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# Hepatitis B virus (HBV) and hepatitis C virus (HCV) infections in health care workers (HCWs): guidelines for prevention of transmission of HBV and HCV from HCW to patients

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[1] The consensus meeting and final report was organised by R.N. Gunson, D. Shouval and W.F. Carman. R.N. Gunson and D. Shouval are primary co-authors of this report.

*Abbreviations:* Anti HBc, antibody to hepatitis B core protein is a marker of current (in the presence of HBsAg) or past infection with HBV; Anti HBe, antibody to hepatitis e antigen can be a marker for low infectivity (in the presence of HBsAg, especially in wild type infection); Anti HCV, antibody to HCV is a marker of current (in the presence of HCV RNA) or past infection with HCV; CDC, centres for disease control; EPP, exposure prone procedures is the term for invasive procedures where there is potential for contact between the skin of the HCW and sharp surgical instruments, needles or sharp tissues in body cavities or poorly visualised/confined body sites; HBeAg, hepatitis B e antigen is a marker of level of infectivity; HBsAg, hepatitis B surface antigen detectable in serum in the majority of HBV infected patients; HBV, hepatitis B virus; HBV DNA, hepatitis B nucleic acids. Can be used to monitor infectivity

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**Abstract**

The transmission of viral hepatitis from health care workers (HCW) to patients is of worldwide concern. Since the introduction of serologic testing in the 1970s there have been over 45 reports of hepatitis B virus (HBV) transmission from HCW to patients, which have resulted in more than 400 infected patients. In addition there are six published reports of transmissions of hepatitis C virus (HCV) from HCW to patients resulting in the infection of 14 patients. Additional HCV cases are known of in the US and UK, but unpublished. At present the guidelines for preventing HCW to patient transmission of viral hepatitis vary greatly between countries. It was our aim to reach a Europe-wide consensus on this issue. In order to do this, experts in blood-borne infection, from 16 countries, were questioned on their national protocols. The replies given by participating countries formed the basis of a discussion document. This paper was then discussed at a meeting with each of the participating countries in order to reach a Europe-wide consensus on the identification of infected HCWs, protection of susceptible HCWs, management and treatment options for the infected HCW. The results of that process are discussed and recommendations formed. The guidelines produced aim to reduce the risk of transmission from infected HCWs to patients. The document is designed to complement existing guidelines or form the basis for the development of new guidelines. This guidance is applicable to all HCWs who perform EPP, whether newly appointed or already in post.


*Keywords:* Virus; Hepatitis; HCW; Guidelines; Prevention; Europe

## 1. HBV and HCV in HCW

### *1.1. Methods*

In order to reach a consensus statement on the management of health care workers (HCWs) infected with hepatitis B virus (HBV) and hepatitis C virus (HCV), experts in blood borne viruses in HCWs from around Europe and the US were questioned on their national protocols. A questionnaire was devised which requested information on various aspects of HCW management including:

a) Estimated seroprevalence of HBV and HCV in HCWs and the general population.
b) HBV vaccination policies for HCWs.
c) HBV and HCV screening policies for HCWs.
d) Management and restriction of infected HCWs.
e) The lifting of restrictions.
f) Unpublished data on HBV and HCV transmissions to patients.
g) Availability, validation and standardisation of viral load assays for HBV and HCV.

In total, 16 countries were sent the questionnaire and of these, 13 supplied comprehensive answers (Table 1). The replies given by each participating country formed the basis of a literature review. This paper was then discussed at a meeting with each of the participating countries in order to reach a consensus on the identification of infected HCWs, protection of susceptible HCWs, occupational management and treatment options for the infected HCW.

## 2. HBV transmission from HCW to patients

### *2.1. Protecting the patient from the infected HCW*

Since the introduction of serologic testing in the 1970s there have been over 45 reports of HBV transmission from HCWs to patients, which have resulted in more than 400 infected patients (Mele

and viral load (quantitative PCR); HCV, hepatitis C virus; HCV RNA, hepatitis C RNA is a marker of active replication and infectivity; HCW, health care workers include all individuals, including students and trainees, whose activities involve contact with patients or body fluids from patients; HICPAC, CDC Hospital Infection Control Practices Advisory Committee; IFN, interferon is an antiviral agent used in the treatment of both HBV and HCV infections; IVDU, intravenous drug user; Peg-IFN, pegylated interferon alpha is a modified interferon with prolonged action used in the treatment of HCV.

Table 1
The countries participating in this consensus meeting.

| Countries participating | Countries not participating |
|---|---|
| Austria | Spain |
| Belgium | Switzerland |
| France | Turkey |
| Germany | |
| Greece | |
| Holland | |
| Israel | |
| Italy | |
| Portugal | |
| Republic of Ireland | |
| Sweden | |
| UK | |
| US | |

et al., 2001). The majority of the documented HBV transmissions have been associated with HCW performing exposure prone procedures (EPP) and transmission rates have varied between 6 and 15%. Most of these occurred prior to 1991, before hepatitis B vaccination was widely used and before standard (universal) infection control precautions were implemented. Since 1991, 11 episodes of HBV transmission to patients from infected surgeons have been reported, nine from the United Kingdom (Oliver et al., 1999; Sundkvist et al., 1998; Molyneaux et al., 2000; The Incident Control Team, 1997; Personal communication with Dr W.F. Carman and Personal Communication with Dr H. Nicholas), one from the Netherlands (Spijkerman et al., 2002), and one from the United States (Harpaz et al., 1996). All but one of the cases in the United Kingdom involved HCWs who were infected with pre-core mutants and were negative for HBeAg.

Data from our questionnaire shows that the seroprevalence of practising HBsAg positive HCWs in some countries can be high, ranging from 0.3 to 3% (Fig. 1). Consequently, HBV infected HCWs may still pose a significant risk to patients in some participating countries. Evidence of past infections is significantly higher, ranging from 4 to 30%.

Protecting the patient from the infected HCW relies upon three main strategies: preventing infection in the HCW, identifying infected HCWs and restricting infected HCWs from performing high-risk procedures likely to transmit the virus. However, there are significant differences in the number and types of prevention policies implemented by different countries.

## 3. Preventing HBV infection in the HCW

Reducing the incidence of HBV infection in HCWs will reduce the risk of transmission to patients. At present protecting the HCW from infection comprises two core elements: adoption of standard precautions and HBV vaccination.

