Public Health England

Protecting and improving the nation's health

Hepatitis B vaccine recommendations during supply constraints

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Outline of the presentation

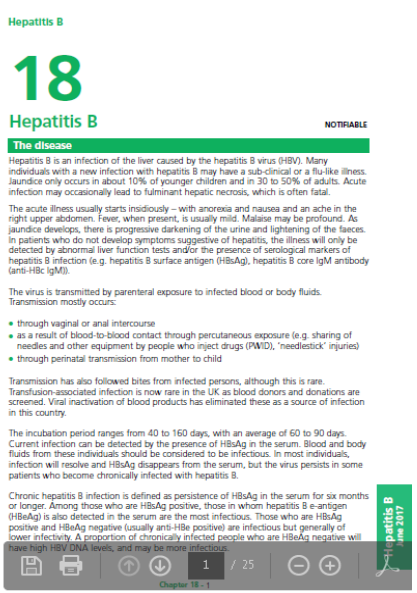
- UK context: hepatitis B vaccination
- Alert and escalation
- Response and risk mitigations
  - Guidance: temporary recommendations
  - Controlled central stock management
  - Communications and publications
- Impact of countermeasures
- Recovery plan
- Challenges

Hepatitis B vaccination in the UK

- Selective and universal immunisation policy
  - Routine infant immunisation since 2017
  - Selective immunisation since 1990s: neonatal, adult risk groups
- Vaccine procurement –no national tender
  - Monovalent HepB and bivalent Hep A/HepB : non-centrally procured vaccine; purchased by providers directly from manufacturers (GSK and MSD) or wholesalers
  - Infanrix-hexa (DTaP/IPV/Hib/HepB): centrally procured for national programme
- Providers = NHS and non-NHS organisations:
  - NHS Trusts (acute and mental health hospitals, ambulance trusts), retail pharmacies, General Practice, travel clinics, occupational health services, private hospitals and clinics, sexual health clinics, community drug and alcohol services, prison services
- Commissioners “contract” providers to deliver services such as vaccination
  - Primary care (GP): Clinical Commissioning Groups
  - Sexual health, community drug services: Local Government
  - NHS secondary care services: NHSE

Broad indications for hepatitis B vaccination

- *Green Book: Immunisation against infectious disease*
- Post exposure vaccination
  - Babies born to hepatitis B infected mothers
  - Significant exposures (e.g. community needle-stick injury)
- Pre exposure vaccination: behavioural, clinical, and occupational risk groups
  - MSM, people who inject drugs, prisoners, foster parents, travellers, household contacts
  - Patients with renal insufficiency, people with chronic liver disease
  - Health and social care staff – including laboratory workers and ancillary staff
  - Non-health first responders (police, fire, mountain rescue), custodial (prison guards)



Hepatitis B

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Hepatitis B

NOTIFIABLE

The disease

Hepatitis B is an infection of the liver caused by the hepatitis B virus (HBV). Many individuals with a new infection with hepatitis B may have a sub-clinical or a flu-like illness. Jaundice only occurs in about 10% of younger children and in 30 to 50% of adults. Acute infection may occasionally lead to fulminant hepatic necrosis, which is often fatal.

The acute illness usually starts insidiously – with anorexia and nausea and an ache in the right upper abdomen. Fever, when present, is usually mild. Malaise may be profound. As jaundice develops, there is progressive darkening of the urine and lightening of the faeces. In patients who do not develop symptoms suggestive of hepatitis, the illness will only be detected by abnormal liver function tests and/or the presence of serological markers of hepatitis B infection (e.g. hepatitis B surface antigen (HBsAg), hepatitis B core IgM antibody (anti-HBc IgM)).

The virus is transmitted by parenteral exposure to infected blood or body fluids. Transmission mostly occurs:

- through vaginal or anal intercourse
- as a result of blood-to-blood contact through percutaneous exposure (e.g. sharing of needles and other equipment by people who inject drugs (PWID), 'needlestick' injuries)
- through perinatal transmission from mother to child

Transmission has also followed bites from infected persons, although this is rare. Transfusion-associated infection is now rare in the UK as blood donors and donations are screened. Viral inactivation of blood products has eliminated these as a source of infection in this country.

