



health

Department:  
Health  
REPUBLIC OF SOUTH AFRICA



## South African National Essential Medicine List Primary Healthcare Medication Review Process Component: Emergencies and injuries

### MEDICINE REVIEW:

#### 1. Executive Summary

**Date:** 21 February 2018  
**Medicine (INN):** Hepatitis B immunoglobulin  
**Medicine (ATC):** J06BB04  
**Indication (ICD10 code):** Z29.8  
**Patient population:** Patients exposed to hepatitis B  
**Prevalence of condition:** 0.2 - 16% ([Pruss-Ustun, 2005](#); [Kew, 2008](#); [Firnhaber, 2008](#)) (1-3)  
**Level of Care:** Primary level of care  
**Prescriber Level:** Nurse prescribers  
**Current standard of Care:** Nil (Administered at secondary level of care)  
**Efficacy estimates: (preferably NNT):** unknown  
**Motivator/reviewer name(s):** Sandy Picken  
**PTC affiliation:** n/a

#### 2. Name of author(s)/motivator(s)

Sandy Picken

#### 3. Author affiliation and conflict of interest details

*Affiliation:* Primary Health Care Expert Review Committee member; Knowledge Translation Unit, University of Cape Town.

*Conflict of interest:* None

#### 4. Introduction/ Background

Hepatitis B immunoglobulin (HBIG) currently forms part of the post-exposure prophylactic (PEP) regimen, at hospital level care, for health care workers (HCW) following hepatitis B exposure. Indications for administration depend on the vaccination status and antibody response of the exposed HCW and source patient's hepatitis results: See table 1.

With the aim of providing equity for HCW working in different settings, the PHC Technical Subcommittee of NEMLC, proposed the inclusion of HBIG for the same indications in the PHC STG/EML. In response and due to supply challenges of immunoglobulin at tertiary and quaternary facilities, the NEMLC recommended that evidence for effectiveness of hepatitis B vaccine and immunoglobulin be reviewed (i.e. proportion of patient that would benefit from this intervention) for PEP.

Table 1: Extract from Hospital level STG, 2015

**10.4 POST-EXPOSURE PROPHYLAXIS**

(...)

**PEP for Health Care workers following hepatitis B exposure**

| Vaccination status and antibody response status of HCW        | Source patient  |   |   |
|---|---|---|---|
|   | HBsAg positive  | HBsAg negative  | HBsAg unknown   |
| Unvaccinated or vaccination incomplete                        | <ul style="list-style-type: none"> <li>• HBIG, IM, 500 units*</li> <li>• Hep B vaccine (3 doses at monthly intervals)</li> </ul>        | <ul style="list-style-type: none"> <li>• Initiate Hep B vaccination (month 0, 1 and 6)</li> </ul> | <ul style="list-style-type: none"> <li>• HBIG, IM, 500 units*</li> <li>• Hep B vaccine (3 doses at monthly intervals)</li> </ul>        |
| Vaccinated AND known to have HBsAb > 10 units/mL <sup>#</sup> | No treatment  | No treatment  | No treatment  |
| Vaccinated AND HBsAb < 10 units/mL or level unknown           | <ul style="list-style-type: none"> <li>• HBIG, IM, 500 units*</li> <li>• Repeat Hep B vaccine (3 doses at monthly intervals)</li> </ul> | No treatment  | <ul style="list-style-type: none"> <li>• HBIG, IM, 500 units*</li> <li>• Repeat Hep B vaccine (3 doses at monthly intervals)</li> </ul> |

\* HBIG and first dose of vaccine to be given simultaneously, but at different sites.  
<sup>#</sup> If the delay in obtaining HBsAb results is more than 24 hours initiate treatment as for vaccinated AND HBsAb < 10 units/mL.  
 After vaccination ensure the health care worker has a HBsAb > 10 units/mL 1 – 2 months after the last vaccine dose.

2015

10.28

The exact prevalence of blood borne viruses infection in South African HCWs is unknown, but is estimated to mimic that of the general population: Hepatitis B virus (HBV) 0.2 - 16%; HIV 17.9% and Hepatitis C virus (HCV) ~2.4%.

