Guidelines for the Detection of a Common Source of Hepatitis B Virus Infections

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Hepatitis B virus (HBV) is an important threat to global public health. Despite the availability of safe and effective prophylactic vaccines, the existence of a large reservoir of chronic carrier patients impedes the eradication of this virus; therefore, HBV-related diseases still rank ninth on the global-ranking of causes of mortality (1). Moreover, HBV is considered the fifth most important infectious agent leading to death, with approximately 1 million HBV-related deaths occurring per year (2). Previous studies showed that the infectivity rate of HBV is higher than that of other blood-borne viruses. The risk of infection after percutaneous exposure to the 3 major blood-borne viruses—HBV, hepatitis C virus (HCV), and human immunodeficiency virus (HIV)—varies greatly, and the risk of infection in non-immune individuals exposed to HBV may be over 30% if the source is hepatitis B e antigen (HBeAg) positive. The average infection rate for HCV and HIV is 1.8% and 0.3%, respectively (3). The residual risk of post-transfusion infection with HBV is higher than that with HIV and HCV (4). Furthermore, the findings of recent studies indicate that HBV is more viable in needle syringes at room temperature than other blood-borne viruses (5). The transmission pattern of HBV in different geographical regions depends on the local prevalence of chronic HBV carriers. For instance, in high prevalence (prevalence rate > 8%) regions such as South Asia, mother-to-child (vertical) transmission is the main route of transmission; in European countries with a low prevalence (prevalence rate < 2%), sexual transmission and unsafe injection practices are the main modes of HBV transmission. Nosocomial transmission and unsafe injection practices are responsible for more than 60% of HBV infections in Central Europe (6). The main mode of HBV transmission in East Asia, a highly endemic region, is vertical. In West Asia and the Middle East, the route of transmission and HBV seroprevalence are variable depending upon the region. For instance, Iran has low HBV endemicity (around 2%), and intravenous drug injections, tattooing, and phlebotomy are considered major potential risk factors and transmission routes of HBV infection in the country (7). Further, socioeconomic statuses, life styles, occupations, and cultural attitudes in different ethnic groups greatly impact the route of HBV transmission in Iran (8).

During the last decade, several HBV outbreaks caused by nosocomial and iatrogenic transmissions have been reported in developed countries (9-16). These findings indicate that several routes of transmission (i.e. multi-
of infection is likely when the all the HBV strains of the outbreak cluster in a separate exclusive branch with a high bootstrap value and when the control and reference strains are distributed in different branches of the phylogenetic tree. In addition to phylogenetic analyses, other evolutionary tests should also be applied. It is useful to calculate the genetic distances between sequences in the HBV outbreak strain collection and in the control group. If the outbreak has a common source of infection, only a limited number of nucleotide variations will be observed among the sequences of the outbreak group and a much higher genetic divergence will be observed among the control samples. In addition, other evidences like a statistical model of distribution for infected cases over a period could support arguments for or against the existence of a common source. In conclusion, we would like to highlight some important steps to investigate an HBV outbreak, and either confirm or refute a common source of an HBV infection:

1. The study should be designed as a cohort study.
2. The control cases should be selected from HBV-infected patients living in the same geographical region who had no previous contact with the presumed source of infection.
3. Phylogenetic analysis should be conducted using a sufficiently large number of complete HBV genomes.
4. The genetic distances between sequences in the control group and the outbreak group should be calculated.
5. Additional analyses such as investigation of the distribution model of HBV-infected cases in the population over a period can help corroborate the existence of a common source of infection.

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