

Slightly abnormal blood test may point to a 'silent' form of hepatitis B

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Silence isn't always golden. In the case of hepatitis B, people with a past — and seemingly resolved — infection often don't know that they still have a silent form of the disorder. Now, new research suggests that slightly abnormal results from a blood test, once thought to be a fleeting curiosity, can tip off doctors to the presence of this potentially infectious and lethal viral renegade.

In the first study to screen for multiple markers of hepatitis A, B and C in more than 100 patients entering an opiate-addiction treatment program, researchers at Rockefeller University were able to look at the coinfection of these liver diseases and reveal a startling fact: that a high percentage of recovering injection-drug users who had hepatitis B in the past are still infected with hepatitis B DNA in the absence of actively replicating virus.

This report, led by Mary Jeanne Kreek, head of the Laboratory of the Biology of Addictive Diseases, raises a public health concern in the midst of an ongoing debate about whether to treat patients with this asymptomatic yet potentially infectious disease. The scientists published their findings in the March 17 issue of *Addiction*, making a broader cross section of clinicians and researchers aware of the ethical and medical concerns surrounding silent hepatitis B.

Kreek and her colleagues, including Gavin Bart, a coauthor of the study, identified and first reported on the silent form of the virus in 2002, when blood tests from patients with past hepatitis B infection came back with



a slightly unusual test pattern. Those with a past infection usually develop two main hepatitis B antibodies, molecules made by the immune system to fight off the virus when it is actively replicating. Kreek and Bart, however, found that 40 percent of the patients tested for these markers had one antibody, not two.

"This test pattern is slightly unusual but normally, when you see this pattern you would say this person has had past infection and you would look no further,"? says Bart, who is now the director of the division of addiction medicine at the Hennepin County Medical Center in Minnesota and an adjunct faculty member at Rockefeller University.

But Kreek and Bart went further.

In addition to screening for hepatitis B antibodies (among other protein markers of the disease), the researchers, in collaboration with David Ho, scientific director of the Aaron Diamond AIDS Research Center, created a highly sensitive test to look for low levels of hepatitis B DNA that wouldn't typically be detected by commercially available DNA kits. When a patient recovers from a hepatitis B infection, the antibodies usually neutralize the viral DNA, according to Bart. Yet, of the patients with the unusual test pattern, Kreek and Bart found that 20 of them, or 60 percent, had hepatitis B DNA.

"That's a huge percentage," says Kreek, who is also Patrick E. and Beatrice M. Haggerty Professor and senior attending physician at Rockefeller. "When you think about the number of persons with heroin addiction, this adds up to a lot of people."

The presence of hepatitis B DNA in the absence of actively replicating virus means that these patients are not ill with the disease but could be infectious. However, in the event that a patient requires immunosuppressive therapy for cancer or has an immune disorder such



as AIDS, the virus could conceivably replicate and further compromise the patient's health. Kreek and Bart also report that 13 of the 20 patients who had silent hepatitis B also had chronic hepatitis C, an entirely different liver disease that affects more than 80 percent of injectiondrug users. Labs around the world, including Kreek's, have shown that patients coinfected with silent hepatitis B and hepatitis C may respond less well to treatment than those without the silent virus.

While some physicians recommend treating silent hepatitis B as soon as it is diagnosed, others recommend treating it only if patients develop other immune-compromising illnesses in order to avoid unforeseen complications and limit costs. However, it is still unclear whether treatment of silent hepatitis B will improve the response to treatment for hepatitis C. Fortunately, a vaccine against hepatitis B is available and can help protect people from becoming infected with the virus. "That's why we are recommending that everyone get vaccinated," Kreek says, referring to her team. "Everyone."

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