### *3.1. Standard precautions*

In 1987 the Centre for Disease Control (CDC) developed universal precautions aimed at protecting both HCWs and patients from infection with blood borne pathogens in the health care setting. These recommendations highlight that blood is the most important source of HBV infections and preventing exposure to blood is as important as vaccination. In 1995 the CDC Hospital Infection Control Practices Advisory Committee (HICPAC) introduced the concept of standard precautions, which place all universal precautions and body substance isolation guidelines into a single set of precautions. Standard precautions should be applied to all patients receiving medical care regardless of their presumed infectious status. Blood, body fluids (including secretions and excretions), broken skin and mucous membranes are considered potentially infectious. The core elements are hand disinfection after contact with patients, use of barrier precautions (gloves), and minimal manipulation and safe disposal of sharp instruments. The implementation of standard precautions has been shown to reduce the risk of blood exposure. Studies (Beltrami et al., 2000) from the US using self-reported questionnaires showed that the introduction of standard precautions reduced the mean number of blood exposures per HCW from 35.8 to 18.1 per year. However, the implementation of standard precautions alone will not prevent all transmissions to, and from, HCWs.

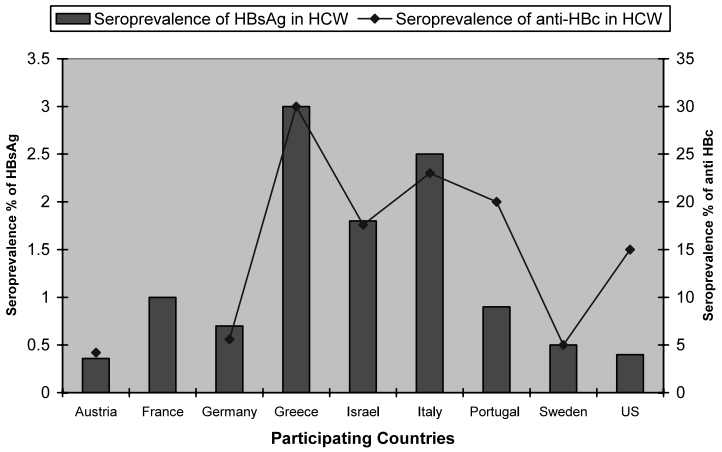


Fig. 1. The seroprevalence of HBsAg and anti-HBc in HCW. The UK, Republic of Ireland, Holland and Belgium did not have any recent data. France had no data on the sero-prevalence of anti-HBc in HCW.

### 3.2. HBV vaccination

Reducing the incidence of HBV infection in HCWs by vaccination will reduce the risk to patients of acquiring HBV. The HBV vaccine is both safe and efficacious (provides protective response in 80–95% of those vaccinated) and provides protection both pre- and post-exposure to infected material (Bonanno and Bonaccorsi, 2001). Studies (Mahoney, 1999; Whittle, 2002; European Consensus group on Hepatitis B Immunity, 2000) carried out in high-risk groups have demonstrated that persons who develop anti-HBs titres $>10$ IU/l will have virtually 100% protection against acute disease and chronic HBV infection. After vaccination protective antibody levels may decrease to low or undetectable levels in 13–60% of persons after 9–15 years, however, long term follow up studies in HCW and other risk groups have demonstrated that the protective antibody response and immune memory remains intact (Table 2). Twenty years after hepatitis B vaccine became commercially available, no breakthrough chronic HBV infections have been documented in vaccinated adults who responded to the first series. Although asymptomatic seroconversions have been detected, it is unclear whether these infections included a viremic phase during which HBV could have been transmitted to others. Currently, there is no proof that booster injections are indicated for the first two decades after successful immunisation. Further studies will determine the need for booster doses in the third decade post-vaccination.

#### 3.2.1. Which HCWs should be vaccinated

Ideally all HCWs should be vaccinated against HBV. Although transmission to patients has occurred during non-EPP (Smellie, 2002) most transmissions have occurred during EPP (Heptonstall, 1991). Therefore, although vaccination should be offered to all HCWs who work with blood or sharps, it would be most useful to vaccinate HCWs involved in EPP. In 1991, the US required that employers offer hepatitis B vaccine to all persons at occupational risk of HBV infection. As a result of this regulation, which increased immunisation to $>70\%$ of at-risk HCWs, and widespread adoption of standard precautions, the estimated annual number of newly infected HCWs in the US declined from $>10\,000$ in 1983 to $<400$ in 2001 (CDC, unpublished data). Vaccination should occur before a HCW begins specialist training for an EPP position and should include all medical, nursing and dental students, as they will be at risk of acquiring HBV during the course of their training.

#### 3.2.2. Mandatory or voluntary vaccination policies

Voluntary vaccination approaches have been shown to be ineffective. Recent data from Canada

Table 2
Long term protection among adult responders to primary HBV vaccination

| Group | Number of patients | Length of follow up (years) | Asymptomatic infections | Chronic infections |
|---|---|---|---|---|
| HCW | 144 | 11 | 0 | 0 |
| Homosexual men | 127 | 11 | 0 | 0 |
| Eskimos | 1194 | 10 | 13 | 0 |
| Homosexual men | 634 | 9 | 48 | 0 |
| Military | 190 | 6 | 4 | 0 |
| Medical students | 100 | 5 | 1 | 0 |
| HCW | 41 | 5 | 0 | 0 |
| HCW | 143 | 5 | 4 | 0 |
| HCW | 32 | 5 | 0 | 0 |
| HCW | 31 | 7 | 0 | 0 |
| HCW | 72 | 5 | 0 | 0 |

Table reproduced from F.J. Mahoney.

highlighted that between 10 and 60% of all EPP-performing HCWs were not vaccinated under a voluntary system (Paton et al., 2002). Therefore, optimal vaccine coverage would be best achieved by the mandatory vaccination of all HCWs who are training to perform EPP. However, the mandatory vaccination of HCWs raises many human rights issues. Consequently, HBV vaccination should be highly recommended in HCWs who perform EPP and those who refuse HBV vaccination should be tested for HBV to determine their infectivity status.

### 3.2.3. *Follow up of vaccination*

All HCWs performing EPP should have their response documented in order to differentiate responders, hypo-responders (10–100 IU/l) and non-responders. Non-responders ( $<10$ IU/l) to the HBV vaccine should be given up to three further doses of HBV vaccine and then have their response re-checked. A study (Averhoff et al., 1998) of 2000 vaccinated HCW showed that 47% of non-responders would develop seroprotection after one additional dose; 42% of the remainder would respond after a further two additional doses, resulting in a cumulative response rate to three additional doses of 69%.

