Vaccines Against Viral Hepatitis

by Prof. Arie J. Zuckerman*

VIRAL hepatitis is a major public health problem in all parts of the world. This is a generalised infection with the liver as the target organ, and the infection is caused by at least three and probably four different viruses.

Hepatitis virus type A, which is responsible for infectious or epidemic jaundice, and hepatitis type B or serum hepatitis can now be differentiated by specific laboratory tests. The more recently identified and unrelated type of hepatitis referred to as non-A, non-B hepatitis is probably caused by more than one virus.

CULTIVATED IN TISSUE CULTURE

Hepatitis A is usually spread by person to person contact by the faecal-oral route and major outbreaks result most frequently from faecal contamination of water and food.

The responsible virus has been identified and characterised in the laboratory. It has very recently been cultivated in tissue culture and developments towards a vaccine can be expected.

Hepatitis B, on the other hand, is an entirely different matter and its importance may be considered under a variety of headings. These include its effect on every field of medical practice, the impact it has on blood transfusion services, its progression in a significant number of patients to chronic liver disease, and the strong association between hepatitis B virus and primary liver cancer.

Hepatitis B virus is transmitted by various body fluids, especially blood but also saliva, menstrual discharges, seminal fluid, breast milk and serous exudates — but infectivity is especially related to blood.

MILLIONS OF CARRIERS

An additional factor of great importance is that infection with hepatitis B virus may be followed by the chronic carrier state. Such a carrier state constitutes a reservoir of infection and in addition it may be associated with liver damage of varying degrees of severity.

There are about 176 million carriers of hepatitis B virus in the world, particularly among blood donors.

In northern Europe, North America and parts of Australia the prevalence is 0, 1% or less of the population. In central and eastern Europe it is up to 5%, with a higher frequency in southern Europe and the countries bordering the Mediterranean. There is a similar frequency in Central and South America. In some parts of Africa, Asia and the Pacific up to 20% of the population may be carriers.

Although the virus has been identified, and infection can be transmitted experimentally to chimpanzees and other apes, the virus has not yet been cultivated in tissue culture — so conventional vaccines cannot be prepared.

PEOPLE AT RISK

There is, however, an urgent need for a hepatitis B vaccine, particularly for groups of people that are at an increased risk of acquiring this infection.

These include health care and laboratory personnel, patients and staff of haemodialysis and transplant units, and oncology units. Also at increased risk are residents and staff of institutions for the mentally handicapped, and individuals living in regions where hepatitis B infection is prevalent and especially where liver cancer is common.

Several other approaches have recently been used to devise and develop vaccines against hepatitis B. Firstly, since it has been shown that the separated coat proteins of the virus, containing the surface antigen, lead to the production of protective antibody, it is now possible to use purified, non-infective and inactivated small spherical hepatitis B surface antigen particles as vaccines.

NEW APPROACH

However, the preparation for use in people of such vaccines from human viral antigens not grown in cell culture, but obtained from plasma of infected persons — namely, from persistent carriers — is an entirely new approach in preventive medicine. It demands special consideration both for safety and for tests applied to the production and control of such preparations.

A second approach is aimed at the isolation of constituent polypeptides of the intact surface antigen particles for the preparation of vaccines. Vaccines prepared from such polypeptides would have an added margin of safety since they would be even less likely than the spherical particle vaccine to contain live virus or contaminating host proteins that might, in theory, lead to untoward reactions in some individuals.

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Recently, methods have been developed, at the Department of Medical Microbiology of the London School of Hygiene and Tropical Medicine, which permit the separation of large quantities of polypeptides free from contamination with host protein. Such preparations are being evaluated for their immunogenicity and safety.

BETTER CONTROL

An alternative source of hepatitis B surface antigen is the use of antigen produced by a cell line derived from human liver cancer cells. The advantage here, as was shown in a recently published study from the London School of Hygiene and Tropical Medicine, is that both the production and the quality of the antigen may be more precisely controlled.

The results obtained by the team of the school's Hepatitis Research Unit confirm that the surface antigen produced by this cell line is very similar to the antigen of the circulating particles in carriers.

Although rigorous purification of the antigen is required to eliminate any contaminants, including any nucleic acid fragments, the findings indicate that the relatively simple biochemical composition of the cell line antigen, and its ready availability, make this an attractive source of material either for a highly purified intact particle or polypeptide hepatitis B vaccine.

TOWARDS SYNTHETIC VACCINE

There are two other approaches to vaccine production, although perhaps more for the future. These include the potential use of hepatitis B proteins expressed in bacterial clones after the insertion of the genome of hepatitis B virus into plasmids — as demonstrated recently by Professor K. Murray of Edinburgh University, Scotland — and, perhaps even more attractive, the preparation of synthetic vaccines, which is being pursued at the London School of Hygiene and Tropical Medicine.

There are obvious advantages in attaining multivalent synthetic vaccines to replace current vaccines, which often contain many irrelevant microbial antigens, proteins and other material which contaminate the essential immunogen and which may lead to undesirable side effects. (6D380/SH) □□

H.E. Shaikh Hamad Bin Isa Al-Khalifa listening to an explanation from H.E. Dr. Ali Fakhro The Minister of Health about the Laboratory of the Isa Town Health Centre.