HEPATITIS B VIRUS: COMPREHNSIVE REVIEW OF EPIDERMIOLOGY, PATHOGENESIS AND TREATMENT

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ABSTRACT

When Hepatitis-B is diagnosed, the quest for a reliable curative treatment in any medical system starts. Which physician should I see? Which doctor specializes in treating Hepatitis B or C infections, or the gastroenterologist with the largest list of alphabets after his name? How is the doctor chosen? Excellent question as well. You should see a physician with extensive clinical experience in treating infections caused by Hepatitis B or C. Instead of choosing someone with book knowledge of Hepatitis B or C, look for a physician with a long history of treating Hepatitis B and C cases alone. Practice is only focused on clinical abilities and knowledge, whereas study allows one to earn more degrees.

Hepatitis B virus (HBV) infection is a major public health issue; in 2019, there were an estimated 820,000 deaths worldwide and 296 million people with chronic HBV infection. While serological testing for HBsAg is necessary for the diagnosis of HBV infection, further testing for IgM hepatitis B core antibody (IgM anti-HBc) is necessary for acute infections within the window of time when neither HBsAg nor anti-HBs are detectable. Analyzing HBV replication status entails testing for HBV DNA to guide treatment choices, but assessing liver disease activity and staging mostly depends on aminotransferase levels, platelet counts, and elastography. The best method for preventing chronic HBV infection is to vaccinate all newborns, including those who receive a birth dose.

INTRODUCTION

Hepatitis refers to the general condition of liver inflammation. This condition can arise not only from excessive activity of the immune system but also due to external factors, most commonly viral infections. An immunological response elicited by the replication and other components of a virus may lead to either an acute or chronic infection. The effects of this condition can vary significantly depending on both the host and the specific virus involved in the infection.

The predominant cause of viral hepatitis is the Hepatitis B virus (HBV), which represents a significant contributor to end-stage liver disease globally. Despite the availability of an effective vaccine for HBV infection, new cases continue to emerge, attributable in part to inadequate vaccination coverage as well as challenges related to the accessibility, availability, and cost of vaccines in regions most affected by the disease. Additionally, another source of new infections arises from viral breakthrough, which may occur in up to 5% of infants who have received the anti-HBV birth-dose vaccine in a timely manner.

Deregulated immune function is a hallmark of some liver diseases, in which the body's attempt to eradicate the insult is either prolonged beyond containment or made worse beyond control. As a result, the body's aggravated mechanism tends to destroy self-cells, a phenomenon known as "collateral damage." Hepatocytes may be destroyed and scar tissue may form in certain situations where the reaction is prolonged and persistent rather than necessarily aggravated. The body's repair systems might not be able to keep up with the hepatocytes' ongoing damage.

NATURAL HISTORY OF HEPATITIS B VIRUS INFECTION

The hepatitis B virus was identified in 1965 by Dr. Baruch Blumberg, who was awarded the Nobel Prize for this significant discovery. Initially, the virus was referred to as the "Australia Antigen," a name derived from a blood sample of an Australian aborigine that exhibited a reaction with an antibody found in

the serum of an American patient with hemophilia. Collaborating with Dr. Blumberg, microbiologist Irving Millman contributed to the creation of a blood test for the hepatitis B infection. This test was received by blood banks in 1971 to screen blood gifts, coming about in a 25 percent lessening in the hazard of hepatitis B contaminations related with blood transfusions. Four a long time taking after the recognizable proof of the hepatitis B infection, Drs. Blumberg and Millman defined the to begin with hepatitis B immunization, which was initially a heat-inactivated adaptation of the infection. Perinatal transmission and horizontal infection during early childhood are the primary modes of hepatitis B virus (HBV) transmission in regions with high endemicity, including Southeast Asia, much of Africa, and the Arctic. In contrast, in areas with low endemicity, such as Western countries, hepatitis B predominantly affects adolescents and adults, primarily due to high-risk sexual behaviors and the use of injection drugs. The process of HBV infection is dynamic, encompassing both replicative and non-replicative phases of virus-host interaction, which are observed in various forms among all infected individuals.