True non-responders are susceptible to HBV infection and should be screened for HBV infection at regular intervals (to be decided by each individual country) and after any significant exposure.

Hypo-responders should be given a further dose of vaccine in order to boost the anti-HBs response to $>100$ IU/l. Anti-HBs levels of $>100$ IU/l are desirable as they are less likely to reflect non-specific reactivity in the assays, take into account inter-test variation, and are generally above the levels commonly seen in HBV carriers with concurrent HBsAg and anti-HBs. Cases of HBV infection in HCWs accompanied by high titres of anti-HBs are rare (Personal communication with Dr W.F. Carman). For example, recently in the UK a surgeon transmitted HBV to three patients, one of whom subsequently died, despite the surgeon having a documented anti-HBs level of 252 IU/l, following vaccination. After a fourth dose anti-HBs levels between 10 and 100 IU/l should be confirmed using another assay to take into account specificity differences between assays.

### 3.2.4. *Screening for HBV in HCW with a hypo-response to vaccine*

Anti-HBs levels between 10 and 100 IU/l may falsely suggest immunity (i.e. non-specific results). Furthermore, it may mask HBV infection as a number of HBV carriers and those with acute infection have been shown to produce anti-HBs at low levels (Ngg and Saw, 1994; Wang et al., 1996; Hayashi et al., 1990; Tsang et al., 1986; Zaaijer and Lelie, 2002). Therefore, all EPP performing HCWs with an anti-HBs level of 10–100 IU/l should be screened for HBV infection.

### 3.3. Recommendations

- All HCWs should apply standard precautions to every patient.
- It is highly recommended that all HCWs in contact with patients, blood or other body secretions should be vaccinated for HBV and have their response checked within a month after the final dose. Initial non-responders should be given one to three more doses of vaccine and have their response determined. Non-responders should have an individual risk assessment based on job description to determine whether they will be investigated for persistent HBV infection.
- All HCW who perform EPP (including dental, medical and nursing students) should provide proof of anti-HBs response before starting a post. If negative or unavailable then the HCW should receive a booster dose of vaccine and have their response determined at least 1 month after. Continued non-responders should be investigated for persistent HBV infection (presence of HBsAg or anti HBc in the absence of HBsAg). Those found to be HBsAg negative should be allowed to perform EPP but should be tested regularly (frequency to be decided by each individual country) and after any significant exposure.
- All HCWs who refuse to be vaccinated must understand the implications of his/her actions.
- The implication of the anti-HBs response differs between non-EPP and EPP HCWs.
  - i) In non-EPP HCWs:
    - 1) Anti-HBs levels $>100$ IU/l are desirable.
    - 2) HCWs with anti-HBs levels between 10 and 100 IU/l should have their response confirmed using another assay. A further dose should be given.
    - 3) HCWs with anti-HBs levels $<10$ IU/l should be given up to three additional boosters and have their response re-checked.
    - 4) HCWs with anti-HBs levels $<10$ IU/l (non-responder) should consult a specialist advisory group to assess risk.
  - ii) In EPP performing HCWs:
    - 1) Anti-HBs levels $>100$ IU/l are preferred.
    - 2) HCWs with anti-HBs levels 10–100 IU/l should be given a booster and have their response re-checked using another assay.
    - 3) All HCWs with a confirmed anti-HBs level between 10 and 100 IU/l should be tested for HBsAg. However, it is not imperative that anti-HBs titres reach a level of $>100$ IU/l.
    - 4) Those HCWs who have anti-HBs levels $<10$ IU/l (non-responders) should be tested for HBsAg. Those found to be negative should consult a specialist advisory group to assess risk.

## 4. Managing the HBV infected HCW

The management of an HBV-infected HCWs should be dependent upon the presence of HBeAg and/or the HBV DNA level. Generally HBeAg positivity is linked to high virus replication and viral load, and therefore, infectivity. Seroconversion to anti-HBe can indicate low infectivity and thus little, or no, risk of transmission. Currently the US excludes HCWs from performing EPP based only on the presence of HBeAg (MMWR, 1991). However, infected HCWs with anti-HBe or no HBe markers may have high levels of HBV DNA. In the UK there have been several transmissions to patients from HBeAg negative/anti-HBe positive HCWs to patients (Table 3).

Currently, the UK and Republic of Ireland exclude all HBeAg positive HCWs and quantify HBV DNA levels in all HBV carriers without HBeAg (HSC 2000/020). The Netherlands excludes HCWs on the basis of their HBV level only, irrespective of HBeAg status. Quantifying the HBV DNA levels in all patients will incur additional costs.

Table 3
The cases of HBe negative HBV transmission from HCW to patients

| HCW | Risk factor | HBV DNA level | Number of patients infected | Illness outcome |
|---|---|---|---|---|
| Orthopaedic surgeon | EPP | Not published | 1 | Patient died |
| Cardiothoracic surgeon | EPP | $1 \times 10^6$ genome equivalents/ml | 2 | Acute infection |
| General surgeon | EPP | $1 \times 10^7$ copies/ml[a] | 1 | Acute infection |
| Obstetrics/gynaecology surgeon | EPP | $4.4 \times 10^6$ copies/ml[a] | 1 (possible 2 more) | Acute infection |
| Obstetrics/gynaecology surgeon | EPP | $5.5 \times 10^6$ copies/ml[a] | 1 | Acute infection |
| General surgery, urology | EPP | $2.5 \times 10^5$ copies/ml[a] | 1 | Acute infection |
| Orthopaedic surgeon | ? | $\sim 10^9$ copies/ml | 1 | Patient died |
| General surgeon | EPP | $> 2 \times 10^5$ genome equivalents/ml | 3 | Patient died |

[a] These values were then retested using the ROCHE Amplicor Monitor assay and the lowest HBV DNA determined was determined to be $4 \times 10^4$ copies/ml.

