issues

The main subject of this training program is to enhance medical education in the field of viral hepatitis. The content of this program does not include any patient related information, and we pay careful attention to protecting patient privacy by for example, not disclosing patient identity in our presentations and avoiding photographing patient faces in presentations. Therefore, our basic standpoint is that there is no need for further protection during transmission of the lectures during face to face conferences or over the internet/telemedicine sessions. This being a learning program, ILBS or any of its faculty/speakers or project PRAKASH staff will not be liable or legally accountable for any clinical or administrative, management complications and or any mishap that arise in any patient or hospital setting. It shall be the responsibility of the participating healthcare professional to utilize their skills and acumen for rendering most appropriate and ethical treatment to their patients.



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