First Commercial Hepatitis B Vaccine

In 1981, the FDA asserted a more present-day plasma-derived hepatitis B counter acting agent for human utilize. This “inactivated” sort of counter acting agent included the collection of blood from hepatitis B virus-infected (HBsAg-positive) advocates. The pooled blood was subjected to diverse steps to torpid the viral particles that included formaldehyde and warm treatment (or “pasteurization”). Merck Pharmaceuticals made this plasma counter acting agent as "Heptavax," which was the to start with commercial hepatitis B contamination counter acting agent. The utilize of this immunization was suspended in 1990 and it is no longer open in the U.S.

ETIOLOGY

Hepatitis B is spread through a variety of routes from infected individuals to non-immune individuals. The following are the main ways that hepatitis B is spread:

1. Horizontal transmission: This refers to the spread of hepatitis B via intercourse or contact with mucosal surfaces. In regions with low to intermediate prevalence, unprotected sex and injectable drug use are the main ways that the disease is spread.

2. Vertical transmission: The virus can spread vertically from mother to newborn during the perinatal period. In regions with a high prevalence, it is the most common mode of transmission. Unprotected intercourse (vaginal, oral, or anal) is considered sexual contact, while any contact with an infected patient's blood, semen, saliva, or vaginal secretions is considered mucosal contact.

The percentage of the population with hepatitis B surface is used to determine prevalence areas.

1. Causative Agent

Hepatitis B Virus (HBV):

HBV is a little infection characterized by somewhat double-stranded DNA and is classified inside the Hepadnaviridae family. Its replication prepare is particular, including turn around translation, which adjusts it with certain retroviruses.

2. Transmission

HBV spreads through blood and body fluids. Common routes include:

Vertical transmission:

From an infected mother to her baby during childbirth (most common in high-prevalence areas).

Horizontal transmission:

Through contact with contaminated blood or bodily fluids, often in childhood (cuts, scrapes, or bites).

Sexual contact: Unprotected intercourse with an infected person.

EPIDERMIOLOGY

❖ Virus Structure And genome

The Hepatitis B virus (HBV) is the prototype virus of the *Hepadnaviridae* family of viruses. Members of this family are hepatotoxic DNA viruses known mammals (Orthohepadna viruses). Additionally, fish and amphibian *Hepadnaviruses* have These viruses share similarities in their genome organization as well as their replication approach, with up to 40% and 20% sequence diversity amongst orthohepadna viruses and avihepadna viruses, respectively. Three types of HBV-virion particles are usually observed in the serum of infected persons.