Hepatitis B infection is serious. The spectrum of clinical manifestations of hepatitis HBV infection varies in both acute and chronic disease. During the acute phase, manifestations range from subclinical or anicteric hepatitis to icteric hepatitis and, in some cases, fulminant hepatitis. The sequelae of chronic HBV infection vary from an inactive carrier state to the development of cirrhosis, hepatic decompensation, hepatocellular carcinoma, extrahepatic manifestations, and death.

In 1995 the South African Department of Health incorporated the HBV vaccine, administered as a monovalent, into the Expanded Programme on Immunisation (EPI) at 6, 10, and 14 weeks of age, and studies conducted thereafter have found it to be safe and highly effective (4). In 2015, South Africa became the first country in Africa to introduce a fully liquid hexavalent vaccine (6-in-1) by replacing the pentavalent (5-in-1) and hepatitis B vaccines (5) – 6,10, 14 weeks and 18 months. Furthermore, HCWs are required to be vaccinated against HBV before they start their training, but no compulsory systems are in place to document immunity or to exclude pre-existing chronic HBV infection (6).

The mean immunization rate of health-care workers for HBV is estimated to be only 18% for our region<sup>1</sup> (3). In local study of 333 HCWs from Gauteng and Mpumalanga, 70.9% reported to have had at least one dose of HBV vaccine. However on serological review, 47.8% were immune due to vaccination (7). HBV vaccination is approximately 92% effective in immunocompetent adults <40 years of age, and only 84% effective in those aged ≥40 years (6). As from 2014, a new cohort of

<sup>1</sup> Afri E: Botswana, Burundi, Central African Republic, Congo, Côte d'Ivoire, Democratic Republic of the Congo, Eritrea, Ethiopia, Kenya, Lesotho, Malawi, Mozambique, Namibia, Rwanda, South Africa, Swaziland, Uganda, United Republic of Tanzania, Zambia, Zimbabwe.

potentially Extended Program on Immunization (EPI)-vaccinated healthcare students started their training. Only 16% of persons vaccinated at age < 1 year are estimated to have detectable anti-HBs  $\geq 10$  mIU/mL 18 years later. However, they generally show good immunological memory, with 60 - 97.4% showing protective anti-HBs levels after a booster dose of HBV vaccine (8).

A regional estimate for of the mean number of sharps injuries per HCW per year was 2.10 (9, 10). The risk of transmission following an accidental exposure is highest for HBV (30%), followed by HCV (1 - 2%) and HIV (0.3%). It has been estimated that globally 66 000 HCWs have been infected with HBV through occupational exposure (1, 10).

Hepatitis B immunoglobulin (HBIG) contains a high titre of antibody to hepatitis B surface antigens and provides immediate passive protection against infection with hepatitis B virus, after acute exposure to infection. Internationally, it is now generally combined with active immunisation with hepatitis B vaccine. The principal indications for administration of HBIG are: a single acute percutaneous exposure to hepatitis B virus (HBV); mucocutaneous exposure; unprotected sexual exposure; mother-to-infant transmission; prevention of re-infection after liver transplantation; non-responders to hepatitis B vaccine and immunosuppressed patients (11).

Health-care workers are frequently exposed to percutaneous injuries with contaminated sharps, which cause a large proportion of all HCV, HBV and HIV infections in this group. These infections could largely be prevented, as shown by the lower numbers of infections in regions where efforts, which include the administration of HBIG immunoglobulin in their PEP regimens, have been made to reduce such exposures (10).

## 5. Purpose/Objective i.e. PICO question

### PICO #1

- P (*patient/population*): occupational exposure to contaminated sharps in HCWs
- I (*intervention*): combination Hepatitis B immunoglobulin (HBIG) and hepatitis B vaccine series
- C (*comparator*): Hepatitis-B vaccine series alone (active immunization)
- O (*outcome*): occupational Hepatitis B infection, hepatitis, acute hepatitis, seroconversion, disability, cirrhosis, hepatic decompensation, hepatocellular carcinoma

In health care workers exposed to hepatitis B through occupational exposure or needlestick injuries/contaminated sharps injuries, what is the effect of combined Hepatitis B vaccine series and HBIG (hepatitis B immunoglobulin) compared to hepatitis B vaccine series alone on occupation hepatitis B infection rates?