Some countries have determined a HBV DNA cut off level, below which transmissions are deemed unlikely to occur. The Netherlands has chosen a HBV DNA cut off level at $10^5$ copies/ml. Although a transmission have been documented below this level ($4 \times 10^4$ copies/ml) (Corden et al., 2002), concerns were raised as to the accuracy of this finding as it was quantified some time after the transmission took place. Furthermore, setting a cut off below this level would prevent the majority of HBeAg negative HCWs from performing EPP (Table 4a). The Netherlands chose $10^5$ copies/ml as they felt that, based on risk of transmission; there are two largely exclusive groups of HBV carriers (Fig. 2). Corden et al. showed that most anti-HBe carriers have viral loads $< 10^5$ copies/ml whereas viral loads $> 10^5$ copies/ml are representative of HBeAg carriers and associated with an increased risk of transmission. Apart from the case discussed above the remainder of HCWs involved in transmission had viral loads $> 10^5$ copies/ml. Although natural fluctuations do occur in HBV carriers (Perrillo, 2001), further studies showed that HBV DNA levels in anti-HBe carriers were unlikely to rise into the high-risk category. For example, Martinot-Peignoux et al. (2002) followed 85 anti-HBe carriers with HBV DNA levels below $10^5$ copies/ml over a mean period of 3 years (range 0.5–11 years). In 96% of these patients the HBV DNA level remained unchanged. However, other studies have contradicted these findings (Tedder et al., 2002). Tedder et al. followed 120 anti-HBe carriers (non-HCW) over a mean period of 6.5 years (range 1–18 years). On closer examination of 20 anti-HBe carriers they found the anti-HBe carrier state to be a dynamic host–parasite relationship with natural, short lived, fluctuations of viral load, which, in rare cases, lead to an $\sim 3$ log increase in viral load (mean 0.89 log) (Fig. 3). Similar rises (from $10^2$–$10^3$ to $10^4$–$10^5$ copies/ml) have been observed between annual samples in some UK based HCWs (Personal Communication with Dr H. Nicholas). If similar increases were to be seen in an infected HCW practising in the Netherlands this could result in an intermittent HBV DNA level of up to $10^8$copies/ml, a level associated with a significant risk of transmission.

Table 4
HBV DNA levels

| HBV DNA level (copies/ml) | Number of HCW with a HBV DNA |
|---|---|
| *(a) In HBV carriers in HCW in the Netherlands* | |
| $\leq 10^3$ | 1 |
| $> 10^3$–$10^4$ | 2 |
| $> 10^4$–$10^5$ | 6 |
| $> 10^5$–$10^6$ | 3 |
| $> 10^6$ | 5 |
| Total | 17 |
| *(b) In HBe negative HCW in the UK* | |
| $\leq 10^3$ | 184 |
| $> 10^3$–$10^4$ | 96 |
| $> 10^4$–$10^5$ | 110 |
| $> 10^5$–$10^6$ | 45 |
| $> 10^6$ | 1 |
| Total | 436 |

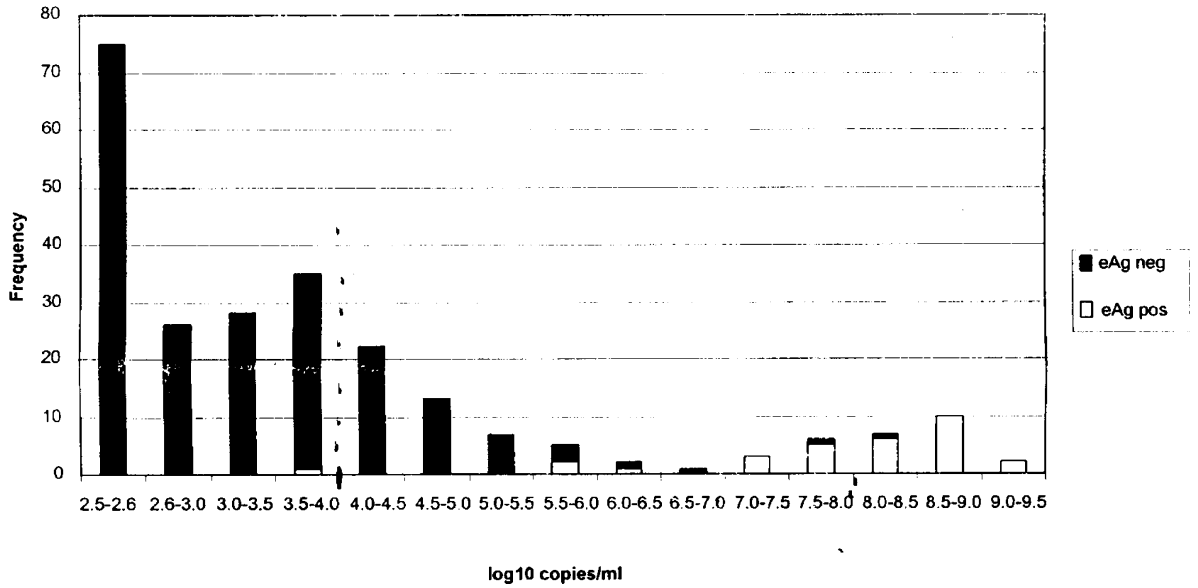


Fig. 2. Distribution of HBV DNA levels, expressed as copies/ml, in 31 carriers whose serum contained HBeAg and 211 carriers whose serum did not. Vertical axis displays numbers of carriers, horizontal axis displays HBV DNA levels (Figure reproduced from Corden et al.).

Therefore, mandatory testing (every 6 months) is carried out to identify EPP performing HCWs who may have moved from below $10^5$ copies/ml into the high-risk group.