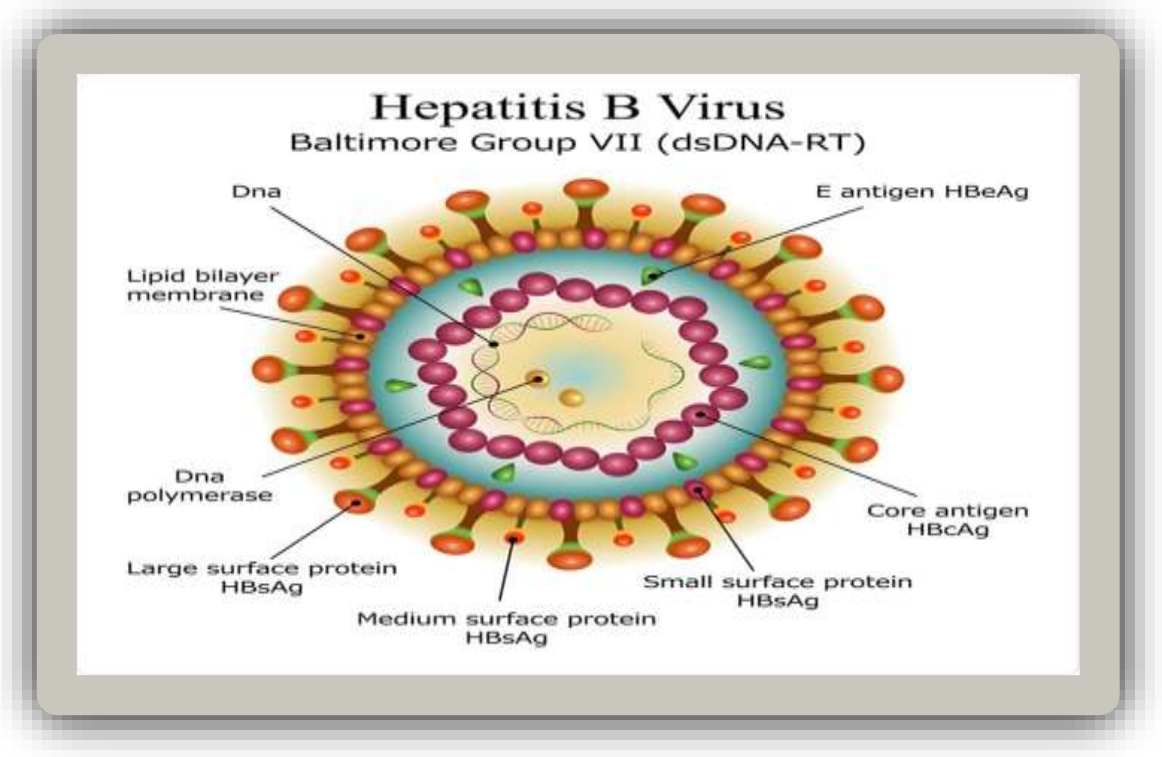

Figure of: Hepatitis of B Virus

The infectious virion, also known as the Dane particle, is 42–45 nm in diameter, made up of HBsAg embedded in a lipid envelope, encasing the viral nucleo capsid containing a reverse transcriptase tethered to the nucleic-acid material.

The other two are sub viral particles (22–24 nm), filamentous and spherical in shape, both comprising HBs Ag embedded in a host-derived lipid membrane but lacking viral DNA. Interestingly, the sub viral particles outnumber the infectious particles by 100 to 100,000-foldin the blood and play immune modulatory and immune inhibitory roles.

HBV infection has the potential for progression to a chronic state and thus presents as a global public health threat for its associated morbidity and mortality. While hepatitis B vaccines are available, limited access to healthcare and lack of proper health education contributes to the increasing global prevalence of hepatitis B.

Lower incidence of hepatitis B in the United States compared to Asia and Africa is due to better access to healthcare and better use of vaccinations and other preventive measures of diagnostics, is an obstacle to those requiring therapy. However, they observed that there is a lack of education and awareness, poor access

to relevant laboratory tests and imaging, and inconsistent access to appropriate medication. This is particularly pertinent in resource-constrained settings.

PATHOGENESIS

HBV can be acquired through two main routes parenatally, from infected mothers to their new-born, which accounts for a majority of cases worldwide, and horizontal transmission through contact with an infected person's body fluids, equipment for body piercing, tattoos, and injecting-drug use. Generally, the mechanisms by which HBV accesses and gains entry into hepatocytes is not fully understood.

The heparin Sulphate proteoglycans (HSG's), sodium taurocholate co-transporting peptide (NTCP), and the epidermal growth factor receptor (EGFR) are some of the receptors that mediate this internalization although there are likely to be others. Both the NTCP and HSG's are hepatocyte-specific receptors, thus explaining the virus' hepatotropic nature. In-depth studies into these receptor interactions could significantly contribute to finding a cure to HBV through inhibition of viral spread within the liver. Recently, some compound leads have been shown to selectively inhibit the virus-receptor function of NTCP.

Virus replication often results in the induction of an innate immune response which is heralded by rapid induction of IFNα/β by the infected cell. Production of IFNα/β induces the transcriptional expression of a large number of interferon inducible genes (ISGs) which in turn exert a variety of intracellular antiviral mechanisms that have the potential to minimize pathogenetic processes by limiting viral production and spread.

CAUSES AND RISK FACTORS OF HEPATITIS-B

Hepatitis B follows a similar mode of transmission as the human immunodeficiency virus (HIV), the agent responsible for AIDS. Both are transmitted through exposure to infected blood or blood products, sexual contact and from mothers to infants primarily at birth. However, hepatitis B appears to be far more infectious than HIV. In addition to the ways in which HIV is spread, hepatitis B appears to be spread by casual contact. It can be acquired by close contact within families, or from person to person through contact with open skin lesions.

