Occult hepatitis B virus infection among anti-HBc positive blood donors: Necessitates substitution of screening by HBV NAT

Safe blood transfusion still remains a major concern and so far all the efforts in this direction have failed to achieve zero residual risk of transfusion transmitted hepatitis B virus (HBV) infection. In this direction the recently published work by Silva et al. in Journal of Infection has revealed remarkable observations.[1] This report shows 3.3% HBV DNA positivity of the blood donor's samples that were anti-HBc positive, more enlightening finding is the HBV DNA positivity among the high level anti-HBs positive donors. At this tertiary care centre of Saudi Arabia out of 26 606 blood units collected during 2000–2003, isolated anti-HBc positivity was 3.2% and HBsAg positivity 1.9%, where as 10.1% of the blood units were anti-HBc and anti-HBs positive. As per policy of health ministry, the anti-HBc and anti-HBs positive blood units were utilized and the isolated anti-HBc blood units were rejected.[2]

The blood units which are anti-HBc and anti-HBs positive do not appear to transmit HBV infection and there is inverse correlation between anti-HBs level and infectivity, only 10% of the blood units with low level (<0.1 IU/ml) anti-HBs are infectious.[3] The observation by Silva et al. that HBV DNA positivity among anti-HBc and high level anti-HBs positive blood donors is a pointer towards the transfusion transmitted risk involved by transfusion of anti-HBc and anti-HBs positive blood units. Though the viral load in these samples was low (<1000 copies/ml) but this can be highly infectious if transfused to an immunocomprised patient. Considering the volume of infectious blood transfused any amount of HBV DNA will be infectious as the minimum infecting dose of HBV in chimpanzees is only 100 virus particles.[4] In many of the developed countries and most of the developing countries the blood units collected are still being screened for HBsAg, anti-HBc and anti-HBs by enzyme immuno assay. On many occasions the results are indeterminate and has to be repeated leading to higher per unit cost of blood screening and lot of rejection of the invaluable units of collected blood or exclusion of the generous donor because of isolated anti-HBc positivity and still the safety of transfusion transmitted HBV is compromised. This high rate of rejection of collected blood units and the exclusion of the anti-HBc positive blood donors leads to the unceasing blood shortage in the blood banks. The HBV screening policy for the collected units of blood needs reassessment in light of the present report[1] and HBV DNA testing should be preferred instead of three enzyme immuno assay tests. HBV DNA testing by NAT of all the collected units of blood should be adopted by all the blood banks, in order to possibly achieve zero risk of transfusion transmitted HBV infection and also to reduce the rejection rate of the precious units of collected blood by testing for anti HBc.

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Proposal for vaccination against SARS coronavirus using avian infectious bronchitis virus strain H from The Netherlands

The outbreak of severe acute respiratory syndrome (SARS) in 2003 has resulted in a number of infections and deaths among healthcare workers (HCWs) and those in contact with SARS-infected persons. The virus, now classified provisionally as a coronavirus in group 4, is highly contagious and treatment of infected persons has so far been disappointing.

The first evidence of successful treatment in monkeys (cynomolgus macaques) was reported recently using alpha-interferon (IFN-alpha)[4] administered from 1 to 3 days after experimental

exposure. This gave only some success, whereas the drug given at 3 days before experimental infection significantly reduced viral replication and excretion from their throats. Lung damage was also reduced by 80% as compared with non-treated monkeys.

In a review article on avian infectious bronchitis (IB) vaccine strain H,[1] various characteristics of this vaccine were outlined. Here I shall mention the most valuable properties of this IB vaccine so far known to underline the hypothesis that it may be beneficial in people at risk from SARS coronavirus.

(1) It has been observed that the IB vaccine H is able to protect against a broad spectrum of different heterologous serotypes of IB challenge viruses.[12] These serotypes differ in their surface proteins (spikes-S1) which are responsible for the induction of neutralizing antibody. Differences in S1 of only 2–3% can change the serotype of an IB virus.[3] Therefore, it can be concluded that the protection provided by the vaccine strain H is not only dependant on the production of neutralizing antibody, but is also due to the induction of other immunological reactions.

(2) The role of the nucleocapsid protein (N) is still not well understood but it may play an important role in protection, inducing specific cytotoxic T lymphocytes.[2,7-10] Thus, the vaccine strain H may be responsible for the induction of protection through its nucleocapsid protein.[13] In order to evaluate the importance of cellular mediated immunity (CMI) in protecting against IBV infections more studies would be necessary to explain all the mechanisms of cross-protection of the vaccine strain H, for instance the induction of interleukine 2 (IL 2).

(3) The observation that interferon (IF) is poorly induced by IBV and may not be induced by the vaccine strain at passage level 52, could be an indication that IF plays a limited role in heterologous protection.[5]

(4) In a study by Marra et al.[6] it was concluded that the SARS coronavirus is a novel coronavirus. Stavrinides and Guttman[11] concluded recently that the SARS coronavirus is mammalian-like through the replicase protein, and avian-like through the M and N proteins. They also observed a mammalian-avian mosaic in the S protein. These observations are of extreme importance to the consideration of an avian coronavirus as a possible candidate for a vaccine against SARS coronavirus.

In adequately equipped laboratory facilities (P4):

(a) It is proposed to use passage 52 of the H strain of vaccine in preliminary experimental studies in monkeys. This passage level has been chosen for its retention of cross-protective characteristics. The vaccine strain H at passage 120 induces only a low level of interferon[5] but has lost its heterologous protection characteristics due to the attenuation of the virus.

(b) In order to produce a valuable immunological reaction in monkeys with the IB H52 vaccine it will be necessary to inoculate a high dose of live virus vaccine, for example 10^8 median embryo infectious doses (100.000.000 EID_{50}) intranasally, intramuscularly and/or subcutaneously. It is not expected that the virus will be infectious for macaques, therefore, a high dose will be required in order to achieve an adequate response of the immune system. For more than 50 years avian IB infections have occurred worldwide and there are no reports of infection among human beings, including in poultry farmers or other people who have had direct contact with highly contagious IB viruses of chickens.

(c) In the study using alpha IF in macaques the amount of SARS coronavirus virus (SCV) used for challenge was 1×10^6 median tissue culture infectious dose ($TCID_{50}$) in 5 ml of PBS administered intratracheally.[4] However, it was not mentioned in that publication whether or not a prechallenge titration of this virus was performed. It is very important to establish the amount of challenge virus, which will provoke disease and eventually death. Therefore, before starting the experiment titration of the challenge virus in these monkeys should be performed in order to determine the amount of virus, which will produce clinical symptoms in not more than 90% of the infected animals. If an overdose is applied no real effect of the treatment will be demonstrable and if insufficient challenge virus is used no results will become available.

(d) It is of extreme importance that the H52 vaccine virus should be free of all microorganisms other than IB live vaccine virus, therefore, its production and passage in specific pathogen free (SPF) embryonated eggs is a prerequisite.

(e) It is proposed to challenge the vaccinated monkeys at 2 and 14 days after vaccination with a challenge SCV which has been titrated in macaques (see point c). This proposal is based on the likely immediate effect of the vaccine at 2 days through immunostimulation mechanisms and at 2 weeks, if protection is observed,

through the heterologous cross-protective activity of the vaccine virus.

It is without question that careful consideration by the relevant official health authorities must be given before an animal live virus vaccine is applied to human beings.

The application of the IB vaccine strain H in humans should be restricted and only HCWs and other persons at risk but not yet showing any signs of the disease will be considered as candidates for vaccination. If clinical symptoms are observed other methods of treatment, such as administration of alpha IF are recommended.

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