**PICO #2** – see appendix 2

## 6. Methods:

- a. **Data sources:** *Pubmed, Cochrane Library*
- b. **Search strategy (pubmed)**  
**Search#1 (6 items retrieved - only 1 relevant to PICO)**

("prevention and control"[Subheading] OR ("prevention"[All Fields] AND "control"[All Fields]) OR "prevention and control"[All Fields] OR "prevention"[All Fields]) AND ("hepatitis b virus"[MeSH Terms] OR "hepatitis b virus"[All Fields]) AND HBV[All Fields] AND (("infection"[MeSH Terms] OR "infection"[All Fields]) AND ("delivery of health care"[MeSH Terms] OR ("delivery"[All Fields] AND "health"[All Fields] AND "care"[All Fields]) OR "delivery of health care"[All Fields] OR ("health"[All Fields] AND "care"[All Fields]) OR "health care"[All Fields]) AND ("manpower"[Subheading] OR "manpower"[All Fields] OR "workers"[All Fields]) AND after[All Fields] AND ("accidents"[MeSH Terms] OR "accidents"[All Fields] OR "accidental"[All Fields]) AND exposure[All Fields])

**Search#2 (3 items retrieved -1 relevant to PICO – same article as search#1)**

Combined[All Fields] AND ("hepatitis b"[MeSH Terms] OR "hepatitis b"[All Fields]) AND ("immunoglobulins"[MeSH Terms] OR "immunoglobulins"[All Fields] OR ("immune"[All Fields] AND "globulin"[All Fields]) OR "immune globulin"[All Fields]) AND ("vaccines"[MeSH Terms] OR "vaccines"[All Fields] OR "vaccine"[All Fields]) AND postexposure[All Fields] AND ("prevention and control"[Subheading] OR ("prevention"[All Fields] AND "control"[All Fields]) OR "prevention and control"[All Fields] OR "prophylaxis"[All Fields]) AND ("hepatitis b"[MeSH Terms] OR "hepatitis b"[All Fields] OR "hepatitis b virus infection"[All Fields])

**Search #3 (58 items retrieved – 8 potentially relevant/abstracts reviewed– only 1 relevant to PICO – same article as search#1)**

((exposure[All Fields] AND ("hepatitis b"[MeSH Terms] OR "hepatitis b"[All Fields])) AND ("health personnel"[MeSH Terms] OR ("health"[All Fields] AND "personnel"[All Fields]) OR "health personnel"[All Fields] OR ("health"[All Fields] AND "care"[All Fields] AND "worker"[All Fields]) OR "health care worker"[All Fields])) AND (("hepatitis b"[MeSH Terms] OR "hepatitis b"[All Fields]) AND ("immunoglobulins"[MeSH Terms] OR "immunoglobulins"[All Fields] OR "immunoglobulin"[All Fields])) AND ("hepatitis b vaccines"[MeSH Terms] OR "hepatitis b vaccines"[All Fields] OR "hepatitis b vaccine"[All Fields])

**Search #4 (4 items retrieved - 0 relevant to PICO)**

(effective[All Fields] AND ("hepatitis b vaccines"[MeSH Terms] OR "hepatitis b vaccines"[All Fields] OR "hepatitis b vaccine"[All Fields])) AND (percutaneous[All Fields] AND exposure[All Fields])

**Search#5 (2 items retrieved - 0 relevant to PICO)**

((effectiveness) AND hepatitis B vaccine) AND post exposure prophylaxis

**Serach#6 (4 tiems retrieved - 0 relevant to PICO)**

comparison [All Fields] AND (("hepatitis B hyperimmune globulin"[Supplementary Concept] OR "hepatitis B hyperimmune globulin"[All Fields] OR "hbig"[All Fields]) AND HBV[All Fields] AND ("vaccines"[MeSH Terms] OR "vaccines"[All Fields] OR "vaccine"[All Fields])) AND (HBV[All Fields] AND ("vaccines"[MeSH Terms] OR "vaccines"[All Fields] OR "vaccine"[All Fields]) AND only[All Fields])