❖ SYMPTOMS OF HEPATITIS B VIRUS

Symptoms and signs of hepatitis B can range from none to minimal in the early stages of the illness, to jaundice (yellowing of the skin), nausea, abdominal pain, fever, and malaise in the acute phase. Appetite loss, fatigue, itching, dark urine and pale stools are some common symptoms.

➢ Acute Hepatitis B Symptoms

1. Fever
2. Fatigue or general malaise
3. Loss of appetite
4. Nausea and vomiting
5. Abdominal pain (especially in the upper right side near the liver)

➢ Chronic Hepatitis B Symptoms

1. Persistent fatigue and weakness
2. Joint pain
3. Abdominal pain or discomfort
4. Jaundice (if liver function deteriorates)

Early diagnosis and treatment can help manage symptoms, prevent complications, and reduce the risk of liver damage for those with chronic HBV.

➢ TREATMENT OF HEPATITIS B

Getting advice or professional opinion is NOT a free service, as you are communicating with the world's one & only clinical specialist on Hepatitis B. Once you are diagnosed to have Hepatitis B or C, you have only 2 options, either meet Dr. John K C OR die of Liver Cancer/Cirrhosis. This statement looks awkward, but it is a frank reality, you should admit it. Public behaves like a fool or idiot when this health issue occurs to them or to any family members. They select a doctor on what basis? They assume that if they meet a specialist in a very big hospital, their all problems would be solved permanently. They do not know anything that is happening in a medical field. All specialists work in any hospital for a monthly pay of 2 lakhs rupees after signing an agreement with management to provide that hospital, a fixed income on monthly basis -'target' it is called.. In short, their monthly salary is based on this 'target'. So specialists do wanted and mostly unwanted tests on the patients like blood tests, , CT scan, Endoscopy, MRI scan, Biopsy etc... Patients do not know the key point in a treatment. Patients think that, by doing all these tests, Hepatitis B viruses/Hepatitis C viruses would be removed from the body.This is the foolishness or idiocy of the public. On doing these tests, you are just trying to study the nature of viruses. Treatment means taking something to kill viruses.

Hepatitis Delta Drug Watch

DRUG	MECHANISM	COMPANY	STATUS
Lambda (Pegylated Interferon)	Immune Response Stimulator	Eiger BioPharma, USA	*FDA Orphan Drug Designation* Phase III (Projected 2018)
Myrcludex B	Entry Inhibitor	MYR-GmbH, Germany	*EMA PRIME Eligibility* Phase II
Lonafarnib	Prenylation Inhibitor	Eiger BioPharma, USA	*FDA Fast Track Designation* Phase II
Ezetimibe	NTCP Inhibitor	Ziauddin University Hospital, Pakistan	Phase II
REP 2139 REP 2165	HBsAg Inhibitor	Replicor, Canada	Phase II
GI-18000	Immune Response Stimulator	GlobeImmune, USA	Pre-clinical
ALN-HDV	RNAi Gene Silencer	Alnylam, USA	Pre-clinical

Table 1: Hepatitis Delta Drug

Key point in a treatment is the use of drugs or any procedure to handle the enemy, in this case Hepatitis B or C viruses. Identify the enemy and start a battle to kill that enemy using weapons called drugs/medicines. In homoeopathy around five hundred anti-viral drugs have been identified which can eliminate almost all viruses that attack human beings. Although there are highly effective treatments available to manage hepatitis B, there are few available treatments for hepatitis D, and none are U.S. Food and Drug Administration (FDA)

approved. Hepatitis D is the most severe form of viral hepatitis, and coinfection can accelerate liver damage and cause cirrhosis or liver cancer in as little as 5 years for some patients.

