**Hepatitis B in a vaccinated soldier: A case report**

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**Competing Interests:**

The authors have no competing interest to declare.

**Word count** *(excluding title page, abstract, references, figures and tables):*

1198 of 1200 limit

**Keywords:** Hepatitis B, Hep B, Vaccine.

**ABSTRACT:**

Assessing for an adequate immunological response to a pre-exposure course of Hepatitis B vaccine is not routinely recommended in all vaccinated individuals. Current UK guidelines advise checking Hepatitis B surface antibody titres only in those considered at high occupational risk such as healthcare and laboratory workers. We present a case of an infantry soldier who developed acute Hepatitis B despite having a complete course of Hepatitis B vaccinations. This case emphasises that Hepatitis B is still an important differential diagnosis for all returning military personnel who present with compatible symptoms despite being vaccinated.

**INTRODUCTION:**

Hepatitis B (HBV) is a viral infection of the liver, which predominantly causes a flu-like illness associated with anorexia, nausea and right upper abdominal pain, with jaundice occurring in approximately 30-50% of adults*.*[1](#_ENREF_1) However, severe disease may occasionally lead to fulminant hepatic necrosis that can be fatal.[2](#_ENREF_2) Most individuals clear the infection but approximately 5% of previously healthy, infected adults develop chronic infection.[3](#_ENREF_3) This is defined as the persistence of Hepatitis B Surface Antigen (HBsAg) in the serum for longer than six months.[2](#_ENREF_2) Chronic HBV can lead to cirrhosis and increased the risk of developing hepatocellular carcinoma.[2](#_ENREF_2)

The virus is usually transmitted by parenteral exposure to infected blood or body fluids; with an average incubation period of 60-90 days but this can range from 40-160 days.[1](#_ENREF_1) It can also survive outside the body for up to seven days.[4](#_ENREF_4) Whilst the prevalence of Hepatitis B in the United Kingdom is low, believed to be between 0.1% and 0.5%,[5](#_ENREF_5) it is much higher in other parts of the world.[1](#_ENREF_1) Such as the Western Pacific region, Africa and South-East Asia; where 6.2%, 6.1% and 2% of the general population are infected, respectively.[6](#_ENREF_6)

An inactivated HBV vaccine, which consists of three doses for pre-exposure immunisation, is available and recommended for those at increased risk of HBV because of their lifestyle, occupation or other factors. Table 1 lists groups recommended to have the Hepatitis B vaccine under current Public Health England recommendations. The vaccine has been effective in reducing the incidence of HBV and hepatocellular carcinoma, however, 10-15% of adults have an inadequate immune response to the initial three doses.[1](#_ENREF_1)[2](#_ENREF_2)

**Table 1:** Public Health England recommendations for the use of the Hepatitis B Vaccine, Adapted from The Green Book, Hepatitis B, Chapter 18[1](#_ENREF_1)

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| --- |
| **Recommendations for the use of the vaccine:** |
| **Born on or after 1 August 2017*** Infants as part of the routine childhood immunisation programme (pre-exposure)
* Individuals at **high risk\*** of exposure to the virus or complications of the disease (pre-exposure)
* Individuals who have already exposed to the virus including infants born to hepatitis B infected mothers (post-exposure)

**Born up to and including 31 July 2017*** Individuals at **high risk\*** of exposure to the virus or complications of the disease (pre-exposure)
* Individuals who have already exposed to the virus including infants born to hepatitis B infected mothers (post-exposure)
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| ***\*Those considered at high risk of exposure to the virus or complications of the disease:**** Persons who inject drugs
* Individuals who changed sexual partners frequently
* Close family contacts of a case or individual with chronic hepatitis B infection
* Family adopting children from countries with a high or intermediate prevalence of HBV
* Foster carers
* Individuals receiving regular blood or blood products and their carers
* Patients with chronic renal failure
* Patients with chronic liver disease
* Inmates of custodial institutions
* Individuals in residential accommodation for those with learning difficulties
* People travelling to or going to reside in areas of high or intermediate prevalence
* Individuals at occupational risk: *healthcare worker in UK and overseas, laboratory staff, staff of residential and other accommodation for those with learning difficulties, occupation risk i.e prison staff, morticians, embalmers, emergency services.*
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Current UK guidelines recommend checking antibody titres one to four months after completing a primary course of vaccine only for those at risk of occupational exposure, particularly healthcare and laboratory workers, and provide a booster at this time if the response in inadequate.[1](#_ENREF_1) A 5-year booster vaccine is recommended for those who are at continued risk of Hepatitis B but fall outside the previous category; however antibody titre levels (Hepatitis B surface antibody, anti-HBs) to assess response are not recommended at any point.[1](#_ENREF_1)

We present a case of an infantry soldier who developed acute Hepatitis B despite having a complete course of Hepatitis B vaccinations.

**CASE REPORT:**

A twenty-four year old male infantry soldier with no medical history but recent occupational travel presented with acute jaundice and flu-like symptoms.

