UK National Screening Committee

A pilot of the triage approach to assess whether existing population screening programmes should be continued

Screening Topic

Antenatal screening for hepatitis B

V. Final consultation

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1. Executive Summary

Triage reviews are high level reviews which scan the literature to identify 'red flags' suggesting that further exploration of programme cessation may be necessary. These reviews have a surveillance function and are not intended as a comprehensive review of the programme.

This triage review identified no studies that reported outcomes related to the possible harms of an antenatal hepatitis B screening programme.

A similar review was conducted by the United States Prevention Task Force in 2009 and this came to the same conclusion. Because of the similar aims of the US and UK screening programmes, the conclusions made in the USPSTF review are likely to be applicable to the UK screening programme where they note that any harms associated with screening for hepatitis B are likely to be minimal.

The UK National Screening Committee last reviewed the recommendation to offer antenatal hepatitis B screening in 2010 and considered the benefits of screening to outweigh the harms.

It is the conclusion of this report that there is no evidence suggesting that programme cessation should be explored further.

2. Background

Introduction to the condition

Hepatitis B (HBV) is a viral disease that is transmitted through contact with infected blood and/or bodily fluids. Hepatitis B infections are generally described in either acute or chronic terms, where a chronic infection is usually defined as infection lasting more than 6 months.

The likelihood that an individual will go on to develop a chronic infection is predominantly dependant on the age at which the individual is exposed to the virus. Around 90% of untreated infants who are infected before 12 months will develop a chronic infection whereas fewer than 50% if exposed at 5 years of age. This decrease to less than 5% in those exposed in adulthood.

Symptomatic acute infections are uncommon in both adults and in infants. In those that do experience symptoms, most are likely to only have "flu-like" symptoms. In a minority of cases, acute infections can lead to sever liver disease, which can be fatal.

It is not uncommon for individuals with a chronic hepatitis B infection to be asymptomatic for many years after the initial exposure. Other individuals with chronic HBV infection develop symptomatic disease. This is reported to be associated with cirrhosis, significantly increased risk of liver cancers and liver failure. The risk of symptomatic chronic infection is increased in individuals who contract the disease in infancy.

Hepatitis B infections can be passed from mother to child during pregnancy (vertical transmission). The most common route for vertical transmission is through exposure to the virus during delivery, with a very small minority arising from intrauterine transmission (crossing the placental barrier). The risk of transmission is increased in women that are hepatitis B e-antigen positive. More recently it has been suggested that high viral load increases the risk of mother to child transmission.

Mother to child transmission remains an important cause of chronic hepatitis B infections. This, the long term risks associated with exposure to Hepatitis B in infancy and the availability of a vaccine which can be administered during the child's first 12 months provide the logic for antenatal screening as a strategy to minimise the risk of infection.

3. National Guidance

The UK National Screening Committee has formally recommended hepatitis B screening in pregnant women since 2003. The NHS Infectious Diseases in Pregnancy Screening (IDPS) Programme has oversight of the screening programme in England and provides the standards to which service providers should adhere.

In addition to the screening recommendation, there are a number of national policies and guidelines for the prevention, diagnosis and management of hepatitis B in newborns and pregnant women, notably:

- Vaccination recommendations outlined in Chapter 18 of the Joint Committee for Vaccination and Immunization (JCVI) green book (PHE 2013).
- Recommendations on antiviral therapy in the third trimester for women with increased viral load is covered in Diagnosis and Management clinical guidelines and quality standards from the National Institute of Health and Social Care Excellence (NICE) (NICE 2014; NICE 2013).
- United Kingdom National Guideline on the Management of the viral Hepatitis A, B & C from the British Association for Sexual Health and HIV (BASH 2015)

Acute hepatitis B is a notifiable disease in England and Wales. The screening lab must report all confirmed positive results to Public Health England (PHE).

In addition to the antenatal screening programme, there is a dried blood spot testing service provided by Public Health England (PHE). The service provides tests for infants aged 12 months who are born to hepatitis B positive mothers. The governance for this programme is outside of the remit for the UK NSC (PHE 2013a).

4. Review methodology

Triage review

The UKNSC has committed to assess the viability of all national screening programmes every three years. Triage reviews will be the starting point for each of these assessments.

The purpose of a triage review is to search for evidence that indicates that a screening programme may cause harm in the screened population. The definition of harm in these reviews can be a clinical risk, a social complication or consider a reason for disinvestment. Evidence associated with the modification of the existing screening programme, for example diagnostic studies regarding improvements to the screening test accuracy, is outside the scope of these triage reports.