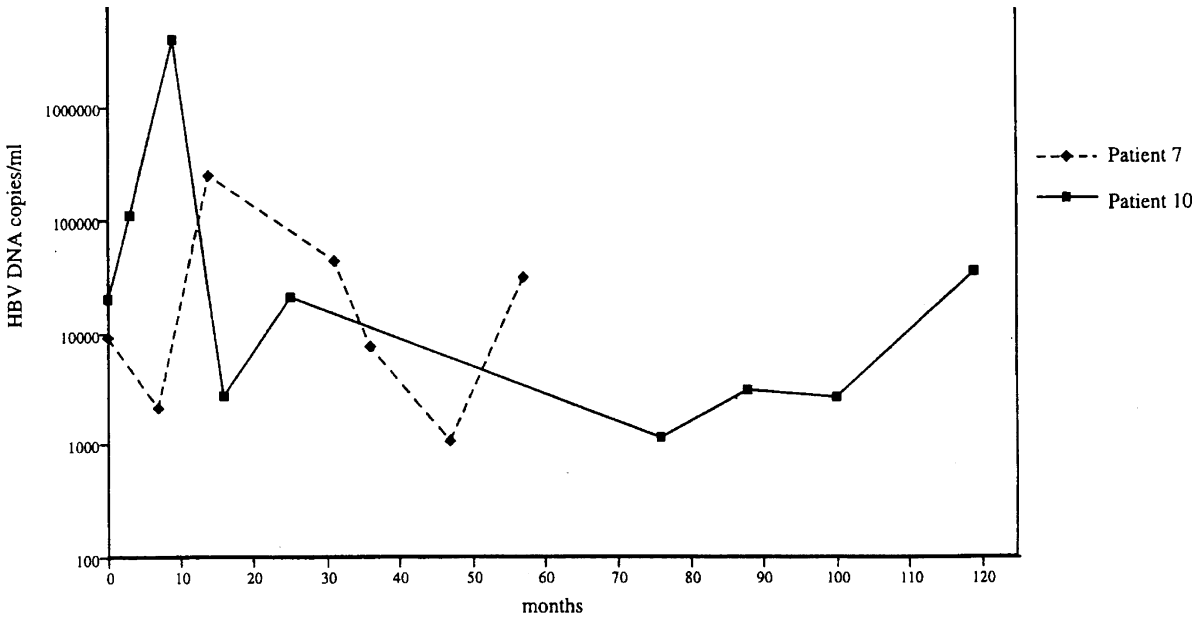


Fig. 3. Changes of HBV DNA levels over time in two anti-HBe patients closely sampled over 60 and 120 months (Figure reproduced from Tedder et al.).

The UK and Republic of Ireland use a HBV DNA cut off level of $10^3$ copies/ml. Implementing the lower cut off level reduces the risk of transmission as fluctuations in viral loads are unlikely to result in rises above $10^6$ copies/ml. In the UK this policy has lead to the restriction of $\sim 58\%$ HBV infected HCWs (Personal communication with Dr W.F. Carman) (Table 4b). However, this may not be applicable to other countries as it may lead to the restriction of the majority of infected HCWs. For example, in the Netherlands a cut off of $10^3$ copies/ml would result in the restriction of $> 94\%$ of all infected HCWs.

The consensus panel agreed that each country should individually determine the HBV DNA level cut off on an individual basis. However, we propose that a cut off of $10^4$ copies/ml would provide a balance between risk of transmission and loss of specialist HCWs. This cut off would also take into any account sudden rises of HBV DNA levels seen due to natural fluctuations or the potential emergence of resistant virus during lamivudine mono-therapy (see below). HCWs with HBV DNA levels equal to or below the cut off are allowed to practice EPP and should be annually tested to ensure they remain below this threshold. Transmission of HBV from HCWs with low levels of HBV DNA has yet to be documented but may occur. A single mother to child (Personal communication with Dr W.F. Carman) HBV transmissions has occurred at DNA levels below $10^3$ copies/ml, which raises the possibility that an infected HCW with HBV DNA levels below the current cut offs may still pose a transmission risk to patients. Therefore, the cut off HBV DNA level should be reviewed as more data become available.

### 4.1. Recommendations

- All HBV infected HCWs with HBeAg should not perform EPP. If HBeAg positive HCWs wish to have their HBV DNA level determined they will first have to be referred to an expert panel. If the panel recommends testing and HBV DNA is below that country's cut off, a HCW can perform EPP. However, the HBV DNA level should be examined every 3 months.
- All HBV infected HCWs negative for HBeAg who are performing EPP should have their HBV DNA level determined. At present the consensus panel recommends a cut off level[2] of $10^4$ genome equivalents/ml. However, the consensus panel agreed that each country could determine the HBV DNA level cut off on an individual basis based on risk to patients and loss of experienced HCWs. All HCWs with HBV DNA levels above the determined cut off level should not perform EPP. All those equal to or below this level are allowed to practice EPP.
- All HCWs with HBV DNA levels equal to or below their country's cut off should be annually tested for HBV DNA and managed as above.
- All HCWs shown to be a source of transmission to patients, regardless of HBV profile, should not perform EPP.

## 5. Lifting the restrictions on the infected HCW

### 5.1. HBV infected HCW

#### 5.1.1. Currently available treatments

There are currently two approved antiviral agents (a third, adefovir was recently licensed in the US and tenofovir is likely to become available in the future) for the treatment of chronic HBV infection (Leung, 2002a,b) (Table 5). The first antiviral agent approved was interferon (IFN), an immunomodulating agent licensed for use in 1992 and now available in most countries for HBV treatment. Lamivudine, a nucleoside analogue, was licensed by the US FDA in 1998 and is now also approved for the treatment of chronic HBV infection.

Although IFN treatment is of short duration, its route of administration, serious side effects, cost, and lack of activity in anti-HBe/DNA positive HBV carriers has restricted its use for the treatment of HCWs. Lamivudine offers many advan-

[2] The consensus panel agreed that each country could determine the HBV DNA level cut off on an individual basis based on risk to patients and loss of experienced HCW.

Table 5
Advantages and disadvantages of IFN and lamivudine in HBV therapy

| Anti-viral agent | Benefits | Disadvantages |
|---|---|---|
| IFN | Short duration of treatment | Parental administration |
| | >30% eAg loss | Side effects |
| | 8–10% HBsAg loss | As efficacious as lamivudine |
| | No resistant mutations | No efficacy in HBe negative/DNA positive carriers |
| | Long term improvement | Patients with cirrhosis |
| Lamivudine | Convenient | Longer duration of treatment |
| | No side effects | No HBsAg loss |
| | >30% eAg loss | Promotes resistance (YMDD mutation) |
| | Equivalent to IFN | ?long term side effects |
| | Effective in IFN non-responders | Lower rate of HBeAg seroconversion |
| | Suppresses HBV DNA while on treatment | |

tages over IFN as it can be given orally, has little side effects, and is as efficacious as IFN. Also, of importance to the treatment of HCWs, lamivudine can suppress viral replication in most carriers (by at least 2 logs), including low viremic HBV carriers, within 6 weeks of therapy. However, once therapy is stopped in HBe negative/DNA positive HBV carrier viral rebound is the rule rather than the exception.

### 5.1.2. *Aim of treatment for a restricted HCW*

The lifting of EPP restrictions on an infected HCW depends on the outcome of therapy and the exclusion criteria applied. If we accept that the most protective restriction policies are those based on the level (or presence) of HBV DNA then, in most countries, EPP restrictions will only be lifted if treatment results in a sustained reduction of viral replication 6–12 months after the cessation of therapy. However, complete DNA loss after treatment is rare (2–10%) and restricted to only HBeAg positive carriers receiving IFN treatment. Therefore, very few HBV infected HCWs could return to practice EPP after treatment.

