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DEVELOPMENTS IN VIRAL HEPATITIS BIOLOGY AND EPIDEMIOLOGY

Edited by

Paolo PASQUINI

Istituto Superiore di Sanità, Rome, Italy
FOREWORD

Viral hepatitis, particularly type B, represents an important public health problem in both the developing and the developed world: every year tens of millions of people are infected by viral hepatitis; chronic HBsAg carriers are about 200,000,000.

In Italy about 30,000 cases of hepatitis (all types) are reported every year; and this, of course, is only the tip of the iceberg. Chronic carriers in Italy are estimated to be between 1,500,000 and 2,000,000.

In the Mediterranean area there is a high prevalence of delta infections associated with an increased risk of fulminant hepatitis and evolution toward chronicity.

There are about 18,000 liver cirrhosis deaths per year and viral hepatitis is one of its main causes. Moreover, viral hepatitis B infection is associated with primary liver carcinoma. Post-transfusional hepatitis is presently due mostly to non-A non-B viruses; however post-transfusional B hepatitis still occurs in Italy.

Viral hepatitis B infection is not only an important cause of morbidity (acute hepatitis, chronic hepatitis, cirrhosis, primary liver carcinoma) but is also an important social and financial problem in terms of hospital admission, primary health care, laboratory test, sickness-absence, years of life and work lost.

The public health relevance of viral hepatitis and the recent successes and anticipated further developments of active immunization, make it particularly important to better understand the biology and epidemiology of viral hepatitis infections so that prevention could be carried out on a sound scientific basis.

With these objectives in mind, the Istituto Superiore di Sanità has recently started a number of research activities in the area of viral hepatitis ranging from basic research in virology and biochemistry to epidemiologic research and mathematical modelling; the public health orientation of the viral hepatitis project of the Istituto Superiore di Sanità is reflected in one of its first contributions: the reformulation of hepatitis vaccination policy in Italy based on the evaluation of regional vaccination programs carried out in collaboration with the Ministry of Health.

The present issue of the Annali dell'Istituto Superiore di Sanità devoted to hepatitis is an indication of the increasing interest and activities of our Institute in this area; in this issue current scientific knowledge in some important areas of viral hepatitis research is reviewed and new developments are discussed.

From a virological viewpoint, thanks to the recent introduction of animal models, new perspectives exist for the understanding of the structural biochemical characteristics, replication, and mechanism of persistent infections.

In the first paper H. Will and M. Rapicetta review the molecular biology of hepadnaviruses; this review summarizes recent data on the structure and function of genomes, genes and proteins and the replication strategy of the hepadnaviruses family to which belong human hepatitis B virus and the closely related woodchuck, ground squirrels and Pekin duck hepatitis viruses.

In the second paper G. Realdi and co-workers review current knowledge on pathogenesis with particular reference to the mechanism of evolution into chronic persistent or active hepatitis; an inadequate immune response to viral antigens seems to be the major component in the evolution to chronic infection and in the persistence of liver damage.
The evaluation of the infectivity of a serum sample has many implications, both for the individual patients and their contacts, and for the community as a whole, which is interested in valid screening procedures and efficient public health practices. In the third contribution by F. Bonino and co-workers, criteria for infectivity assessment and recent laboratory techniques are discussed, with particular reference to HBV-DNA detection by molecular hybridization, a simple, reproducible and sensitive procedure, that allows rapid examination of multiple samples.

The use of laboratory tests for serological markers of viral hepatitis is widespread in Italy. The importance of laboratory quality control in this area, like in many others, cannot be overemphasized, for its obvious public health, research and finance implications. The assays for hepatitis B markers were included in the interlaboratory quality control program sponsored by the Italian National Research Council (CNR). The fourth paper by R. Malvano and co-workers reports the first two years of experience of this interlaboratory quality control of immunometric assays of HBsAg and anti-HBs in Italy.

Descriptive epidemiology of hepatitis in Italy based on notifications of cases and seroepidemiology surveys is presented in the fifth paper, by L. Dardanoni, A. Mele and M.C. Polizzi. Most recent data from the type specific acute viral hepatitis information system (SEIEVA) are discussed in reference to public health practices.

In the evaluation of alternative preventive strategies, mathematical models, based on the natural history of hepatitis B infection and its dynamics in populations, may have a role to play. A simple deterministic model of hepatitis B infection and its application to the Italian epidemiological situation, are presented in the sixth paper by P. Pasquini and B. Cvjetanović.

Primary liver carcinoma is one of the most common cancers in the world. The hepatitis B virus is second only to cigarette smoking as the most important known human carcinogen. The epidemiologic evidence, based on ecologic correlations, case-control and prospective studies, on the association between primary liver carcinoma and hepatitis B infection is discussed by D. Trichopoulos and co-workers in the seventh paper.

The role of immunological and molecular markers of hepatitis B and hepatitis delta virus in predicting the course and the outcome of chronic HBsAg positive liver disease is evaluated by A. Craxi and co-workers in its survival analysis in the eighth paper.

General control measures against hepatitis B infection including immunoprophylaxis are reviewed by G.G. Frössner and E. Franco in the ninth paper.

Maternal-neonatal transmission of hepatitis B is a major problem in population with a high rate of HBV infections and a high prevalence of HBeAg among HBsAg carrier mothers. Babies born to HBeAg-positive carrier mothers are at very high risk of acquiring perinatal HBV infection and of becoming HBsAg chronic carrier. The specific problem of maternal-neonatal transmission of hepatitis B virus, its epidemiology and prevention are discussed in the tenth paper by A.R. Zanetti; the current recommendation is to initiate the vaccination of neonates in conjuction with the HBIG administration within 12 hours of birth.

The main four lines of developments of hepatitis B vaccines, and their results (human plasma-derived, subunit polypeptide, recombinant DNA, synthetic vaccines) are reviewed in the eleventh paper by A.J. Zuckerman, with particular emphasis on new vaccines.

In Italy the great majority of post-transfusional hepatitis is classified as non-A non-B hepatitis. Despite a decade of intensive investigation, the nature of the non-A non-B agents remains elusive. The contribution by F. Tremolada and co-workers in the last paper, on non-A non-B post-transfusional hepatitis provides a good example of how, even in the absence of etiologic information and specific laboratory tests, effective prevention program, based on relatively simple epidemiologic knowledge, can be implemented with success.

Francesco Pocchiari
Director General