Depending on the direction and volume of the evidence identified, the triage review may recommend that further investigation through a more rigorous evidence review is warranted or that no further investigation is required until the next three-year cycle. If no studies are identified then this report will recommend continuation of the programme without any further review until the next cycle. As such, triage reviews have a surveillance function.

Each triage review will undergo a three month public consultation on the UKNSC website. The screening committee will then make the final recommendation on the next stage of the review based on the findings of the triage review and the stakeholder consultation comments.

Search strategy and Inclusion criteria

The triage review will be based on a literature search over the last 10 years or since the publication date of the last formal UK NSC review, whichever is most recent. As noted above, studies will only be included that report on outcomes that highlight a reason for the cessation of the existing national

screening programme. The search and inclusion criteria will therefore only consider studies that are relevant to one or more of the criteria below:

- The study reports outcomes that address screening programme cessation (including publications about the ending of screening programmes in countries similar to the UK)
- The study reports on the harms of screening for hepatitis B
- The study reports on the balance of harms and benefits of screening for hepatitis B

Triage reviews prioritise higher quality studies; systematic reviews, randomised controlled trial and large prospective cohort studies. Lower quality of evidence (i.e. case-series, narrative reviews etc.) are considered if they report a significant finding and there is no higher quality evidence to refute or support the outcome(s).

The process for study inclusion was undertaken in two stages. The first stage was undertaken by a UKNSC information scientist and aimed to remove studies that are clearly not relevant to the review (for example, animal studies, studies in a foreign language and duplicates). The second stage was undertaken by a single reviewer and considered the remaining studies and applied the above criteria; all studies excluded at this stage are noted in the excluded studies table in the appendix.

5. Evidence summary

Description of the evidence

The literature search identified nine studies that matched the specifications outlined in the methodology. Of the nine studies, five were conference abstracts. No studies met the inclusion criteria outlined above. The full search strategy is outlined in appendix 1 and the rationale for the exclusion of each of the studies included after the first stage of the review can be found in the table in appendix 2.

While no new evidence was identified, two reviews from the U.S. Preventative Services Task Force (USPSTF) were published in 2009 that are relevant to this report (Lin et al., 2009; USPSTF., 2009) Both publications reported the outcomes of the same literature search on the benefits and harms of the U.S. antenatal hepatitis B screening programme. The literature search was from 2001 (the search cut-off of the previous USPSTF review) to March 2008. The review also identified no studies that met their inclusion criteria.

The screening policy recommended by the USPSTF in 2004 is largely analogous with the one recommended by the UKNSC. Therefore the findings (or lack of) in the USPSTF review could be transferrable to a UK context, albeit with a cautionary note about the differences of US screening practice and any demographic differences between of the two populations.

The USPSTF 2009 update concluded that the potential harms of an antenatal screening programme for hepatitis B are “at most, minimal”.

Conclusion

No new evidence was identified on the harms of antenatal Hepatitis B screening. A similar review, undertaken by the USPSTF in 2009, also found no new evidence that would challenge the ongoing delivery of the recommended screening programme in the USA.

Antenatal hepatitis B screening is part of routine care in most developed countries. It is the conclusion of this report that there is no evidence suggesting that programme cessation should be explored further.

6. References

BASHH 2015

British Association of Sexual Health and HIV 2015, United Kingdom National Guideline on the Management of the Viral Hepatitides A, B & C 2008 Clinical Effectiveness Group British Association of Sexual Health and HIV, British Association of Sexual Health and HIV, London available at: http://www.bashh.org/documents/1927.pdf

Department of Health 2011

Department of Health 2011, Hepatitis B antenatal screening and newborn immunisation programme Best practice guidance (2011), Department of Health, London, https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/215622/dh_132637.pdf

Lin et al., 2009

Lin K, Vickery J. Screening for hepatitis B virus infection in pregnant women: evidence for the U.S. Preventive Services Task Force reaffirmation recommendation statement. Annals of Internal Medicine 2009;150(12):874-6

NICE 2013

National Institute for Health and Social Care Excellence 2013, NICE Clinical Guideline: Hepatitis B (chronic): diagnosis and management, National Institute for Health and Social Care Excellence, London

NICE 2014

National Institute for Health and Social Care Excellence 2014, Hepatitis B: NICE quality standard, National Institute for Health and Social Care Excellence, London

