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Hepatitis E Virus (HEV) and Blood Components:

Information for clinical and transfusion laboratory staff

v1.1 March 2016

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Introduction

- Hepatitis E Virus (HEV)
  - RNA virus
  - Four genotypes:
    - 1 + 2 are human viruses
    - 3 + 4 are animal viruses (transmitted zoonotically)

- Increase in the reported cases of HEV arising from infection acquired within the UK (i.e. ‘non-travel associated’)
- Cases of non-travel associated infection are most likely to be:
  - caused by the genotype 3 strain (associated with pigs)

Incidence of clinical acute HEV hepatitis in the UK

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Year	Number of confirmed cases
2003	124
2004	149
2005	329
2006	289
2007	162
2008	176
2009	**175**
2010	**274**
2011	**456**
2012	**578**
2013	**692**
2014	**869**
2015	616 (Jan to Sept)

Data: Public Health England. *Hepatitis E: symptoms, transmission, treatment and prevention*.
Accessed online via: https://www.gov.uk/government/publications/hepatitis-e-symptoms-transmission-prevention-treatment on 8th February 2016

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HEV infection

- Most cases are asymptomatic.
- Symptomatic cases present as an acute but mild transient illness requiring supportive management only
- Average incubation period is approximately 40 days
- Symptoms can last on average 1-4 weeks
  - mild non-specific illness (fatigue, fever, nausea/vomiting)
  - derangement in liver enzymes and jaundice

HEV infection

- Immunocompetent patients are usually able to clear the virus
- In immunosuppressed patients, such as those undergoing transplant, HEV is more difficult to clear
  - lead to chronic changes including chronic inflammation and potential to develop cirrhosis

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HEV transmission

- HEV is passed via oral-faecal route (contaminated sewage) in developing countries
- In developed counties, transmission potentially linked to:
  - eating under-cooked pork and game, processed pork products and some shell fish
  - transmission via blood components and organ transplantation
  - also via SD treated FFP, but now prepared from HEV negative plasma.

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Hepatitis E virus in blood components: a prevalence transmission study in southeast England (The Lancet, July 2014)

- Samples from blood donations given in the southeast of England from October 2012 – September 2013 were screened retrospectively for HEV RNA.
- Prevalence of HEV RNA in donations was **1 in 2848**
  (79 out of the 225,000 donations tested)
  - 54 of the 79 HEV RNA positive samples were genotyped: all were genotype 3.
- 129 blood components were manufactured from the 79 donations:
  62 of these were transfused before identification of infected donation.
- Follow up of 43 recipients showed 18 (42%) had evidence of infection.
- HEV transmission via Red Cells, Platelets (pooled and apheresis), Fresh Frozen Plasma, and Granulocytes was identified.

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Hepatitis E virus in blood components: a prevalence transmission study in southeast England (The Lancet, July 2014)

Conclusions

- HEV genotype 3 infections are widespread in the English population and in blood donors.
- Transfusion transmission linked to viral load/ serological status of donor.
- Transfusion-transmitted infection rarely caused acute morbidity.
- In some immunocompromised patients, infection became persistent, but could be influenced by reducing/ modifying immunosuppression or treating with Ribavirin.

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SaBTO recommendations

- Advisory Committee on the Safety of Blood, Tissues and Organs (SaBTO) set up a specific Hepatitis E working group in response to the Lancet article.

Key Recommendations:

- Introduce donor blood component testing to provide HEV negative blood components for patients undergoing solid organ or allogeneic stem cell transplants.
- Provide advice to allogeneic stem cell transplant and solid organ patients regarding risk of eating poorly-cooked pork or pork products including sausages and offal.

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Indications for HEV negative blood components

- SaBTO expanded on the specific patient groups who should receive HEV negative blood components (see Box 1 on slide 15).
- Applies to cellular blood components (red cells, platelets and granulocytes) and plasma components (FFP and cryoprecipitate).
- No evidence at present to support a requirement for HEV negative blood components for pregnant women.

