The Hepatitis B and Delta Viruses

A subject collection from *Cold Spring Harbor Perspectives in Medicine*

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Front cover artwork: Hepatitis B virus. Colored transmission electron micrograph (TEM) of the hepatitis B virus and its naturally occurring antigen. The rounded spheres (called Dane particles) are the complete virus. Hepatitis B virus occurs typically in clusters of three types of particles (as seen here): the virus itself, as well as smaller spheres and rod-shaped forms made from the protein coat of the virus. The smaller noninfectious spheres are antigenically identical to the virus and provide raw material for hepatitis B vaccines. Infection by this virus is more serious than by hepatitis A, can be sexually transmitted, and causes chronic hepatitis. (Image provided by Dr. Linda M. Stannard, University of Cape Town and reprinted with express permission from *Science Source* © 2014.)

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Preface

IT HAS BEEN 50 YEARS SINCE BARUCH BLUMBERG REPORTED the presence of a novel antigen in the blood of an Aboriginal Australian. This "Australia antigen," now known as the hepatitis B surface antigen, persists in the blood of more than 200 million people worldwide chronically infected with the hepatitis B virus (HBV). Soon after the discovery of HBV it was realized that this virus not only caused jaundice but also contributed to the development of end-stage liver disease, cirrhosis, and hepatocellular carcinoma, a fatal cancer of the liver. A more aggressive form of hepatitis is associated with a second agent, the hepatitis delta virus (HDV) discovered by Mario Rizzetto in 1977. HDV is a satellite of HBV, as it requires the HBV envelope proteins to complete its life cycle.

Because of rapid advances in clinical and basic research and the successful development of both, an effective vaccine, and nucleos(t)ide-analog-based antiviral therapies, the burden of HBV infections and their deleterious effect on public health have been substantially reduced, but by no means eliminated. HBV, a DNA virus, turned out to use reverse transcriptase for genome replication, like retroviruses and HIV. In contrast, HDV carries an RNA genome, resembling certain plant agents called viroids. The course of HBV infections is intertwined with the host's immune response, and as such, it can be transient or chronic depending on the mode of transmission, age of infection, immune competence of the host, and other unknown factors. Although a wealth of information related to the molecular biology and pathogenesis of HBV and HDV infections has accumulated over the past 40 years, a major challenge remains: finding a cure for chronic HBV infections.

The purpose of this volume is to provide clinical and laboratory investigators, physicians, teachers, and students with a comprehensive overview of the state of the art of clinical and molecular facets concerning HBV and HDV infections. The book comprises 23 chapters authored by experts who have made major contributions to advance the HBV and HDV fields over four decades. The first four chapters provide a historical perspective and clinical and molecular overview of HBV and HDV. Subsequent chapters focus on HBV virology, pathogenesis and natural history, and animal models, prevention, treatment, control, and eradication. The volume concludes with four reviews on HDV, including discussions of its unusual life cycle and role as a modulator of HBV sequelae. We are hopeful that this book encourages readers to apply the information gained to develop new ideas that will eventually lead to a cure for chronic hepatitis B and reduce the burden of liver disease, and importantly liver cancer.

This book would not have been possible without the generous help of Barbara Acosta and Richard Sever at Cold Spring Harbor Laboratory Press. We would also like to acknowledge our colleagues who provided help during the editing phase, including Siddharth Balachandran and William Mason at the Fox Chase Cancer Center.

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