### 5.1.3. *Mono-therapy*

A possible alternative would be to consider allowing HCWs on long-term mono-therapy, with successful suppression of HBV DNA, to return to performing EPP. This is based on the theory that the absence/suppression of HBV DNA level reduces the risk of HBV transmission. The cost of treatment and the repeated testing needed to measure DNA levels may be high, but would be compensated by the reduction in compensation payouts, retraining costs and loss of experienced HCWs.

Both lamivudine and adefovir are suitable for long-term mono-therapy as they are easy to administer and have minimal side effects. Both drugs have been shown to suppress HBV DNA in the majority of those undergoing treatment (Mailliard and Gollan, 2003). The response to lamivudine in anti-HBe/DNA positive HBV carriers has been shown to improve with the duration of treatment (20% after year 1 rising to $\sim$70% after year 4).

However, there are problems. Although resistant virus is yet to be described in adefovir mono-therapy, lamivudine mono-therapy often results in the emergence of resistant virus. The resistant virus, known as the YMDD mutant, is detectable in 14% of patients after 1 year of lamivudine treatment and rises to >60% after year 4. The appearance of resistant virus has been associated with high pre-treatment HBV DNA levels. Three to 6 months after the appearance of resistant virus, a significant rise in the HBV DNA level may occur, sometimes to levels greater than before treatment, which may increase the risk of transmissions occurring. Studies show that the replicative activity of the resistant virus is less than the wild type. This would suggest that it is less transmissible but further studies will need to be carried out to substantiate this. Therefore, frequent viral load testing would need to be carried out to identify HCWs with resistant virus.

Further concerns were raised over whether HBV DNA suppression will prevent transmission (Kazim, 2002). Kazim et al. recently demonstrated

vertical transmission from a Hepatitis B chronically infected mother despite successful DNA suppression after long-term lamivudine mono-therapy. Other important aspects include the possible side effects after long-term use and the ethical issues of offering a treatment aimed at preventing transmission, rather than treating illness, which may not be available for patients.

A HCW who stops mono-therapy should have their viral load measured immediately and then every 3 months and should not perform EPP if their level rises above the cut off level. Data show that the majority of anti-HBe/DNA positive HBV carriers will suffer viral rebound levels 3–6 months after the cessation of lamivudine therapy. In some cases this can be to above pre-treatment levels.

### 5.2. Recommendations

All infected HCWs should be referred to a hepatologist for specialist advice. Some HCWs may elect to take treatment. In order to return to performing EPP, infected HCWs receiving treatment should demonstrate that their HBV DNA levels have fallen below the $10^4$ genome equivalents cut off level[3]. Each HCW who has successfully reduced the HBV DNA level to below the cut off should be retested every 3 months. HCWs who default on mono-therapy should have their HBV DNA level tested immediately and then retested every 3 months. All HCWs with HBV DNA levels above this cut off should not perform EPP. All those below this level are allowed to practice EPP.

## 6. HCV transmission from HCW to Patient

### 6.1. HCV transmission from HCWs to patients: the concerns

The lower risk of HCV transmission compared with HBV is offset by the greater risk of chronic infection (Lauer and Walker, 2001). Eighty percent of all those infected will develop chronic HCV infection, which may develop into cirrhosis and, more rarely, carcinoma.

Most countries have no national policy for HCV infected HCWs and some only restrict the practice of an infected HCW if they have been shown to be a source of transmission to a patient (Table 6). However, the largely asymptomatic nature of HCV infection may have resulted in an underestimation of the number of HCWs to patient transmissions.

The questionnaire showed that the current prevalence of HCV infected HCWs in the participating countries ranged from 0.2 to 3% (Fig. 4), which, in most cases, is comparable to the prevalence of HCV infection in the general population.

### 6.2. HCV transmission from HCW to patients: the published evidence

There have been six published reports (Estaban, 1996; Duckworth et al., 1999; Cody et al., 2002; Ross et al., 2000, 2002a,b) of transmissions of HCV from HCWs to patients resulting in the infection of 14 patients (Table 7). Further cases are known of in the US and UK (CDR, 2000, 1999, 2000; Brown, 1999; CDR, 1995; Newsday, 2002; Sehulster et al., 1997; Bosch, 1998, 2000; Hepatitis C lookback exercise, 2000) but the investigations are unpublished. However, overall there appears to be a low risk of HCV transmission from HCWs to patients during EPP. This is supported by look-

Table 6
Countries by presence of absence of national guidelines for HCV infected HCWs

| Countries with national guidelines for HCV infected HCWs | Countries without national guidelines for HCV infected HCWs |
|---|---|
| Belgium | Austria |
| Germany | France |
| Italy | Greece |
| UK | Holland |
| US | Israel |
| | Portugal |
| | Republic of Ireland |
| | Sweden |

[3] The consensus panel agreed that each country could determine the HBV DNA level cut off on an individual basis.

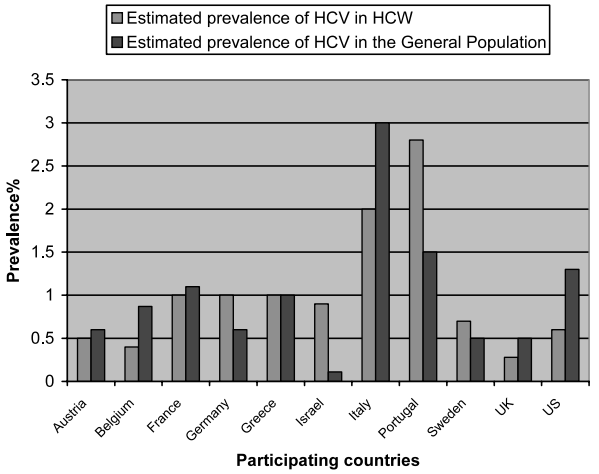


Fig. 4. The estimated prevalence of HCV in HCW.

back exercises. In the US a recent exercise (Personal Communication with Dr M. Alter) involving an HCV infected reconstructive surgeon found no transmissions in 268 patients (Table 8).

### 6.3. The benefits to the HCW of knowing their HCV status

Screening for and restricting HCV infected HCWs is not justified, based on current published data. However, it is recommended that HCWs (including dentists, midwives, nurses etc.) who perform EPP should know their HCV status. Most data suggest that little of the HCV infection in HCW is acquired occupationally (Thornburn et al., 2001; Cooksley and Butterworth, 1996; Thomas et al., 1996; Jagger et al., 2002; Mihaly, 2001; Thomas, 2001; Moens et al., 2000). Therefore, it should be recommended that HCWs determine their status before they begin EPP posts. This would allow the HCW to make informed career choices, could also provide evidence of occupational infection, and would enable a HCW to undergo counselling and treatment.