NHS England 2016

NHS England 2016, *NHS public health functions agreement 2016-17 - Service specification no.15 NHS Infectious Diseases in Pregnancy Screening Programme*, NHS England, London, available at https://www.england.nhs.uk/commissioning/wp-content/uploads/sites/12/2016/02/serv-spec-15.pdf

PHE 2013

Public Health England 2013, *Hepatitis B: the green book, chapter 18,* Public Health England, London available at: https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/503768/2905115_Green_Book_Chapter_18_v3_0W.PDF

PHE 2013a

Public Health England 2013, The national dried blood spot (DBS) testing service for infants of hepatitis B positive mothers, Public Health England, London, available at https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/343748/The_national_DBS_service_for_infants_of_hepatitis_B_positive_mothers.pdf

PHE 2015

Public Health England 2015, Acute hepatitis B (England): annual report for 2014, Public Health England, London, available at: https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/457408/hpr3015_hbv-ann.pdf

PHE 2015a

Public Health England 2015, *Antenatal screening for infectious diseases in England: summary report for 2014,* Public Health England, London, available at: https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/482642/hpr4315_ntntlscrng.pdf

PHE 2016

Public Health England 2016, *NHS Infectious Diseases in Pregnancy Screening Programme Laboratory Handbook 2016 to 2017*, Public Health England, London available at https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/539828/NHS_Infectious_Diseases_in_Pregnancy_Screening_Programme_Laboratory_Handbook_2016_2017_with_gateway_number.pdf

PHE 2016a

Public Health England 2016, *NHS Infectious Diseases in Pregnancy Screening Programme Standards 2016 to 2017, Public Health England, London, available:* https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/529070/IDPS_Programmeme_Standards_2016_to_2017.pdf

PHE 2016b

Public Health England 2016, Professional Briefing for PHE and NHS England Screening KPIs (Q3 2015 to 2016), Public Health England, London, available at https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/544000/Professional_Briefing_Screening_KPIs_Q3_2015_to_2016pdf.pdf

USPSTF 2009

US Preventive Services Task Force. Screening for hepatitis B virus infection in pregnancy: U.S. Preventive Services Task Force reaffirmation recommendation statement.[Summary for patients in Annals of Internal Med. 2009 Jun 16;150(12):I36; PMID: 19528547]. Annals of Internal Medicine 2009;150(12):869-73, W154

Appendix 1 – Search strategy

SCOPE OF THE SEARCH:

- Addressing screening programme cessation
- Reporting harms from screening
- Reporting balance of harms and benefits from screening

SOURCES SEARCHED:

- Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present)
- Embase 1996 to 2016 Week 17
- Cochrane Library Issue 4 April 2016

DATES OF SEARCH: January 2005 – April 2016

SEARCH STRATEGY:

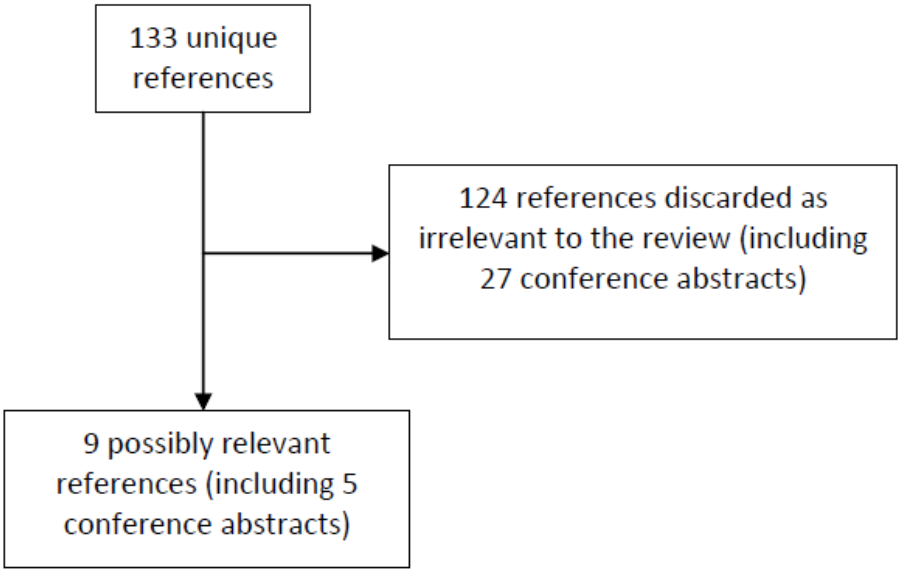
1. exp Hepatitis B/ (49743)
2. (hepatitis B or HBV).tw. (69781)
3. 1 or 2 (80891)
4. Prenatal Diagnosis/ (32831)
5. ((antenatal or prenatal or pregnan$) adj2 screen$3).tw. (6137)
6. Mass Screening/ae [Adverse Effects] (589)
7. 4 or 5 or 6 (37286)
8. (ceas$ or cessation or stop or stopped or continu$ or discontinu$).tw. (1018207)
9. (appropriate$ or inappropriate$ or unnecessary or question$).tw. (1185472)
10. (harm$ or adverse).tw. (463259)
11. (benefit$ and (risk$ or harm$)).tw. (125360)
12. ((side or adverse) adj effect$).tw. (305158)
13. (overdiagnos?s or over diagnos?s).tw. (2746)
14. Programme Evaluation/ (50822)
15. Patient Safety/ (9182)
16. Patient harm/ (60)
17. exp Health Services Misuse/ (8368)
18. Risk Assessment/ (198291)
19. 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 (2864810)
20. 3 and 7 and 19 (106)
21. limit 20 to yr="2005 -Current" (52)

