

## Viral Coinfections

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### Abstract

The occult infections are widely found in co-infections with viral agents of hepatitis C (HCV) and human immunodeficiency virus (HIV). These three viruses share similar transmission routes, so that cases of co-infections are common. People infected with HCV or HIV is more prone to infection occult. The cases of co-infections are characterized by an exacerbation of liver disease and a very strong increase in the risk of developing hepatocellular carcinoma HCC.

**Keywords:** Hepatitis C; HIV; Liver; Carcinoma

### Coinfection HBV/HCV

The hepatitis C virus belongs to the family Flaviviridae. It is estimated that 130 million people are infected with HCV worldwide and that cases of co-infections HBV / HCV concern 7-20000000 people. These two viruses share the same liver tropism. The case of co-infections is associated with increasing severity of liver disease, faster development to stages of fibrosis, cirrhosis and HCC than in the case of mono-infection whether HBV or HCV [1]. Studies conducted *in vitro* have shown that HCV played a dominant negative effect which inhibit HBV replication and which is mediated by the HCV Core protein [2,3]. A second study, meanwhile, found the opposite effect, suggesting that HBV inhibit replication of HCV [4]. However, or interactions between HBV and HCV are still very difficult to study and this mainly because of lack of appropriate studies *in vitro* systems. BELLECAVE team was able to demonstrate that these two viruses could replicate in the same cell without bias interact directly. Viral interference would be indirect and mediated by molecular mechanisms that might be responsible for these mutual inhibitions observed [5-8]. HCV is capable of inducing an interferon response, then we can think that this molecular mechanism could contribute to the establishment of occult HBV infection in co-infected patients. The data show that patients infected with HCV population represent a particular risk for the OBI. It is very likely that viral interference mechanisms contribute to the status occult but surely not explain all cases. In this context of HBV DNA is detectable in a third of HCV carriers + / AgHBs- Mediterranean [9,10], an even higher prevalence of between 37 and 95% has been reported in Asian populations [11].

### Coinfection HBV/HIV

HIV belongs to the lentivirus family, it shares only few features with HBV. However, each of these viruses have a reverse transcription step which is one of the major targets for antiviral therapy. Currently 33 million people worldwide are infected with HIV, the global distribution of the virus is very heterogeneous. In areas of high endemicities for HIV and HBV, it is estimated that 6-14% of patients infected with HIV + are also HBV [12]. In areas of low prevalence cases of co-infections are less common. If coinfection with HBV appears to have little impact on diseases related to HIV infection the opposite is not true:

- The likelihood that an HBV infection progresses to acute ÷ chronic HBV infection is higher among the infected persons are with HIV [13].
- During chronic infection of HBV replication is higher.
- The probabilities of 84 anti-HBs or anti-HBe seroconversion in people are lower than in coinfectées mono-infectées HBV.

- The progression to fibrosis and cirrhosis is faste

The phenomena of HBV co-infection/AIDS, however, remain poorly understood. The treatment of co-infections is tricky

- Molecules active against both viruses, targeting reverse transcriptase step exist and are 'well tolerated', but the risk of the emergence of mutant HBV or HIV resistant to these molecules is very high.
- Certain drugs used in antiretroviral therapy may be hepatotoxic.
- There are many interactions between drugs used against both viruses. With the improvement of anti-HIV treatment, co-infections with viral hepatitis (HBV and HCV) have become one of the new major causes of morbidity and mortality in HIV (+) patients. This is only true for people in developed countries where access to treatment is facilitated.

The prevalence of occult infection with HBV has been widely sought in HIV (+) patients and according to studies it varies between 0 and 89% [14]. Lack of standardized tools for the detection of occult infection is the cause of such an aberrant gap. However, the HIV infection is clearly an infection risk factor occult HBV and prevalence in HIV (+) patients is higher than what is found in the general population [15]. In HIV (+) patients, it is not known if an indirect molecular interaction for example between the two viruses exists and could inhibit HBV replication. A major problem in the case of co-infections HIV / HBV occult reactivation of HBV infection. The reactivation phenomena of occult HBV infections are not fully understood but are frequently observed following discontinuation or interruption of HAART against HIV [16]. Although patients are treated against HIV with active molecules also against HBV, HBV reactivation resistant strain is rare. Interestingly cases of reactivation of occult infections were reported independently of the appearance of resistance mutations in the lamivudine, but associated with the disappearance of anti-HBs antibody or immune depressed states [17]. The molecular analysis of HBV strains shown in these two studies had shown the mutation accumulation in the HBsAg

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at key positions Y100C, P120T, sK122R, sD144A. In two studies are reported sK122R mutations and involve genotypes A, substitutions extremely rare in this genotype. The absence of antibody at the time of reactivation was not possible to perform functional analysis of the recognition of HBsAg and anti-HBs antibodies of patients. One can imagine that the appearance of mutation is the result of immune selection pressure on the virus. But that reactivation of HBV was made possible by the absence of anti-HBs antibodies. The reactivation of occult infections in HIV patient's phenomena (+). Another study showed that reactivation of occult infection in two HIV (+) patients was independent of resistance mutations to lamivudine and state of immunosuppression [18].

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