The incubation period ranges from 40 to 160 days, with an average of 60 to 90 days. Current infection can be detected by the presence of HBsAg in the serum. Blood and body fluids from these individuals should be considered to be infectious. In most individuals, infection will resolve and HBsAg disappears from the serum, but the virus persists in some patients who become chronically infected with hepatitis B.

Chronic hepatitis B infection is defined as persistence of HBsAg in the serum for six months or longer. Among those who are HBsAg positive, those in whom hepatitis B e-antigen (HBeAg) is also detected in the serum are the most infectious. Those who are HBsAg positive and HBeAg negative (usually anti-HBe positive) are infectious but generally of lower infectivity. A proportion of chronically infected people who are HBeAg negative will have high HBV DNA levels, and may be more infectious.

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Chapter 18 – 1

Hepatitis B June 2017

Alert and escalation

- May-June 2017: Notification from manufacturers that UK supplies will be affected by manufacturing issue
  - some stock restrictions implemented
- June 2017: PHE issues warning and initial advice in e-bulletin *Vaccine Update*
- July 2017: PHE notified that situation will become critical
  - Usual demand ~150k adult doses and 10k paediatric doses per month
  - 1/3 of usual GSK stock available over August and MSD will be out of stock
- July 24 – Aug 7: PHE develops temporary guidance and communications
- 4 August 2017: PHE National Enhanced Incident declared; CMO alerted
- PHE National Incident Management Team (IMT) established
  - Strategic aims: to prioritize vaccine supply to those at highest immediate risk and preserve scarce stock during the period of constraint for these individuals
  - Strategic and operational response agreed to mitigate risks
  - De-escalation when assurance of sufficient supply to meet current and future demand
  - Official letters from PHE and DH to manufacturers

Response – reduce demand

- PHE Guidance
  - Temporary recommendations (Aug 2017)
  - Advice for people whose vaccination has been deferred (Aug 2017)
  - Use of combination vaccine for travellers (Nov 2017)
  - Recovery plan for phased re-introduction of vaccine as supplies improve (Feb 2017)
  - NaTHNaC: travel health advice
- Scientific “sign off” and endorsement
  - DH sponsored independent expert committee: Joint Committee on Vaccination and Immunisation (NITAG)
  - Chief Medical Officer
  - NHSE Hepatitis clinical lead
- Managed central stock control
  - Forecasting based on estimated demand and need
  - PHE /DH /manufacturer agreed vaccine ordering restrictions
- Communications

Temporary recommendations – key principles

- Prioritise scare supply for those at highest IMMEDIATE risk
- Provide advice to individuals whose vaccination is deferred and flag them for recall
- Advise other ways of avoiding exposure to hepatitis B
- Use alternative vaccines and presentations (e.g. vials vs PFS) where appropriate
- Use dose sparing schedules and defer routine boosters
- Order and manage stock responsibly
  - Liaise with clinical leads (across departments in Trusts)
  - Estimate stock required for highest risk groups
  - Order small amounts frequently
  - Avoid stockpiling

Risk based prioritisation

Prioritisation	Exposure type		Examples of individuals in this category (not exhaustive but for illustration only)
1 Highest risk and urgency	Post exposure	**Substantial exposure to infected blood from a known hepatitis B infected source**	Infants born to hepatitis B infected mothers
2	Post exposure	**Other exposure to a known hepatitis B infected source**	Needlestick or other sharps injury from known positive person, sexual exposure to an acute case of hepatitis B
3	Post exposure	**Exposure to an unknown source**	Needlestick injury from discarded needle in community, sexual assault, mass casualties from a major incident
	Pre-exposure	**Priming for unavoidable, high and imminent risk**	Clinical health care workers with regular blood exposure, particularly those performing exposure prone procedures (e.g. surgeons, dentists), and those working in certain settings (e.g. renal units, hospital laboratory workers). Other first responders required to attend major trauma with likely blood contamination.
	Pre-exposure	**Priming for unavoidable, high and imminent risk, with high risk of onward transmission and co- circulating viruses e.g. HIV, HDV**	Sex workers, MSM with multiple partners, PWID, prisoners, people travelling to endemic countries for medical treatment, patients on renal dialysis units.
4	Pre-exposure	**Priming for those at lower risk and those that can access advice in the event of a recognised exposure**	Household contacts of people with hepatitis B, most other health care workers and ancillary staff in UK healthcare settings, other occupations at risk of percutaneous exposures.
	Pre-exposure	**Priming for those at lower risk or where risk may be avoided or delayed**	Other travel to medium and high endemicity countries. Individuals with cirrhotic liver disease.
5 Lowest risk and urgency	Pre-exposure	**Boosting and reinforcing doses**	For healthy individuals who have completed a primary course of immunisation