Similar searches were also carried out in Embase and the Cochrane Library. All searches carried out on 29 April 2016

Medline	52
Embase	99
Cochrane Library	23
Total	174

After automatic and manual de-duplication, 133 unique references were sifted for relevance to the review.

Inclusions and exclusions



Appendix 2 – Excluded studies table

Full study reference	Rationale for exclusion
Lin K, Vickery J. Screening for hepatitis B virus infection in pregnant women: evidence for the U.S. Preventive Services Task Force reaffirmation recommendation statement. Annals of Internal Medicine 2009;150(12):874-6	Secondary review that does not report any new findings related to the benefits or harms of screening
US Preventive Services Task Force. Screening for hepatitis B virus infection in pregnancy: U.S. Preventive Services Task Force reaffirmation recommendation statement.[Summary for patients in Annals of Internal Med. 2009 Jun 16;150(12):I36; PMID: 19528547]. Annals of Internal Medicine 2009;150(12):869-73, W154	Secondary review that does not report any new findings related to the benefits or harms of screening
Pande C, Sarin SK, Patra S, Gupta E, Kumar A, Trivedi S. Hepatitis B vaccination with or without hepatitis B immunoglobulin (HBIG) at birth to babies born of hbsag positive mothers prevents overt HBV transmission but may not prevent occult HBV infection in babies. Gastroenterology 2012; 142(5 suppl. 1):[S994 p.].	Does not report outcomes associated with a screening programme.
LeFevre ML, US Preventive Services Task Force. Screening for hepatitis B virus infection in nonpregnant adolescents and adults: U.S. Preventive Services Task Force recommendation statement.[Summary for patients in Annals of Internal Medicine. 2014 Jul 1;161(1):I-28; PMID: 24863504]. Annals of Internal Medicine 2014;161(1):58-66	Screening population does not include pregnant women
Ukwu A, Shehu C, Abdulmumini Y, Nasir S, Umar A. Outcome of pregnancy amongst hepatitis B virus positive pregnant women in a tertiary hospital, Northern Nigeria. International Journal of Gynecology and Obstetrics 2015;131:E507	Study cohort is not generalizable to the UK screening population
Salazar Rios L, Lopez M, Garcia-Otero L, Ferreri J, Gonce A, Lens S, et al. Prevention of perinatal transmission of hepatitis B with antiviral treatment. Journal of Perinatal Medicine Conference: 12th World Congress of Perinatal Medicine 2015;43	Does not report outcomes related to the potential harms of antenatal screening
Lao T. Liver complications and hepatitis in pregnancy. International Journal of Gynecology and Obstetrics 2015;131:E7	Narrative review that does not report any new findings related to the benefits or harms of screening
Zhang H Pan CQ, Liu X, Bian Q, Pang Q, Zhu YX, et al. Excellent theraputic response to tenofovir dipivoxil fumarate (TDF) in chronic hepatitis b pregnant women with resistance to prior anti-viral therapy. Hepatology 2014;60:1117A-8A	Does not report outcomes associated with a screening programme.
Chakrabarty G, Clark S, Forton D. Tenofovir use in hepatitis B infection in pregnancy. Gut 2012;61:A133-A4	Does not report outcomes related to the potential harms of antenatal screening