Plasmodium Liver Stage of Infection (Malaria)

Plasmodium is the parasite responsible for malaria, with species like P. falciparum and P. vivax being the most common in humans. The infection starts when a mosquito injects Plasmodium sporozoites into the bloodstream, which travel to the liver and invade hepatocytes. Inside liver cells, Plasmodium sporozoites undergo an asexual multiplication phase, forming merozoites. This phase lasts from 5-16 days, depending on the species. Once the merozoites are mature, they are released from liver cells into the bloodstream to infect red blood cells, leading to the symptomatic blood stage of malaria. In P. vivax and P. ovale, some sporozoites become dormant in liver cells as hypnozoites, causing relapses if reactivated.

1) Hepatitis B Virus (HBV) Infection

HBV is a DNA virus that specifically targets liver cells, leading to hepatitis (inflammation of the liver). The virus enters hepatocytes by binding to specific receptors on the cell surface, initiating a complex replication cycle where the viral DNA integrates into the host's nucleus. HBV infection can be acute or chronic. Chronic HBV infection may lead to liver inflammation, fibrosis, cirrhosis, and even hepatocellular carcinoma (liver cancer). The immune response to HBV-infected hepatocytes contributes to liver damage as immune cells attack infected liver cells. It is a viral infection that primarily affected to the liver, potentially leading to both acute and chronic disease. It is caused by the hepatitis.

❖ PREVENTION

Hepatitis B is preventable with a vaccine. All babies should receive the hepatitis B vaccine as soon as possible after birth (within 24 hours). This is followed by two or three doses of hepatitis B vaccine at least four weeks apart. Booster vaccines are not usually required for people who have completed the three-dose vaccination series. To reduce the risk of getting or spreading hepatitis B: practice safe sex by using condoms and reducing the number of sexual partners avoid sharing needles or any equipment used for injecting drugs, piercing, or tattooing wash your hands thoroughly with soap and water after coming into contact with blood, body fluids, or contaminated surfaces get a hepatitis B vaccine if working in a healthcare setting.

Hepatitis B vaccine is recommended for the following people:

- All infants
- Unvaccinated children aged <19 years
- Adults aged 19 through 59 years
- Adults aged 60 years and older with risk factors for hepatitis B.

The hepatitis B vaccine is the main way to prevent infection with HBV. The vaccine is given as two shots one month apart, or three or four shots over six months. How many shots you get depends on the type of hepatitis B vaccine that you're given. You can't get hepatitis B from the vaccine. In the United States, the Advisory Committee on Immunization Practices recommends that infants get their first shot of the vaccine after they're born. If you didn't get vaccinated as a baby or child, the committee still recommends the vaccine for everyone through age 59.

❖ SCREENING & TESTING

The CDC estimates that 68% of people with chronic hepatitis B are unaware of their infection. The only way to find out if you have hepatitis B is to get tested. Hepatitis B testing is a covered preventive service under many health plans.

Being aware of your hepatitis B status is important because treatments are available that reduce the chance of developing liver disease and liver cancer. If you are diagnosed with hepatitis B, you can also protect your family members by getting them vaccinated. CDC recently published updated recommendations for hepatitis B screening and testing

CDC recommends HBV screening for hepatitis B surface antigen (HBsAg) for all pregnant people during each pregnancy, preferably in the first trimester, regardless of vaccination status or history of testing.

Interpretation of Screening Tests

The three main serologic markers used to determine HBV infection status are hepatitis B surface antigen (HBsAg), antibody to hepatitis B surface antigen (anti-HBs), and antibody to hepatitis B core antigen (anti-HBc) (Table 1).

Serologic markers change over typical courses of resolved acute infection and progression to chronic infection [15].

❖ HEPATITIS B VACCINE

Hepatitis B vaccine is usually given as 2, 3, or 4 shots. Infants should get their first dose of hepatitis B vaccine at birth and will usually complete the series at 6–18 months of age. The birth dose of hepatitis B vaccine is an important part of preventing long-term illness in infants and the spread of hepatitis B in the United States.