Vaccine choice for post exposure

Post-exposure vaccination	Order of preference	Infants born to hepatitis B infected mothers	Other children exposed to a known or unknown source of hepatitis B	Adults exposed to a known or unknown source of hepatitis B
Full risk assessment needed: hepatitis B status of source, significance of exposure, vaccination status of recipient as per Green Book and immunoglobulin handbook Urgent testing of the source should be done if their hepatitis B status if unknown. Give HBIG where indicated (but do not substitute vaccine with HBIG)	1st	Paediatric monovalent HepB vaccine (EngerixB or HBVaxPRO)	Paediatric combination HepA/B vaccine (Twinrix paediatric)	Adult monovalent HepB vaccine (EngerixB or HBVaxPRO)
	2nd	Adult monovalent HepB vaccine (EngerixB or HBVaxPRO)	High dose paediatric HepA/B vaccine (Ambirix)	Adult combination HepA/B vaccine (Twinrix)
	3rd	Paediatric combination HepA/B vaccine (Twinrix paediatric)	Paediatric monovalent HepB vaccine (EngerixB or HBVaxPRO)	High dose paediatric HepA/B vaccine (Ambirix)
	4th	High dose paediatric or adult combination HepA/HepB vaccine (Ambirix or Twinrix)	Adult monovalent HepB vaccine (EngerixB or HBVaxPRO)	Two simultaneous doses of paediatric combination HepA/B vaccine (Twinrix Paediatric)
	5th	Combination DTaP/IPV/Hib/HepB (Infanrix hexa)	Adult combination HepA/HepB vaccine (Twinrix)	Renal HepB vaccine (Fendrix or HBVaxPRO40)

Special considerations for infants born to hepatitis B infected mothers

- About 3000 babies born each year - identified via universal antenatal screening programme
- No delay in birth dose of vaccine for infants born to hepatitis B infected mothers
- Paediatric monovalent HepB vaccine should be prioritised for the birth dose
- Combination DTP/IPV/Hib/HepB is licensed from 6 weeks of age and may be used for second and subsequent doses.
- In infants who have received the birth dose on time and where monovalent hepatitis B is not available, **the second dose may be delayed to six weeks of age and given as DTaP/IPV/Hib/HepB,** with further doses given promptly at 12 and 16 weeks of age**.**
- Boosting at 12 months and/or pre-school can be deferred, although the recommended test for HBsAg at 12 months of age should be done on time

Vaccine choice for pre exposure

Order of preference	Children	Immunocompetent adults	Adults with immunosuppression	Adults of any age with renal failure who are pre-dialysis or on dialysis
1st	Paediatric combination HepA/B vaccine (Twinrix paediatric)	Adult monovalent HepB vaccine (unless requiring hepatitis A) (EngerixB or HBVaxPRO)	Renal HepB vaccine (Fendrix or HBVaxPRO40)	Renal HepB vaccine (Fendrix or HBVaxPRO40)
2nd	Paediatric monovalent HepB vaccine (EngerixB or HBVaxPRO)	Adult combination HepA/B vaccine (Twinrix)	Adult combination HepA/B vaccine (Twinrix)	Adult monovalent HepB vaccine (EngerixB or HBVaxPRO)
3rd	Adult monovalent HepB vaccine (EngerixB or HBVaxPRO)	High dose paediatric HepA/B vaccine (Ambirix)	High dose paediatric HepA/B vaccine (Ambirix)	High dose paediatric or adult combination HepA/HepB vaccine (Ambirix or Twinrix)
4th	High dose paediatric or adult combination HepA/HepB vaccine (Ambirix or Twinrix)	Paediatric combination HepA/HepB vaccine (Twinrix paediatric)	Adult monovalent HepB vaccine (EngerixB or HBVaxPRO)	Two simultaneous doses of paediatric combination HepA/HepB vaccine (Twinrix paediatric)