There are now successful treatments available for HCV. The combination of peg-IFN and ribavirin has shown an average response rate of 56%, ranging from 76% in genotypes 2/3 to 46% in

Table 7
Published HCV transmissions from infected HCWs to patients

| HCW | Year (country) | Number of patients infected | RNA level | Genotype | Risk factor |
|---|---|---|---|---|---|
| Cardiac surgeon | 1988–1993 (Spain) | 5 | $2.2 \times 10^6$ genome equivalents/ml | 3 | IVDU |
| Cardiac surgeon | 1994 (UK) | 1 | $10^6$ genome equivalents/ml | 4a | EPP |
| Anaesthesiologist | 1994 (US) | 1 | $3.7 \times 10^6$ genome equivalents/ml | 1a | Probable IVDU |
| Anaesthesiology assistant | 1998 (Germany) | 5 | $1 \times 10^6$ copies/ml | 1a | Failure to use standard precautions |
| Orthopaedic surgeon | 2000 (Germany) | 1 | $1.3 \times 10^6$ IU/ml | 2b | EPP |
| Gynaecologist | 2000 (Germany) | 1 | $2.6 \times 10^5$ IU/ml | 1b | EPP |
| Surgeon[a] | 2000–? (UK) | 1 | / | 2b | EPP |
| Gynaecologist[a] | 1978–1999 (UK) | 4 | / | 4 | EPP |
| Member of surgical team[a] | 1994–1999 (UK) | 2 | / | 1b | EPP |
| Cardiac surgeon[a] | 1993–1994 (UK) | 1 | / | ? | ? |
| Cardiac surgeon[a] | ? (US) | 3 | / | 1b | ? |
| Operating room technician[a] | 1991–1992 (US) | 40 | / | ? | IVDU |
| Anaesthetist | ? (Spain) | ~217 | / | ? | IVDU |

[a] The investigation into these transmission cases has yet to be published in detail.

Table 8
Transmission rates of patient look-back studies of non IVDU HCV infected HCWs

| HCW | Year | Number of patients infected | Number of patient tested | Transmission rate (%) |
|---|---|---|---|---|
| Cardiac surgeon | 1994 | 1 | 278 | 0.3 |
| Reconstructive surgeon | 1997 | 0 | 268 | 0 |
| Gynaecologist | 1993–2000 | 1 | 2285 | 0.04 |
| Anaesthesiology assistant | 1998 | 5 | 833 | 0.6 |
| Orthopaedic surgeon | 2000 | 1 | 229 | 0.48 |

genotype 1 (Fried et al., 2002). The likelihood of relapse after successful treatment is also small. For example, a French study (Leung, 2002a,b) demonstrated that 96% of patients, who had sustained loss of HCV RNA after treatment were still RNA negative 4 years after the cessation of therapy. Two patients did relapse after 2 years. The successful treatment of a HCW training to perform EPP should reduce the risk of transmission to patients even further, if one assumes the risk is dependent on the presence of HCV RNA.

Also, if a patient is exposed the blood of a HCW known to be HCV infected then post-exposure treatment can be given to the patient. Although there is currently no official post-exposure prophylaxis available for HCV, preliminary studies suggest that IFN therapy may prevent chronic infection if given during acute infection (Table 9) (Viladomiu et al., 1992; Lampertico et al., 1994; Hwang et al., 1994; Jaeckel et al., 2001). This would require transparency and declaration of the HCW status.

### 6.4. Recommendations

- No consensus was reached as to how to manage HCV infected HCWs who perform EPP. On balance it is not recommended that EPP be forbidden for the HCV infected HCW. However, as a minimum, it is recommended that all HCWs performing EPP know their HCV status as it may have implications for their future career. Those found to be infected with HCV should be referred to a hepatologist, as successful treatment will reduce the risk of transmission of HCV to patients. If there is a substantial blood letting into a patients body cavity, then the status of the HCW should be made known to occupational health and the patient informed, and treated if infection occurs; or referred to a hepatologist.

## 7. Informed consent

### 7.1. Should disclosure of seropositivity lead to the lifting of restrictions

In 1991, the CDC issued recommendations, which stated that:

> "a HCW infected with HBV (including HBeAg) and HIV should not perform EPP unless they have sought counsel from an expert review panel and been advised under what circumstances, if any, they may continue to perform EPP. Such circumstances include notifying prospective patients of HCW seropositivity before EPP".

Other countries have implemented similar guidelines, which allow the infected HCW to continue performing EPP after disclosure of status to patients. For example, Canada currently allows all anti-HBe positive carriers to perform EPP after disclosure (Barrigar et al., 2001). Recently in the US, disclosure of HCV serostatus allowed an HCV infected cardiac surgeon to continue EPP after several transmissions to patients. Perhaps we should consider allowing all infected HCWs who disclose their seropositivity to patients, HBV and HCV, to return to EPP posts?

Table 9
Results of selected studies of IFN for the treatment of acute HCV infection

| Study | Weeks after exposure | Duration of treatment | Regimen | Sustained viral response (%) | |
|---|---|---|---|---|---|
| | | | | IFN | Controls |
| Viladomiur et al. | 7 | 3 months | Subcutaneous IFN (3 MIU, three times/week) | 73 | 38 |
| Lampertico et al. | 8 | 3 months | Subcutaneous IFN (3 MIU, three times/week) | 39 | 0 |
| Hwang et al. | 9.5 | 3 months | Subcutaneous IFN (3 MIU, three times/week) | 81 | 12 |
| Jaeckel et al. | 12 | 4 weeks<br>20 weeks | Subcutaneous IFN (5 MIU, daily)<br>Subcutaneous IFN (5 MIU, three times/week) | 98 | Not reported |

*7.1.1. Case for disclosure of seropositivity*

Advocates state that the main aim of disclosure is patient safety. Is it ethical to operate on a patient, knowing there is a small but undeniable risk of passing on a potential life threatening infection? Disclosing the infectious status of the HCW, and discussing the subsequent risks of infection versus the risk of the procedure or the untreated outcome, allows the patient to make informed choices about his/her safety. The patient may then choose a different surgeon or may accept the risks to be small and allow the procedure to take place. Furthermore, the patient may choose to undergo vaccination, which could protect them from HBV, but not HCV. Advocates also point to the important position HCWs, such as surgeons, have in the community. Many feel that the disclosure of seropositivity by an infected HCW could have a positive effect on patients, and colleagues, by reducing the stigma attached to many of these viral infections. The legal issue of risk is also of importance. Failure to disclose risk may result in legal proceedings for both the HCW and the hospital.

