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Review Article

Jaundice: A brief historical perspective

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ABSTRACT

Jaundice is one of the earliest diseases known to mankind. The present article documents the history of documentation of jaundice and its various subtypes. Thus, this brief review serves, in-part, as one ready reference for history of jaundice.

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The Talmud describes Jaundice as a *sign of causeless hatred*.¹ Earliest references to jaundice, other than those depicted in the popular Babylonian Talmud/Sumerian Tablets, are found in Ebers papyrus,² and then in the Ayurveda. The English translators of Ebers papyrus claim that it is a 1500BC document wherein references to the first dynasty are found. This dates the written contents to around 3400BC, whence it will precede Ayurveda (3000BC)³ by at least 400 years. It may be noted that Ayurveda is practised even today and is continuously evolving. This situation makes it difficult to specify the exact date when the treatments of jaundice entered Ayurveda. Despite an error in attributing the date, Issac Asimov considers the Ebers papyrus as the first surviving account of medical remedies in his book 'Chronology of Science and Discovery'.⁴ Subsequent other major references to jaundice are found in the works of Hippocrates (460BC–370BC).^{5,6} Despite this, the readers must

keep in mind that just as understanding of solar system by the scientific community underwent a change of concepts from geo-centrism (Earth-centred) to helio-centrism (Sun-centred), medical community in the late 1800s underwent a paradigm shift from hepato-centrism to cardio-centrism.

The words hepatic, liver and jaundice have their origins in Greek, Sanskrit and Old French respectively.^{7,8} For an interesting discussion on etymology of the words 'hepatic' and 'liver', and their historical usage, the readers are asked to consult an interesting article by Riva and colleagues in the journal of hepatology.⁸ Subsequent letters in the same journal take the discussion on this topic to a crescendo.^{9,10} As per the online etymology dictionary, 'jaundice' has its origin in circa 1300AD in the Old French word 'jaunis' that meant 'yellowness', and the word 'jaunis' itself is derived from an earlier French word 'jalnice'.¹¹

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Researchers prior to 1800s had little idea about the type of Jaundice they were describing. Effects of alcohol were first described by Addison in 1836.¹² By 1937, i.e., a hundred years later, the effects of halothane based anaesthetics on liver were apparent.¹³ Autoimmune hepatitis (AIH), previously referred to as Chronic Active Hepatitis (CAH), was originally described in 1940s. However, only in 1950 it was considered to be autoimmune in nature. The nomenclature AIH which was proposed in 1965 was approved in the year 1993.¹⁴ Put simply, the case of AIH and CAH was akin to 'phthisis' and 'tuberculosis' wherein the authors ended up describing the same disease but were using different terminology.

The concept of obstructive jaundice came up in the year 1935 with Whipple.¹⁵ The terms infective hepatitis (in England) and infectious hepatitis (in USA) were first used in the years 1939 and 1943 respectively.¹⁶ Prior to this, jaundice as an adverse effect of vaccination was noted as early as 1885 by Lührman.^{17,18} McDonald, in the year 1908, suggested that jaundice may probably be caused by an agent much smaller than a bacterium.¹⁹ Only in the year 1923 it was hypothesized that a virus might be involved.¹⁷

World War II (WWII) threw open the field with regard to hepatitis. During WWII, it is estimated that approximately 16 million people were killed as a consequence of hepatitis.¹⁸ This situation led to serious research not only on vaccine induced hepatitis but on other types as well. By 1947, based on the studies in volunteers, it was apparent that there were two types of hepatitis: epidemic/infectious hepatitis and serum hepatitis (SH). Whereas epidemic hepatitis had a short incubation period, long incubation period was the hall mark of SH. In 1953, World Health Organization (WHO) recommended usage of the terms hepatitis A for infectious hepatitis and hepatitis B for SH.¹⁷ Discovery of the respective viruses, however, had to wait at least a decade in each of the cases.^{20,21} Needless-to-say, the Hippocratic corpus described epidemic jaundice.