Dose sparing schedules and boosting

Dose sparing option	Rationale
Schedule options for pre-exposure primary immunisation	
Avoid using 0, 7, 21 day (super-accelerated) schedule - preferentially use standard (0, 1, 6 months) or, if rapid protection required, the accelerated schedule (0, 1, 2 months)	• The super-accelerated schedule is wasteful in the current supply climate. Because the immune response following 3 doses with the super accelerated schedule is lower than that with the standard or accelerated schedules, deferral of the reinforcing/booster dose at 12 months is more risky • For most indications, particularly travel and occupational health, there should be sufficient time to use the standard or accelerated course • Limited data suggest that, in healthy adults over 18 years, two doses at 0 and 1 months will provide equivalent protection to 3 doses at the super-accelerated schedule
Defer third dose of primary pre-exposure immunisation to at least 6 months in those not at immediate risk of exposure who can recognise exposure and access care promptly	• Equivalent protection achieved after 3 doses with 0,1, 6 month and 0,1,2 month schedules • In healthy adults and children, a high proportion will have started to respond after a second dose of hepatitis B vaccine and a completing dose given after an exposure should provide rapid protection.
Boosting deferral	
In immunocompetent individuals who have completed a primary immunisation course at 0, 1, 2 mont… months	• Although knowledge about the duration of protection against infection and …ully
In immunoc… workers, wh… immunisatio… dose currently recommended for five years after the primary course for at least another 12 months	recommending a booster dose of hepatitis B vaccine in routine immunisation programmes.

BOOSTER DOSES NO LONGER RECOMMENDED – JCVI ADVICE, FEB 2018

Controlled central stock management

- PHE estimated vaccine demand from priority groups 1-3 based on NHS and company sales data
- Manufacturers agreed to release vaccine only for priority groups 1-3
- DH and PHE worked with manufacturers to set monthly maximum ordering quantities (MOQs) set to meet estimated demand and prevent stockpiling
  - Allocation based on an assessment of the proportion of vaccines used by those customers for individuals in the highest priority groups 1-3
  - Some providers e.g. NHS Trusts got larger allocations (for A&E PEP, sexual health clinics and staff undertaking EPP) than other customers e.g. GPs, retail pharmacies, universities could not order a stock of adult vaccine
- Override mechanism established for additional doses / volume above MOQ if justification / verification given
- **At-risk infants**: rapid stocktake of birth dose availability in maternity units; Infanrix hexa ordering opened early
- PHE / DH situation weekly monitoring calls with GSK and MSD

Communications and publications

News item on NaTHNaC website
Letter to Dentists
Letter to NHS OH Departments
Letter to GPs
Letter to NHS Medical Directors (includes implications for A&E Departments)
Letter to University Deans
BHIVA / BASHH advice
Letter for NHS111
CAS Alert
Letter to nurses
Letter to community pharmacists
Memo to BVHG/BGS/BASL members
Drug and Drinks News item
Email to liver charities
Post on Royal College of Emergency Medicine website
Email to NHS Trust pharmacists
Letter to NHS Screening and Immunisation Leads and GPs regarding early opening of hexavalent vaccine ordering for babies born to hepatitis B infected mothers

Plan for phased re-introduction of hepatitis B vaccine for lower priority groups 2018

Ref: Gateway number: 2017806
PDF, 247KB, 9 pages

This file may not be suitable for users of assistive technology. Request an accessible format.

Hepatitis B: vaccine recommendations during supply constraints

Ref: PHE gateway number 2017256
PDF, 221KB, 17 pages

This file may not be suitable for users of assistive technology. Request an accessible format.

Temporary Addendum: Combined hepatitis A and B vaccine use in travellers

Ref: PHE publications gateway number 2017585
PDF, 139KB, 1 page

This file may not be suitable for users of assistive technology. Request an accessible format.