Approximately six weeks after returning from jungle warfare training in Thailand (December 2017), he developed central abdominal pain associated with a seven-day history of diarrhoea. He underwent a laparoscopic appendectomy that histologically demonstrated severe acute diffuse suppurative appendicitis and peri-appendicitis with no perforation. During this admission his liver function tests were deranged, 6 February 18, Alanine Transaminase (ALT) 933 IU/L, Alkaline Phosphatase (ALP) 96 IU/L, Bilirubin 51 umol/L. Synthetic liver function was normal; Prothrombin time (PT) 14.5 sec, Activated Partial Thromboplastin Time (APTT) 26.1 secs and Albumin 52g/L.

Twenty-four hours after discharge he developed epigastric pain, associated with nausea and flu-like symptoms. Within a further seventy-two hours he became acutely jaundice and presented to a different hospital. He remained apyrexic with no focal symptoms. He denied a paracetamol overdose, excessive alcohol intake, smoking, recreational drug use, recent tattoos, piercings or injecting drugs. He had a single heterosexual partner for the past two years and denied sexual activity with men or sex workers. He had travelled to Thailand in November 2017 for occupational reasons (jungle warfare training with no freshwater exposure) and returned in December 2017. During the trip he had diarrhoea and vomiting for approximately 24 hours (4December 17); otherwise he was well.

His liver function test were markedly deranged on admission; ALT 8640 U/L, ALP 241 U/L, Bilirubin 130 umol/L and albumin 44 g/L. Positive findings on examination were jaundice and two small lymph nodes in the left inguinal canal. A thickened gallbladder but no signs of stones or biliary dilatation were seen on liver ultrasound.

Hepatitis B serology, core IgM antibody and HBsAg, were positive for acute infection. Serology was negative for Human Immunodeficiency Virus (HIV), Syphilis and Hepatitis C (HCV). Approximately six weeks later his symptoms were much improved; mainly fatigue and intermittent nausea persisted. Liver function tests had almost normalised; ALT 36 U/L, ALP 109 U/L, GGT 74 U/L, bilirubin 26 umol/L and albumin 51 g/L.

All MOD personnel are offered Hepatitis vaccination. The patient received 3 separate doses of Hepatitis B vaccine in June 2015, July 2015 and April 2016. In line with UK guidelines his anti-HBs levels were not checked.

**DISCUSSION:**

The Hepatitis B vaccine is highly effective for the prevention of HBV, however between 10-15% of adults have an inadequate immune response to the initial vaccine course.[1](#_ENREF_1) Vaccine-induced antibody responses to HBV vary greatly, but it is assumed with greater confidence that immunity has been established if anti-HBs levels are above 100 mIU/ml and these individuals do not require any further primary doses.[1](#_ENREF_1) A five-year booster is still recommended. Patients with an anti-HBs level between 10-100mIU/ml should have a fourth primary vaccine and a five-year booster.[1](#_ENREF_1) An anti-HBs less than 10 mIU/ml is classified as a non-response and a repeat course (three doses) of the vaccine is recommended, followed by re-testing the anti-HBs at one to four months after the second course.[1](#_ENREF_1)If they are still a non-responder following this and have no markers or current or past infection, it is recommended they receive Hepatitis B Immunoglobulin (HBIG) if they are exposed to the virus.[1](#_ENREF_1)Such information on anti-HBs levels aids appropriate decisions to be made concerning post-exposure prophylaxis following known or suspected exposure to the virus. Patients with unknown anti-HBs levels would not necessarily receive HBIG post-exposure.

Current UK guidelines recommend checking antibody titres one to four months after the completing a primary course of vaccine only for those a risk of occupation exposure, particularly healthcare and laboratory workers.[1](#_ENREF_1) This excludes many individuals that may be non-responders to the vaccine and thus at higher risk of contracting HBV.

Literature suggests that risk factors for a poor response to the vaccine include age over forty years, obesity, smoking, alcoholics, those with advanced liver disease, immunosuppressed and renal dialysis patients.[7](#_ENREF_7)[8](#_ENREF_8) These do not apply to the case we present; nevertheless it is evident the patient was a ‘non-responder’ to the primary course of the HBV vaccine.

Anti-HBs levels were not tested in this patient after primary vaccination. This is in line with current UK guidelines; as his occupation would not be considered as high risk as those in healthcare or laboratory work. Although this case report is not sufficient evidence to warrant a change in current anti-Hbs guidelines, it highlights vaccine non-response and emphasises Hepatitis B as a differential diagnosis to bear in mind when investigating acute jaundice in vaccinated patients. Particularly those in occupations that require them to travel to areas with a higher prevalence of HBV. Furthermore given this patient did not have risk factors predisposing him as a ‘vaccine non-responder’, this case highlights the continued importance of using additional preventative measures even in those vaccinated; particularly if anti-HBs levels are not routinely checked. This case highlights that Hepatitis B is an important differential in all returning military personnel presenting with febrile jaundice despite vaccination.

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