Hepatitis B serological markers		
Antigens		*Correlates with*
HBsAg	Hepatitis B surface antigen	acute or chronic HBV infection
HBeAg	Hepatitis Be antigen	HBV replication and infectivity
Antibodies		*Correlates with*
Anti-HBc	Antibodies against HBV core antigen	previous or ongoing contact with HBV
IgM anti-HBc	IgM antibodies against HBV core antigen	acute or exacerbation of HBV
Anti-HBs	Antibodies against HBsAg	recovery and immunity (vaccination)
Anti-HBe	Antibodies against HBeAg	lower HBV replication and remission

Table 3: Hepatitis B Serological Markers

- **HBsAg (hepatitis B surface antigen)** is the first serologic marker to appear in a new acute infection, which can be detected as early as 1 week and as late as 9 weeks, with an average of one month after exposure to the hepatitis B virus (HBV).

- Anti-HBs or HBsAb (hepatitis B surface antibody) – this becomes detectable on a blood test after the disappearance of HBsAg in persons who are able to get rid of the virus and avoid a chronic infection. The presence of anti-HBs following a new acute infection generally indicates recovery and a person is then protected (or "immune") from re-infection with hepatitis

- **Anti-HBc or HBcAb (hepatitis B core antibody) –** this blood test remains positive indefinitely as a marker of past HBV infection.

❖ Enhancing The Health Care Team Outcomes

Improving team-based health care outcomes for hepatitis B virus (HBV) requires an integrated approach that includes coordinated care, patient education, preventive measures, and systematic monitoring. Here are some strategies to enhance team outcomes in managing HBV:

1. Integrated Care Team Approach

Multidisciplinary Teams: Incorporate primary care providers, hepatologists, infectious diease specialists, nurses, pharmacists, and social workers to address all aspects of HBV care.

2. Patient Education and Engagement

Education on HBV: Educate patients about HBV transmission, prevention, treatment options, and the importance of adherence to care plans.

Culturally Competent Communication: Tailor educational resources to be culturally and linguistically appropriate, especially important for HBV, which disproportionately affects certain populations.

3. Preventive and Screening Measures

Risk-Based Screening: Screen individuals based on risk factors, such as birth in a high-prevalence area, familial history, or risk behaviors.

Vaccination Protocols: Ensure all team members promote and administer HBV vaccinations to uninfected at-risk individuals and newborns.

❖ CHALLENGES AND DIRECTION

1. Limited Access to Vaccines and Treatment: Cost and availability hinder control efforts, especially in low-income regions.

2. Mother-to-Child Transmission (MTCT): Major transmission route, with limited resources for preventing newborn infection.

3. Asymptomatic and Underdiagnosed Cases: Many people are unaware of their infection, delaying treatment and increasing transmission.

4. Stigma and Cultural Barriers: Stigma deters people from seeking testing, treatment, or disclosing their status.

5. Drug Resistance: Long-term antiviral use risks resistance, complicating treatment.

6. Inadequate Surveillance: Lack of data makes it hard to track and respond effectively to HBV trends.

FUTURE DIRECTIONS FOR HBV CONTROL

The proper understanding and interpretation of diagnostic methods is necessary for successful therapy against hepatitis B, because different type of therapies target various markers of hepatitis B infection differently. Therefore, diagnosis based on different combinations of markers of hepatitis B infection needs to be carried out to monitor the effectiveness of a therapy. The seroclearance of HBsAg and appearance of anti-HBs [26,45], which further indicates protective immunity, can be diagnosed with a combination of HBs and anti-HBs markers. HBsAg serum levels and their source are different in the inactive and immune–tolerant phase and, therefore, need to be diagnosed by different strategies in these phases. In HBeAg-negative patients, less than 100 IU/mL of HBsAg may indicate gradual HBsAg clearance that can only be diagnosed together with HBeAg and HBsAg markers [74]. Both markers, along with knowledge of HBV genotypes, may also be helpful in monitoring the response of antiviral therapy. The genotypes of HBV in the infected patient is known to influence the effect of antiviral therapy [75]. Therefore, the foolproof diagnosis for HBV would be to obtain information on HBsAg, HBeAg, hepatitis B viral load, and genotypes of HBV. These four markers may help in accomplishing the WHO's goal because these will help in determining the stage of infection and further decision-making in the type of therapy to be given.

1. Universal Vaccination Programs:

Increase coverage for newborns and high-risk adults to prevent new infections.

2. Enhanced MTCT Prevention:

Integrate screening and antiviral options in prenatal care to reduce newborn infections.

