Fig1 The discovery of HBV Serum Virological products

In the 1940s, MacCallum proposed the term “hepatitis B” for infectious jaundice associated with parenteral transmission route (“serum hepatitis”) from “infectious epidemic” hepatitis linked to fecal–oral transmission (“hepatitis A”).

In the 1960s, The field of viral hepatitis was revolutionized by Blumberg and Alter's accidental discovery of an HBV surface antigen. Subsequently, it was found that HBsAg was only a part of it.

In the 1970s:
1. Dane particles were discovered and the morphology of HBV was observed under an electron microscope.
2. Methods to detect HBsAg were first described using radioimmunoassays and enzyme immunoassays.
3. Hirchman and others found DNA polymerase in the preparation of three HBsAg positive serum ultracentrifugation.
4. Scientists recognized HBeAg is a part of the core of the virus.
5. Interferon was used for treatment
6. Magnius and Esmark discovered an additional "mystery antigen", "HBeAg", which is endemic in highly infectious HBsag-positive samples but not in low-infectious Hbag-positive samples.

In the 1980s:
1. The first hepatitis B vaccine targeting HBV blood was produced.
2. Summers and others found that circular DNA (rcDNA) was subsequently converted into covalent closed circular DNA (cccDNA).
3. Miller et al. first observed HBV RNA in the form of HBV DNA-RNA heterozygous molecule in the serum of patients with CHB.
4. Pierre Tiollais and his partners genetically engineered the first human vaccine, hepatitis B, from animal cells.
5. it was included in the Hepatophilic DNA Viridae.
6.Gerken and colleagues demonstrated decreased rates of LHBs and MHBs in patients with acute hepatitis B during progression to HBsAg loss.

In the 1990s:
1. With improvements in the detection of HBV DNA by polymerase chain reaction, active HBV viremia has been found in some HBeAg-negative HBsAg positive patients. In addition, a subset of HBsAg negative subjects exhibited "occult" hepatitis B.
2.German scholar Kock and others found the existence of HBV RNA in the serum of patients with chronic HBV infection.
3. Lamivudine, the first drug in the nucleoside drug family, was introduced.

In the 2000s:
1. Fully automated quantitation of hepatitis B virus (HBV) DNA in human plasma by the COBAS AmpliPrep/COBAS TaqMan system.
2. A rapid real-time PCR assay based on the TaqMan system is described in this publication, HBV DNA can be accurately detected and quantified.

In the 2010s:
1. HBsAg CLEIA Lumipulse HBsAg-HQ assay is a very convenient and precise assay for HBV monitoring in clinical practice.
2. The Aptima Quantitative HBV test is the latest NAAT for quantification of HBV DNA in patient plasma and serum samples.
3. HBV RNA in serum was determined to be pgRNA, which is encapsulated and exists in HBV-like virus particles.
4. Researchers suggested that HBV RNA could be a new indicator of functional cure for CHB patients.
5. HBcrAg was identified as an alternative marker for intrahepatic cccDNA and its transcriptional activity, and HBcrAg could be used to evaluate new antiviral therapies.
6. Liver-specific sodium taurocholate cotransporting polypeptide have been identified as essential for HBV cell entry.