**Cochrane library:**

**Search#1: Hepatitis B immunization (9 review retrieved – 1 relevant to PICO, excluded see below)**

**Search#2: Hepatitis B post exposure prophylaxis (15 items retrieved) - 1 relevant to PICO, excluded see below)**

c. **Excluded studies:**

| <b>Author, date</b>                | <b>Type of study</b> | <b>Reason for exclusion</b>  |
|------------------------------------|----------------------|--|
| <a href="#">Chen, 2005</a><br>(12) | Cochrane<br>Review   | Not relevant to PICO<br>Aim of this review: To assess the beneficial and harmful effects of hepatitis B vaccination in health-care workers.  |
| <a href="#">Matthew, 2008</a> (13) | Cochrane<br>Review   | Not relevant to PICO<br>Aim of this review: To assess the benefits and harms of hepatitis B vaccination in people not previously exposed to hepatitis B infection or with unknown exposure status. |

d. **Evidence synthesis –**

Only 3 studies relevant to PICO found ((14-16), old studies with small cohorts- conducted in 1980s.

No relevant reviews were identified except if PICO extrapolated from perinatal setting in which 1 review (17) shows Hepatitis B vaccine plus hepatitis B immunoglobulin were superior to hepatitis B vaccination alone (RR 0.54, 95% CI 0.41 to 0.73, 10 trials).

In absence of sufficient evidence, international guidance consulted (see appendix 1).

| Author, date   | Type of study                      | n                             | Population  | Comparators  | Primary outcome  | Effect sizes  |
|--|------------------------------------|-------------------------------|---|--|--|---|
| <a href="#">Palmović, 1993</a> (14)                      | Controlled trial                   | 111 adults                    | Adult health care workers after accidental exposure | <ul style="list-style-type: none"> <li>Group A - n37 = (active + passive) HBIG + vaccine series</li> <li>Group B – n40 = (active alone) vaccine series only</li> <li>Group C – n34 (control) no immunoprophylaxis</li> </ul> | <ul style="list-style-type: none"> <li>Acute HBV infection</li> <li>10 months F/U</li> </ul> | <ul style="list-style-type: none"> <li>Group A +B = 0 acute HBV infections</li> <li>Group C = 6%, 2/34 developed acute HBV infection</li> </ul> |
| Extrapolated - studies relevant to PERINATAL SETTING     |                                    |                               |   |  |  |   |
| <a href="#">Lee, 2006</a> ((17)                          | Cochrane review                    | 29 randomised clinical trials | -   | -  | -  | Compared with vaccine, vaccine plus hepatitis B immunoglobulin reduce hepatitis B occurrence (F 0.54, 95% CI 0.41 to 0.73 10 trials)            |
| <a href="#">Kabir, 2006</a> (18)<br><i>Abstract only</i> | Cohort study (historical controls) | 823 children                  | children (born to HBsAg positive mothers) in Iran   | Group 1- n 481, no immunoprophylaxis, age > 16 years<br>Group 2 – n157, no immunoprophylaxis, age ≤ 16 years<br>Group 3 - n125, HBV vaccine only<br>Group 4 – n60 neonates, both HBIG + vaccine                              | Prevalence of anti-HBsAb:  | Prevalence of anti-HBsAb:<br>Group 1: 21.8%<br>Group 2: 33.3%<br>Group 3: 68.8%<br>Group 4: 5.7%  |

**a. Evidence quality:**

Available evidence seems to be old, 1980-1990's and predominant focus is on perinatal setting.