3. Development of Functional Cures:

Advance research for curative treatments to reduce reliance on lifelong antivirals.

❖ New Therapies

New therapies for hepatitis B virus (HBV) infection are being developed to improve treatment efficacy, reduce the need for lifelong antiviral therapy, and ultimately find a functional cure. Here are some of the most promising approaches:

1. RNA Interference (RNAi) Therapy

Mechanism: RNA interference (RNAi) therapies use small interfering RNA (siRNA) molecules to target and degrade HBV RNA, reducing the production of viral proteins and inhibiting viral replication.

2. Capsid Assembly Modulators

Mechanism: These drugs target the HBV core or capsid protein, disrupting the assembly of viral capsids and thus preventing replication.

3. Entry Inhibitors

Mechanism: These drugs prevent HBV from entering liver cells, blocking the initial stage of infection.

4. Therapeutic Vaccines

Mechanism: Unlike preventive vaccines, therapeutic vaccines aim to stimulate the immune system to recognize and fight chronic HBV infections.

5. Gene Editing (CRISPR-Cas9)

Mechanism: Gene-editing technologies like CRISPR-Cas9 can target and disrupt HBV DNA, particularly the covalently closed circular DNA (cccDNA) reservoir in liver cells.

❖ CURRENT RESEARCH

Current research on Hepatitis B virus (HBV) is primarily focused on finding a cure, understanding immune system interactions, and improving prevention. Key areas include developing novel antiviral drugs, gene-editing techniques, and therapeutic vaccines to eliminate HBV or enhance the immune response against it. Additionally, there's a focus on discovering biomarkers for better disease monitoring and advancing personalized medicine to tailor treatments. Research also addresses HBV-related liver cancer risks, co-infection with HIV, and expanding vaccination efforts globally to prevent new cases. These efforts aim to improve outcomes for the millions affected by HBV worldwide.

Current HBV research focuses on:

Functional cure:

- ✓ Developing therapies that eliminate the virus and prevent reactivation.

New antiviral drugs:

- ✓ Targeting specific viral proteins or host factors.

Immunotherapy:

- ✓ Stimulating the immune system to fight the virus.

Vaccine development:

- ✓ Improving existing vaccines and creating new ones.

Prevention and control:

- ✓ Implementing public health measures to reduce transmission.
- ✓ These efforts aim to improve treatment outcomes and ultimately eradicate HBV.

LITERATURE REVIEWS:

The point of view on Hepatitis B virus (HBV) centers around its significant public health impact and the urgent need for improved management and a cure. HBV is recognized as a major global cause of chronic liver disease, cirrhosis, and liver cancer. Current perspectives emphasize the importance of advancing antiviral therapies, developing effective therapeutic vaccines, and understanding immune interactions to achieve functional cures. Additionally, there's a focus on expanding prevention strategies, especially in high-prevalence areas, through widespread vaccination and better diagnostics. Ultimately, the goal is to reduce the HBV burden and prevent disease progression, ideally leading to global eradication.

Author Name	Publication Year	Abstract
Nishant Tripathi and Omar Y. Mousa	9 July 2023	Hepatitis B infection is a serious global healthcare problem. Often transmitted via body fluids like blood, semen, and vaginal secretions, the hepatitis B virus can cause liver injury.
Leslie Baumann	9 October 2002	This book provides a comprehensive foundation in cosmetic dermatology, addressing the science of skin types, aging, and treatment modalities.
Richard J. Motley:	1 November 2002	Dermatology is a specialized branch of medicine that focuses on diagnosing and treating conditions affecting the skin, hair, and nails.

CONCLUSION

The observations we made indicate a need for prevention and control of, generally, serum hepatitis in hyperendemic and low-resourced countries, especially in the West African sub-region. There is the need for operative strategies which requires comprehensive investments to interrupt the transmission of serum hepatitis and reduce the consequential morbidity and mortality. The importance of expanding research in the field of HBV cannot be overstated. There is a pressing need to elevate efforts in HBV research to precisely assess prevalence rates, identify at-risk populations, establish treatment priorities, and deepen our comprehension of host-pathogen interactions that could ultimately lead to a cure.

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