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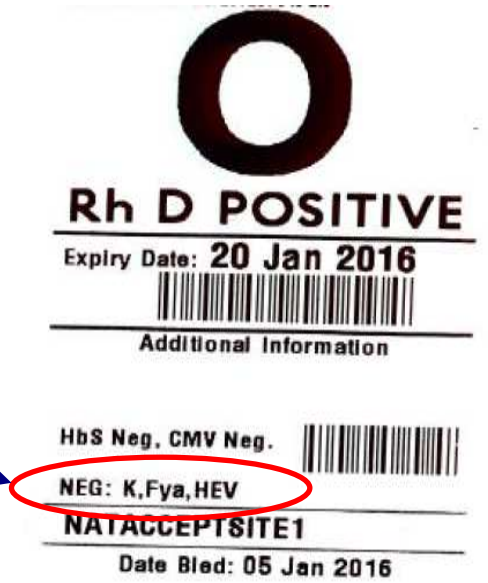
Testing and issue

- NHSBT now issues HEV negative blood components: all types of components are available as HEV negative.
- In 2016/17 a premium of £17.18 is being applied to each unit issued where HEV negative is requested as an additional requirement.
- Some components will be issued HEV negative as standard (see Box 2 on slide 16); the HEV premium does not apply to these components.
- NHSBT will provide HEV negative components for neonates and infants under the age of one year.

Component labelling

- Blood components manufactured by NHSBT that are HEV negative will be labelled ‘NEG: HEV’



- Non-UK plasma components issued by NHSBT, i.e. MB FFP and MB Cryoprecipitate, are already tested and confirmed as HEV negative in the country of donation (Austria); these components do not identify this on the blood pack label.

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Ordering and receipt

- A tick box has been added to OBOS to select HEV negative as an additional requirement for the component
  - this will be in addition to any requirement for the component to be irradiated or CMV negative.
- Components that have HEV negative as part of the mandatory requirements will be automatically provided as HEV negative (see Box 2 on slide 16), and there is no need to tick this box when ordering these components on OBOS.
- Methylene Blue (MB) treated frozen components are already screened for HEV during the manufacturing process; when ordering these components on OBOS, **DO NOT** tick the HEV negative box – if it is ticked our system will not allow for the component to be dispatched; the order will be cancelled and have to be re-ordered.
- HEV negative status of blood components has been added to EDN specification.

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Transfusion laboratory

- No additional handling or storage requirements for HEV negative components.
- Patients who require HEV negative blood components may need to be flagged on your LIMS (see Box 1 on slide 15) – refer to local policy.
- Transfusion laboratory staff should be trained to recognise clinical details on transfusion request forms that may indicate the need for HEV negative blood components.
- Transfusion laboratory should inform any receiving referral hospitals of the need for HEV negative blood components for the patient.
- Any suspected HEV transmission by blood component transfusion should be reported to NHSBT as soon as possible.

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BOX 1

Patients who require HEV negative components

- **Patients awaiting solid organ transplant (SOT)** – from 3 months prior to date of planned elective SOT or from the date of listing for a solid organ transplant.
- **Patients who have had SOT** – for as long as the patient is taking immunosuppressants.
- **Patients with acute leukaemia** – from diagnosis (unless/until decision made not to proceed with stem cell transplant).
- **Patients awaiting allogeneic stem cell transplant** – from 3 months prior to the date of planned transplant and up to 6 months following transplant, or for as long as the patient is immunosuppressed.
- **Extra corporeal procedures** – only included if within above indications.

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BOX 2

Components issued HEV negative as standard

- Red cells for neonatal use (i.e. ‘paedipack’/split pack)
- Platelets for neonatal use (i.e. ‘paedipack’/split pack)
- Red cells for intrauterine transfusion
- Platelets for intrauterine transfusion
- Red cells for large volume transfusion
- Red cells, irradiated, for exchange transfusion (neonatal)
- Pooled granulocytes, irradiated

- Methylene blue fresh frozen plasma (paediatric)
- Methylene blue fresh frozen plasma (neonatal)
- Methylene blue cryoprecipitate (pooled)
- Methylene blue cryoprecipitate (single)