**7. Alternative agents:** no therapeutic alternatives exist.

## EVIDENCE TO DECISION FRAMEWORK

|   | JUDGEMENT   | SUPPORTING EVIDENCE & ADDITIONAL CONSIDERATIONS   |          |             |   |        |   |                         |
|---|---|---|----------|-------------|---|--------|---|-------------------------|
| <b>QUALITY OF EVIDENCE</b>                                      | <p>What is the overall confidence in the evidence of effectiveness?</p> <p>Confident      Not confident      Uncertain</p> <p><input type="checkbox"/>      <input checked="" type="checkbox"/>      <input type="checkbox"/></p>   |   |          |             |   |        |   |                         |
| <b>BENEFITS &amp; HARMIS</b>                                    | <p>Do the desirable effects outweigh the undesirable effects?</p> <p>Benefits outweigh harms      Harms outweigh benefits      Benefits = harms or Uncertain</p> <p><input checked="" type="checkbox"/>      <input type="checkbox"/>      <input type="checkbox"/></p>   | <ul style="list-style-type: none"> <li>• HBV infection is a major occupational risk of HCWs if they are exposed in the workplace (30% transmission risk).</li> <li>• Poor/uncertain pre-exposure vaccine coverage.</li> <li>• Insufficient evidence to conclude that active vaccination alone is as effective as combination active-passive immunoprophylaxis.</li> </ul>   |          |             |   |        |   |                         |
| <b>THERAPEUTIC INTERCHANGE</b>                                  | <p>Therapeutic alternatives available:</p> <p>Yes      No</p> <p><input type="checkbox"/>      <input checked="" type="checkbox"/></p> <p>List the members of the group.</p> <p>List specific exclusion from the group:</p>   | <p>Rationale for therapeutic alternatives included:</p> <p>References:</p> <p>Rationale for exclusion from the group:</p> <p>References:</p>  |          |             |   |        |   |                         |
| <b>VALUES &amp; PREFERENCES / ACCEPTABILITY</b>                 | <p>Is there important uncertainty or variability about how much people value the options?</p> <p>Minor      Major      Uncertain</p> <p><input type="checkbox"/>      <input type="checkbox"/>      <input checked="" type="checkbox"/></p> <p>Is the option acceptable to key stakeholders?</p> <p>Yes      No      Uncertain</p> <p><input checked="" type="checkbox"/>      <input type="checkbox"/>      <input type="checkbox"/></p> |   |          |             |   |        |   |                         |
| <b>RESOURCE USE</b>   | <p>How large are the resource requirements?</p> <p>More intensive      Less intensive      Uncertain</p> <p><input type="checkbox"/>      <input type="checkbox"/>      <input checked="" type="checkbox"/></p>   | <p><b>Cost of medicines/ treatment course</b></p> <table border="1"> <thead> <tr> <th>Medicine</th> <th>Cost (ZAR)*</th> </tr> </thead> <tbody> <tr> <td>Immunoglobulin: Hepatitis B 100IU/2mL 2ml ampoule – single dose</td> <td>669.38</td> </tr> <tr> <td>Vaccine Hepatitis B Adult 20mcg/ml vial – 3 doses</td> <td>24.04 x 3 doses = 72.12</td> </tr> </tbody> </table> <p>* Contract circular HP10-2016BIO</p> <p><b>Additional resources:</b> Blood test to check HBsAb titre.</p> | Medicine | Cost (ZAR)* | Immunoglobulin: Hepatitis B 100IU/2mL 2ml ampoule – single dose | 669.38 | Vaccine Hepatitis B Adult 20mcg/ml vial – 3 doses | 24.04 x 3 doses = 72.12 |
| Medicine  | Cost (ZAR)*   |   |          |             |   |        |   |                         |
| Immunoglobulin: Hepatitis B 100IU/2mL 2ml ampoule – single dose | 669.38  |   |          |             |   |        |   |                         |
| Vaccine Hepatitis B Adult 20mcg/ml vial – 3 doses               | 24.04 x 3 doses = 72.12   |   |          |             |   |        |   |                         |
| <b>EQUITY</b>   | <p>Would there be an impact on health inequity?</p> <p>Yes      No      Uncertain</p> <p><input type="checkbox"/>      <input checked="" type="checkbox"/>      <input type="checkbox"/></p>  | <p>Inequitable to supply at Hospital level without making available to PHC level.</p>   |          |             |   |        |   |                         |
| <b>FEASIBILITY</b>  | <p>Is the implementation of this recommendation feasible?</p> <p>Yes      No      Uncertain</p> <p><input type="checkbox"/>      <input type="checkbox"/>      <input checked="" type="checkbox"/></p>  | <p>Supply issues.</p>   |          |             |   |        |   |                         |