By 1974, it was apparent that there was a third virus other than Hepatitis A virus (HAV) and Hepatitis B virus (HBV), whence it was referred to as non-A, non-B hepatitis (NANBH).²² Subsequent animal model research showed clearly that there are at least two distinct forms of NANBH.²³ Perhaps

Hepatitis C virus (HCV) represents the first of these two. The manner of discovery of HCV using reverse-transcription of the viral nucleic acid represents one major breakthrough in the field of biomedical biotechnology.²⁴ However, this virus continues to remain an enigma to researchers, and the diagnosis of this virus is typically by the detection of virus specific antibodies using Enzyme linked immunosorbent assays (ELISA), and/or by amplifying the viral nucleic acid by reverse transcription polymerase chain reaction (RT-PCR).

Massive epidemics of viral hepatitis between 1950-1970 in India, China and the adjoining regions led to identification of Hepatitis E virus (HEV).¹⁸ The actual discovery of HEV is credited to two groups of investigators. One of them, Khuroo and colleagues, is from India,²⁵ and the other group, Balayan et al, is from Russia.²⁶ The process of identification of HEV by ingestion of infected material by Balayan is indeed heroic and makes interesting stuff for Hollywood story writers.

The year 1977 also marked the discovery of Hepatitis D virus (HDV). With the observation that this virus requires the presence of HBV as helper virus, and the fact that HBV is vaccine preventable, HDV obviously became a neglected disease.¹⁸ 1995 saw the discovery of yet another virus that targets liver, the GB virus - C, increasing the repertoire of hepatitis viruses.²⁷ Two years later in 1997, a seventh virus the transfusion-transmitted virus (TTV) was identified in patients with non-A-B-C-G hepatitis.²⁸ Given the fact that both GBV-C and TTV are transmissible by contaminated blood and related fluids, Bendinelli et al,²⁹ suggest that TTV might be the other virus originally predicted by Shimizu et al, in 1979.³⁰ Needless-to-say, the period between the years 1950-2000 can easily be considered as the *Era of Viral Hepatides*, whence as many as seven viruses that cause hepatitis and target liver have been discovered and described. All of this is summarized as Fig. 1.

Per se the underlying cause of jaundice is difficult to identify symptomatically. Thus, based on the symptoms alone, it is difficult to differentiate between AIH and viral hepatides or drug induced liver diseases. Complicating this scenario is the discovery of seven viruses that target liver exclusively. Therefore laboratory diagnosis and/or histologic examination to exclude various possibilities become mandatory. Molecular

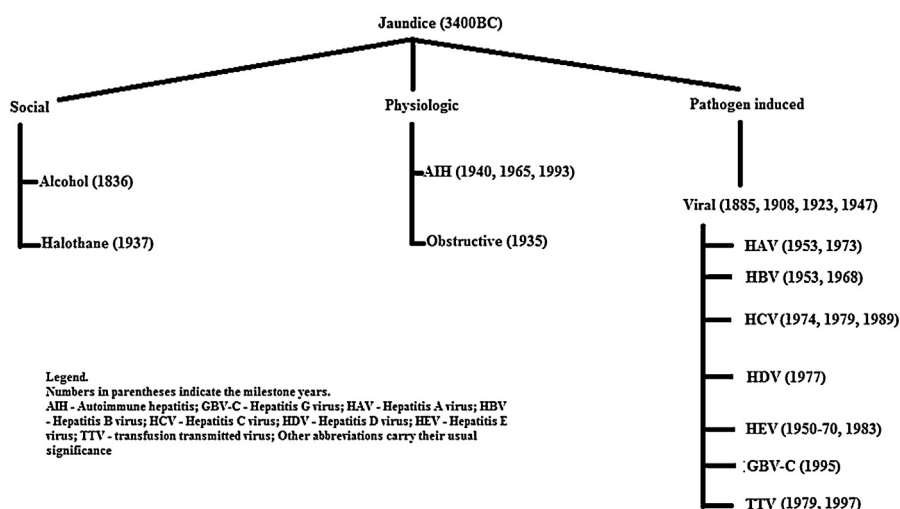


Fig. 1 – Milestones in Jaundice research and documentation.

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