# Exposure to hepatitis B virus activates immunity in young people, suggesting benefits for earlier treatment

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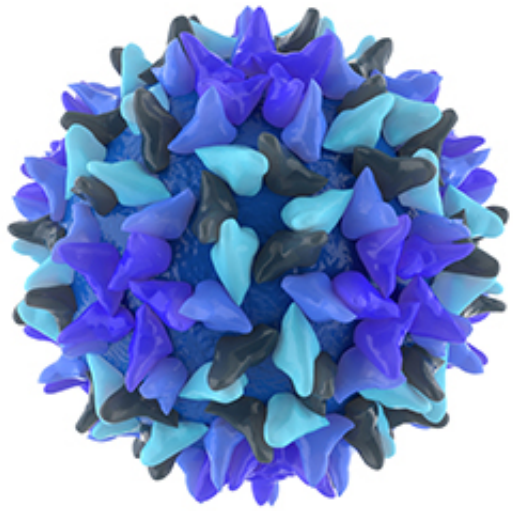

A computer-generated image of the hepatitis B virus. Credit: iStockphoto/Thinkstock

Infectious disease experts have long thought that children, teenagers and young adults who are chronically infected with the hepatitis B virus (HBV) lack the immune cells needed to fight this pathogen. As such, physicians currently withhold therapeutic interventions from younger patients until they have reached an advanced age—typically around 30 years old—at which time the immune system is thought to have 'awakened' to the virus.

Yet, contrary to the conventional medical wisdom, new research from the A*STAR Singapore Institute for Clinical Sciences (SICS) indicates that there is no such inherent age-associated period of so-called 'immune tolerance' to HBV. In fact, older people with chronic hepatitis B seem to have a weaker immune response, represented by weaker antiviral T-cell repertoires, than younger individuals infected with the virus.

"These findings can have major implications for the clinical management of chronic hepatitis B infections," says the SICS's Antonio Bertoletti, who led the research. "It might be better to start treatment early, as young people have a less compromised HBV-specific immune response, and [because] functional recovery of HBV-specific T cells is associated with successful control of the infection."

Scientists from Bertoletti's laboratory, together with clinical collaborators in the UK, isolated T cells from 44 people with chronic HBV infections between the ages of 10 and 30, the majority of whom were of Asian descent. Around 75% of the world's 400 million people with chronic hepatitis B can be found within the region of Asia.

They compared the immune samples to those from healthy age-matched controls, and showed that young patients infected with HBV expressed increased levels of virus-associated T cells, and these T cells displayed the ability to expand and produce pro-inflammatory signaling molecules known as cytokines, which are involved in antiviral responses. Furthermore, these HBV-specific T cells became more dysfunctional with age, the authors found, suggesting that the longer a patient is left untreated, the less effective the immune system becomes at clearing the virus.

The study upends the idea that immune recognition of HBV is somehow averted in certain individuals, thus indicating that all patients, regardless of age, could be suitable for treatment. It also highlights the inadequacy of measuring biomarkers of liver inflammation—the current proxy for immune activity in people with chronic hepatitis B infections. Such

indicators are typically absent in young patients despite the study's suggestion of the presence of active T-cell responses to the virus.

**More information:** Kennedy, P. T. F., Sandalova, E., Jo, J., Gill, U., Ushiro-Lumb, I. et al. Preserved T-cell function in children and young adults with immune-tolerant chronic hepatitis B. *Gastroenterology* 143, 637–645 (2012). dx.doi.org/10.1053/j.gastro.2012.06.009

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