*7.1.2. Case against disclosure of seropositivity*

Many who are against the disclosure of serostatus point to the inherent problems of educating patients about the real risk and consequences of infection with either HBV or HCV. Patients may exaggerate or misinterpret the risks of infection or fail to understand the information being given to them. This may lead to mis-informed decisions and/or unfair discrimination against HCWs. For example, many patients may refuse to be treated by HCWs who come from countries where there is high incidence of HBV or HCV. HCWs are at higher risk of infection from patients, yet it is they, not patients, who have to disclose they infectious status. Therefore, HCW may feel it only fair to ask patients to be tested for HBV, HCV, or HIV before operating.

The privacy of the HCW should also be considered. If we ask all HCWs to disclose their infectious status, could it result in patients requesting information on other aspects of the HCW history, which they may feel could effect their treatment. For example, this may include requests on the HCW legal history, case history, exam results, and criminal records.

*7.2. Recommendations*

- All HCWs with HBV DNA levels above the chosen cut off level should be given the option of disclosure to continue practising EPP. HCWs should ensure that the patient is given accurate and understandable data on the risk of being operated on by an infected HCW. Alternatives should be offered to the patient e.g. HBV vaccination.

## 8. Summary of recommendations

- All HCWs should apply standard precautions to every patient.

- It is highly recommended that all HCWs in contact with patients, blood or other body secretions should be vaccinated for HBV and has their response checked within a month after the final dose. Initial non-responders should be given one to three more doses of vaccine and have their response determined. Non-responders should have an individual risk assessment based on job description to determine whether they will be investigated for persistent HBV infection.
- All HCWs who perform EPP (including dental, medical and nursing students) should provide proof of anti-HBs response before starting a post. If negative/or unavailable then the HCW should receive a booster dose of vaccine and have their response determined at least 1 month after. Continued non-responders should be investigated for persistent HBV infection (presence of HBsAg or anti HBc in the absence of HBsAg). Those found to be HBsAg negative should be allowed to perform EPP but should be tested regularly (frequency to be decided by each individual country) and after any significant exposure.
- All HCWs who refuse to be vaccinated must understand the implications of his/her actions.
- The implication of the anti-HBs response differs between non-EPP and EPP HCWs.
  - i) In non-EPP HCWs:
    - 1) Anti-HBs levels $>100$ IU/l are desirable.
    - 2) HCWs with anti-HBs levels between 10 and 100 IU/l should have their response confirmed using another assay. A further dose should be given.
    - 3) HCWs with anti-HBs levels $<10$ IU/l should be given up to three additional boosters and have their response re-checked.
    - 4) HCWs with anti-HBs levels $<10$ IU/l (non-responder) should consult a specialist advisory group to assess risk.
  - ii) In EPP performing HCWs:
    - 1) Anti-HBs levels $>100$ IU/l are preferred.
    - 2) HCWs with anti-HBs levels 10–100 IU/l should be given a booster and have their response re-checked using another assay.
    - 3) All HCWs with a confirmed anti-HBs level between 10 and 100 IU/l should be tested for HBsAg. However, it is not imperative that anti-HBs titres reach a level of $>100$ IU/l.
    - 4) Those HCWs who have anti-HBs levels $<10$ IU/l (non-responders) should be tested for HBsAg. Those found to be negative should consult a specialist advisory group to assess risk.
- All HBV infected HCWs with HBeAg should not perform EPP. If HBeAg positive HCWs wish to have their HBV DNA level determined they will first have to be referred to an expert panel. If the panel recommends testing and HBV DNA is below that country's cut off, a HCW can perform EPP. However, the HBV DNA level should be examined every 3 months.
- All HBV infected HCWs negative for HBeAg who are performing EPP should have their HBV DNA level determined. At present the consensus panel recommends a cut off level of $10^4$ genome equivalents/ml. However, the consensus panel agreed that each country could determine the HBV DNA level cut off on an individual basis based on risk to patients and loss of experienced HCWs. All HCWs with HBV DNA levels above the determined cut off level should not perform EPP. All those equal to or below this level are allowed to practice EPP.
- All HCWs with HBV DNA levels equal to or below the their country's cut off should be annually tested for HBV DNA and managed as above.
- All HCWs shown to be a source of transmission to patients, regardless of HBV profile, should not perform EPP.
- All infected HCWs should be referred to a hepatologist for specialist advice. Some HCWs may elect to take treatment. In order to return to performing EPP, infected HCWs receiving

treatment should demonstrate that their HBV DNA levels have fallen below the $10^4$ genome equivalents cut off level[4]. Each HCW who has successfully reduced the HBV DNA level to below the cut off should be retested every 3 months. HCWs who default on mono-therapy should have their HBV DNA level tested immediately and then retested every 3 months. All HCWs with HBV DNA levels above this cut off should not perform EPP. All those below this level are allowed to practice EPP.

- No consensus was reached as to how to manage HCV infected HCWs who perform EPP. On balance it is not recommended that EPP be forbidden for the HCV infected HCW. However, as a minimum, it is recommended that all HCWs performing EPP know their HCV status as it may have implications for their future career. Those found to be infected with HCV should be referred to a hepatologist, as successful treatment will reduce the risk of transmission of HCV to patients. If there is a substantial blood letting into a patients body cavity, then the status of the HCW should be made known to occupational health and the patient informed, and treated if infection occurs; or referred to a hepatologist.
- All HCWs with HBV DNA levels above the chosen cut off level should be given the option of disclosure to continue practising EPP. HCWs should ensure that the patient is given accurate and understandable data on the risk of being operated on by an infected HCW. Alternatives should be offered to the patient e.g. HBV vaccination.

## 9. Future research/needs

1) Long-term sero-surveillance to define the risk of acquisition by HCW.
2) Central register of HBV treated HCW and their DNA levels should be kept.
3) Studies on combination therapy for HBV are required.

[4] The consensus panel agreed that each country could determine the HBV DNA level cut off on an individual basis based on risk to patients and loss of experienced HCW.

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