|  |   |  |   |   |  |                      |                  |                 |                                     |                                     |                          |       |           |           |                          |                                     |                          |
|--|---|--|---|---|--|----------------------|------------------|-----------------|-------------------------------------|-------------------------------------|--------------------------|-------|-----------|-----------|--------------------------|-------------------------------------|--------------------------|
| <b>Type of recommendation</b>  | We recommend against the option and for the alternative<br><br><input type="checkbox"/> | We suggest not to use the option or to use the alternative<br><br><input type="checkbox"/> | We suggest using either the option or the alternative<br><br><input type="checkbox"/> | We suggest using the option<br><br><input type="checkbox"/> | We recommend the option<br><br><input checked="" type="checkbox"/> |                      |                  |                 |                                     |                                     |                          |       |           |           |                          |                                     |                          |
| <p><b>Recommendation:</b> Given the following:</p> <ul style="list-style-type: none"> <li>• HBV is a potentially life threatening condition.</li> <li>• HBV transmission risk, if exposed, is high (30% transmission risk).</li> <li>• Variable pre-exposure HCW vaccination coverage and of those vaccinated, adequate immune response is unknown.</li> <li>• Insufficient evidence to conclude that active immunisation alone is as effective as combination active-passive immunoprophylaxis.</li> </ul> <p>The Primary Health Care committee recommends that in the event of an occupational exposure, the exposed health care worker should have access to combination active-passive immunoprophylaxis, as per recommendations outlined in the Hospital Level STG. Such prophylaxis should be tailored according to the vaccination status and immune response of the exposed health care worker and source hepatitis status.</p> <p>Similarly, given the high prevalence of hepatitis B and the high transmission risk associated with exposure to hepatitis B, equal access should be provided for non-occupational exposures including sexual assault and human bite victims in whom skin has been broken, if the exposed person has inadequate anti-HBs antibody titres (see appendix 2).</p> <p><i>Rationale:</i> Aligned with CDC Guidelines.</p> <p><b>Level of Evidence: III Guidelines</b></p> <p><b>Review indicator:</b></p> <table border="0"> <tr> <td>Evidence of efficacy</td> <td>Evidence of harm</td> <td>Price reduction</td> </tr> <tr> <td><input checked="" type="checkbox"/></td> <td><input checked="" type="checkbox"/></td> <td><input type="checkbox"/></td> </tr> </table> <p><b>VEN status:</b></p> <table border="0"> <tr> <td>Vital</td> <td>Essential</td> <td>Necessary</td> </tr> <tr> <td><input type="checkbox"/></td> <td><input checked="" type="checkbox"/></td> <td><input type="checkbox"/></td> </tr> </table> <p><b>NEMLC Recommendation (Minutes of the NEMLC meeting of 5 July 2018): HBIG to be administered at secondary level of care for human bites and occupational PEP.</b></p> <p><i>Rationale:</i> There is a need for equitable access of HBIG for human bites and occupational PEP at both primary and secondary level of care. However, limited availability of HBIG warrants cautious use of this agent for the more common indication that generally presents at secondary level of care – perinatal transmission of hepatitis B.</p> <p><b>Level of Evidence: III Expert opinion</b></p> |   |  |   |   |  | Evidence of efficacy | Evidence of harm | Price reduction | <input checked="" type="checkbox"/> | <input checked="" type="checkbox"/> | <input type="checkbox"/> | Vital | Essential | Necessary | <input type="checkbox"/> | <input checked="" type="checkbox"/> | <input type="checkbox"/> |
| Evidence of efficacy   | Evidence of harm  | Price reduction  |   |   |  |                      |                  |                 |                                     |                                     |                          |       |           |           |                          |                                     |                          |
| <input checked="" type="checkbox"/>  | <input checked="" type="checkbox"/>   | <input type="checkbox"/>   |   |   |  |                      |                  |                 |                                     |                                     |                          |       |           |           |                          |                                     |                          |
| Vital  | Essential   | Necessary  |   |   |  |                      |                  |                 |                                     |                                     |                          |       |           |           |                          |                                     |                          |
| <input type="checkbox"/>   | <input checked="" type="checkbox"/>   | <input type="checkbox"/>   |   |   |  |                      |                  |                 |                                     |                                     |                          |       |           |           |                          |                                     |                          |



|   |
|---|
| <b>Monitoring and evaluation considerations</b> |
| <b>Research priorities</b>                      |