What to do if you have to wait for a dose of hepatitis B vaccine: advice for patients

Ref: PHE publications gateway number 2017260
PDF, 159KB, 4 pages

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Communications and publications

Public Health England

Protecting and improving the nation's health

Issue 263, May 2017

Vaccine update

National Immunisation conference 2017 – third year and going from strength to strength

Dr. Mary Ramsay, head of the Immunisation, Hepatitis, Blood Safety and Countermeasures Response department.

The annual conference (Tuesday 25 and Wednesday 26 April 2017 – The Grand Connaught rooms, London) was completely sold out and we were delighted to welcome a rapt audience of immunisation professionals to an ambitious programme of presentations from the national programmes and from abroad.

Our keynote speaker Professor Peter McIntyre provided insights into the Australian national immunisation programme and highlighted the importance placed on experience and data from the UK programme. In an increasingly global world with communications via the internet, international attitudes to vaccination offer valuable insights into how we can work together to eliminate vaccine preventable diseases.

Contents

SAVE THE DATES

National Immunisation Conference

24-25 April 2018

Subscribe to Vaccine Update here. Order immunisation publications here.
For vaccine ordering and supply enquiries, email: vaccinesupply@phe.gov.uk

Public Health England

Protecting and improving the nation's health

What to do if you have to wait for a dose of hepatitis B vaccine: advice for patients

There is currently a global shortage of hepatitis B vaccine which is now affecting the UK. We have put in place measures so that the NHS and other providers can

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News story

Current global shortage of hepatitis B vaccine

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Hepatitis B Vaccine advice for dental professionals

As you may be aware there is a global shortage of hepatitis B vaccine which is currently impacting severely on the UK supply, a situation that is likely to continue

Challenges - legal & regulatory

- Competition laws prevent release and sharing of stock status between manufacturers or by PHE and other manufacturers
- Manufacturers cannot refer customers to off-label use of alternative vaccine products; they can signpost customers to the PHE temporary guidance
- Only licensed products in UK are from GSK and MSD; UK providers cannot use unlicensed vaccines if they have any licenced stock available
- Legal restrictions in moving vaccine stock between clinical entities

Challenges - strategic

- Stock control: no central procurement, stockpile or supply of hepatitis B vaccine so PHE/DH have no direct control over stock usage
  - No routine stocktake in providers
- Limited manufacturer visibility of supply and reduced allocations – difficult to forecast
- Lack of clarity of clinical responsibility and leadership for non-centrally procured vaccine issues in NHS and DH
- Multiple commissioners, providers, and clinical specialties implicated
  - no single, effective communication channel
- Large uncertainty around estimated numbers of patients/staff in each group where vaccination indicated
  - dependent on sales and reimbursement data which likely reflects demand rather than actual need (e.g. excessive travel use)

Challenges - operational

- Interpretation of guidance as “absolute” “blanket” recommendations
  - Reluctance to undertake individual risk assessment
- Perceived potential for increased pressures on emergency and urgent care services
- Patients being bounced between services as lack of any prior formal agreement on responsibility for vaccination of these groups
  - vaccine shortage used as an excuse not to vaccinate
- Concern that some services simply stopped vaccinating e.g. community drug services – issues:
  - higher cost of alternative products and not contracted to provide them
  - person ordering vaccine different to person immunising
  - no directive in place to allow nurse administration of alternative product
- Parallel market operating in retail pharmacies and private travel clinics can undermine prioritisation
- Concomitant shortage of hepatitis A vaccine and HAV outbreak in MSM

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Thank you

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Resources

- Hepatitis B vaccine recommendations during supply constraints https://www.gov.uk/government/publications/hepatitis-b-vaccine-recommendations-during-supply-constraints
- mmunisation against Infections Disease (the Green Book) Department of Health (2006). Hepatitis B Chapter 18
- https://www.gov.uk/government/publications/hepatitis-b-the-green-book-chapter-18
- Immunoglobulin Handbook Hepatitis B https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/327768/Hepatitis_B_immunoglobulin_Oct_2008.pdf
- The National Travel Health Network and Centre (NaTHNaC) http://nathnac.net/#/
- Information on off-label use of vaccines https://www.gov.uk/government/publications/off-label-vaccine-leaflets
- Vaccine stock situation updates from manufacturers in Vaccine Update: https://www.gov.uk/government/collections/vaccine-update.