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**Appendix 1:**

Post-exposure management of personnel after occupational percutaneous and mucosal exposure to blood and body fluids

**Postexposure management of personnel after occupational percutaneous and mucosal exposure to blood and body fluids**

| Health-care personnel status                                       | Postexposure testing   |                         | Postexposure prophylaxis     |                        | Postvaccination serologic testing ¶ |
|--|------------------------|-------------------------|------------------------------|------------------------|-------------------------------------|
|  | Source patient (HBsAg) | HCP testing (anti-HBs)  | HBIG*                        | Vaccination            |                                     |
| Documented responder <sup>Δ</sup> after complete series (≥3 doses) | No action needed       |                         |                              |                        |                                     |
| Documented nonresponder <sup>◊</sup> after 6 doses                 | Positive/unknown       | – <sup>§</sup>          | HBIG x2 separated by 1 month | –                      | No                                  |
|  | Negative               | No action needed        |                              |                        |                                     |
| Response unknown after 3 doses                                     | Positive/unknown       | <10 mIU/mL <sup>§</sup> | HBIG x1                      | Initiate revaccination | Yes                                 |
|  | Negative               | <10 mIU/mL              | None                         |                        |                                     |
|  | Any result             | ≥10 mIU/mL              | No action needed             |                        |                                     |
| Unvaccinated/incompletely vaccinated or vaccine refusers           | Positive/unknown       | – <sup>§</sup>          | HBIG x1                      | Complete vaccination   | Yes                                 |
|  | Negative               | –                       | None                         | Complete vaccination   | Yes                                 |

\* HBIG should be administered intramuscularly as soon as possible after exposure when indicated. The effectiveness of HBIG when administered >7 days after percutaneous, mucosal, or nonintact skin exposures is unknown. HBIG dosage is 0.06 mL/kg.

¶ Should be performed 1 to 2 months after the last dose of the HepB vaccine series (and 4 to 6 months after administration of HBIG to avoid detection of passively administered anti-HBs) using a quantitative method that allows detection of the protective concentration of anti-HBs (≥10 mIU/mL).

Δ A responder is defined as a person with anti-HBs ≥10 mIU/mL after ≥3 doses of HepB vaccine.

◊ A nonresponder is defined as a person with anti-HBs <10 mIU/mL after ≥6 doses of HepB vaccine.

§ HCP who have anti-HBs <10 mIU/mL, or who are unvaccinated or incompletely vaccinated, and sustain an exposure to a source patient who is HBsAg-positive or has unknown HBsAg status, should undergo baseline testing for HBV infection as soon as possible after exposure, and follow-up testing approximately 6 months later. Initial baseline tests consist of total anti-HBc; testing at approximately 6 months consists of HBsAg and total anti-HBc.

Reproduced from: CDC Guidance for Evaluating Health-Care Personnel for Hepatitis B Virus Protection and for Administering Postexposure Management. MMWR Recomm Rep 2013; 62:1.



## Appendix 2:

Review of evidence for hepatitis B prophylaxis following a human bite

- P - Human bite victims
- I - Hepatitis B immunoprophylaxis
- C - Nil
- O - Hepatitis risk, acute hepatitis, seroconversion, cirrhosis, hepatic decompensation, hepatocellular carcinoma.

### Search strategy #6: 33 results retrieved – 4 relevant to PICO, 2 excluded – see below

("hepatitis"[MeSH Terms] OR "hepatitis"[All Fields] OR "hepatitis a"[MeSH Terms] OR "hepatitis a"[All Fields]) AND ("prevention and control"[Subheading] OR ("prevention"[All Fields] AND "control"[All Fields]) OR "prevention and control"[All Fields] OR "prophylaxis"[All Fields]) AND ("bites, human"[MeSH Terms] OR ("bites"[All Fields] AND "human"[All Fields]) OR "human bites"[All Fields] OR ("human"[All Fields] AND "bites"[All Fields]))

### Search strategy #7 – [ 11 results retrieved – 4 relevant to PICO – duplicates of above)

((("bites, human"[MeSH Terms] OR ("bites"[All Fields] AND "human"[All Fields]) OR "human bites"[All Fields] OR ("human"[All Fields] AND "bite"[All Fields]) OR "human bite"[All Fields]) AND ("hepatitis b"[MeSH Terms] OR "hepatitis b"[All Fields]) AND ("prevention and control"[Subheading] OR ("prevention"[All Fields] AND "control"[All Fields]) OR "prevention and control"[All Fields] OR "prophylaxis"[All Fields]))) AND (("hepatitis"[MeSH Terms] OR "hepatitis"[All Fields] OR "hepatitis a"[MeSH Terms] OR "hepatitis a"[All Fields]) OR (acute[All Fields] AND ("hepatitis"[MeSH Terms] OR "hepatitis"[All Fields] OR "hepatitis a"[MeSH Terms] OR "hepatitis a"[All Fields])) OR ("seroconversion"[MeSH Terms] OR "seroconversion"[All Fields]) OR ("liver cirrhosis"[MeSH Terms] OR "liver"[All Fields] AND "cirrhosis"[All Fields]) OR "liver cirrhosis"[All Fields] OR "cirrhosis"[All Fields] OR "fibrosis"[MeSH Terms] OR "fibrosis"[All Fields]) OR (hepatic[All Fields] AND decompensation[All Fields]) OR ("carcinoma, hepatocellular"[MeSH Terms] OR ("carcinoma"[All Fields] AND "hepatocellular"[All Fields]) OR "hepatocellular carcinoma"[All Fields] OR ("hepatocellular"[All Fields] AND "carcinoma"[All Fields]))) NOT ("malaria"[MeSH Terms] OR "malaria"[All Fields])

#### a. Excluded studies:

| <i>Author, date</i>                 | <i>Type of study</i> | <i>Reason for exclusion</i>                         |
|-------------------------------------|----------------------|---|
| <a href="#">Voigt, 2003 (19)</a>    |                      | Article in German                                   |
| <a href="#">Kupper, 2015 (20)</a>   |                      | Article in German                                   |
| <a href="#">Harrison, 2008 (21)</a> |                      | Retrospective<br>Primary focus not relevant to PICO |
| <a href="#">Liston, 2001 (22)</a>   |                      | Abstract only<br>Abstract no relevant to PICO       |

In absence of sufficient evidence, international guidance consulted (see appendix 3).

### Appendix 3

Recommended post-exposure prophylaxis for percutaneous or permucosal exposure to hepatitis B virus

#### Recommended postexposure prophylaxis for percutaneous or permucosal exposure to hepatitis B virus

|   | Treatment when source is:                       |                            |   |
|---|---|----------------------------|---|
|   | HBsAg positive                                  | HBsAg negative             | Not tested or unknown   |
| <b>Vaccination and antibody response status of exposed person</b> |   |                            |   |
| Unvaccinated  | HBIG x 1; initiate HB vaccine series            | Initiate HB vaccine series | Initiate HB vaccine series  |
| Previously vaccinated   |   |                            |   |
| Known responder   | No treatment                                    | No treatment               | No treatment  |
| Known non-responder   | HBIG x 2 or HBIG x 1 and initiate revaccination | No treatment               | If known high-risk source, treat as if source were HBsAg positive |
| Antibody response unknown   | Test exposed person for anti-HBs                | No treatment               | Test exposed person for anti-HBs                                  |
|   | If adequate*, no treatment                      |                            | If adequate*, no treatment  |
|   | If inadequate*, HBIG x 1 and vaccine booster    |                            | If inadequate*, initiate revaccination                            |

HBsAg: hepatitis B surface antigen; HBIG: hepatitis B immunoglobulin; HB vaccine series: hepatitis B vaccine; anti-HBs: antibody to hepatitis B surface antigen.

For dosing information see "Hepatitis B immune globulin: Drug information" and "Hepatitis B vaccine: Drug information".

\* Responder is defined a person with adequate levels of serum antibody to hepatitis B surface antigen (ie,  $\geq 10$  mIU/mL); inadequate response to vaccination defined as serum anti-HBs  $< 10$  mIU/mL.

Courtesy of David Weber, MD, MPH.

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