

# Hepatitis E & Blood Components:

Dr Fiona Regan

Consultant Haematologist

NHSBT, Colindale & Imperial College  
Healthcare NHS Trust, London

(With thanks to Dr Jayne Peters, Haematology ST5  
NHS Blood and Transplant, Plymouth Grove, Manchester and Prof  
Richard Tedder, PHE England– for some graphics/slides)

## HEV: RNA virus; 4 genotypes:

1 + 2 are human viruses (1 is travel-associated)

3 + 4 are animal viruses (transmitted zoonotically)

5+ years, increase in cases of HEV acquired in UK i.e. 'non-travel associated',  
caused by genotype 3 (associated with pigs)

Year	Number of confirmed cases in UK
2003	124
2004	149
2005	329
2006	289
2007	162
2008	176
2009	<b>175</b>
2010	<b>274</b>
2011	<b>456</b>
2012	<b>578</b>
2013	<b>692</b>
2014	<b>869</b>
2015	190 (Jan to March)

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 8<sup>th</sup> September 2015

# Hepatitis E

- HEV: oral-faecal route (sewage contamination) in developing countries
- In developed countries, transmission by:
  - Diet: eating under-cooked pork/game, processed pork products and some shell fish
  - Blood components and SCT/organ transplant
- **Average incubation period approx 40 days;**
- **Symptoms last on average 1-4 weeks** – then clearance;
  - Some asymptomatic
  - Mild non-specific illness (fatigue, fever, nausea/vomiting)
  - Derangement in liver enzymes and jaundice
  - Care: in SCT setting, can be mistaken for GVHD (if ↑ steroids, HEV worsens; treatment is ↓IS +/- add ribavirin)

# Hepatitis E – if not cleared

- Immunocompetent patients usually able to clear the virus
- In immunosuppressed patients, eg: undergoing SCT or SOT transplants, HEV is more difficult to clear
  - Can lead to chronic changes including chronic inflammation & potential to develop cirrhosis in 3-5 years

THE TIMES  
**Health News**  
News | Opinion | Business | Money | Sport | Life | Arts | Puzzles | Papers

Welcome to your preview of The Times

## Hepatitis E risk from blood donations



Sonia Elks  
Last updated at 2:37AM, July 28 2014

One in almost every 3,000 blood donors in England could be infected with hepatitis E, according to a new study.

Experts said that around 1,200 transfusions containing the virus are likely to be given to patients every year in England.

Researchers said the risk to patients was 'slight' (1/10k) (1)

Print  
Share via  
Facebook  
Twitter

BBC  
Menu


## NEWS

Home | UK | World | Business | Politics | Tech | Science | Health | Education | Entertainment

Health

### Blood donors 'passing on hepatitis E'

© 28 July 2014 | Health



Around 1,200 people each year are infected with the hepatitis E virus (HEV) through donated blood in England, a large study shows.

Most people will not notice any symptoms, although it can cause liver damage and be fatal in some cases.

The study in the Lancet medical journal showed one in 3,000 blood donations

## Hepatitis E virus in blood components: a prevalence transmission study in southeast England (Lancet, July 2014; 384: 1766-73.)

- NHSBT and PHE: Prospective study monitoring hepatitis E detection in 225,000 donations between Oct 2012 – Sept13
- Objectives:
  - Prevalence of HEV RNA in blood donations
  - Outcomes of those patients infected via transfusion
    - (blood testing not at time of blood issue, but afterwards)
- Results: Prevalence in blood donations:
  - 79 /225 000 donations were HEV RNA pos
    - = Prevalence **1 in 2848 blood donations**
  - Most samples were genotyped: all type 3

# Results: Outcome of patients -

	Blood components associated with HEV-viraemic donation	Blood components recalled or discarded	Blood components transfused
Red blood cells	71	48 (68%)	23 (32%)
Pooled platelets	15	3 (20%)	12 (80%)
Apheresis platelets	24	1 (4%)	23 (96%)
Fresh frozen plasma	12	9 (75%)	3 (25%)
Cryoprecipitate	6	6 (100%)	0
Pooled granulocytes	1	0	1 (100%)
<b>Total</b>	<b>129</b>	<b>67 (52%)</b>	<b>62 (48%)</b>

Data are number or number (%).

**Table 1: Blood components associated with viraemic donations**

Further analysis of outcome of 18 patients who received components from a viraemic donor indicated that in the highly immunosuppressed, the virus took a long time to clear

	Recipients of blood components	Infected recipients	Uninfected recipients
Red blood cells	16	4 (25%)	12 (75%)
Pooled platelets	10	4 (40%)	6 (60%)
Apheresis platelets	14	7 (50%)	7 (50%)
Fresh frozen plasma	2	2 (100%)	0
Pooled granulocytes	1	1 (100%)	0
<b>Total</b>	<b>43</b>	<b>18 (42%)</b>	<b>25 (58%)</b>

Data are number or number (%).

**Table 2: Association between transfused blood components and transmission of hepatitis E virus in 43 of 60 exposed patients in whom follow-up was possible**

## Lancet Paper: Conclusions

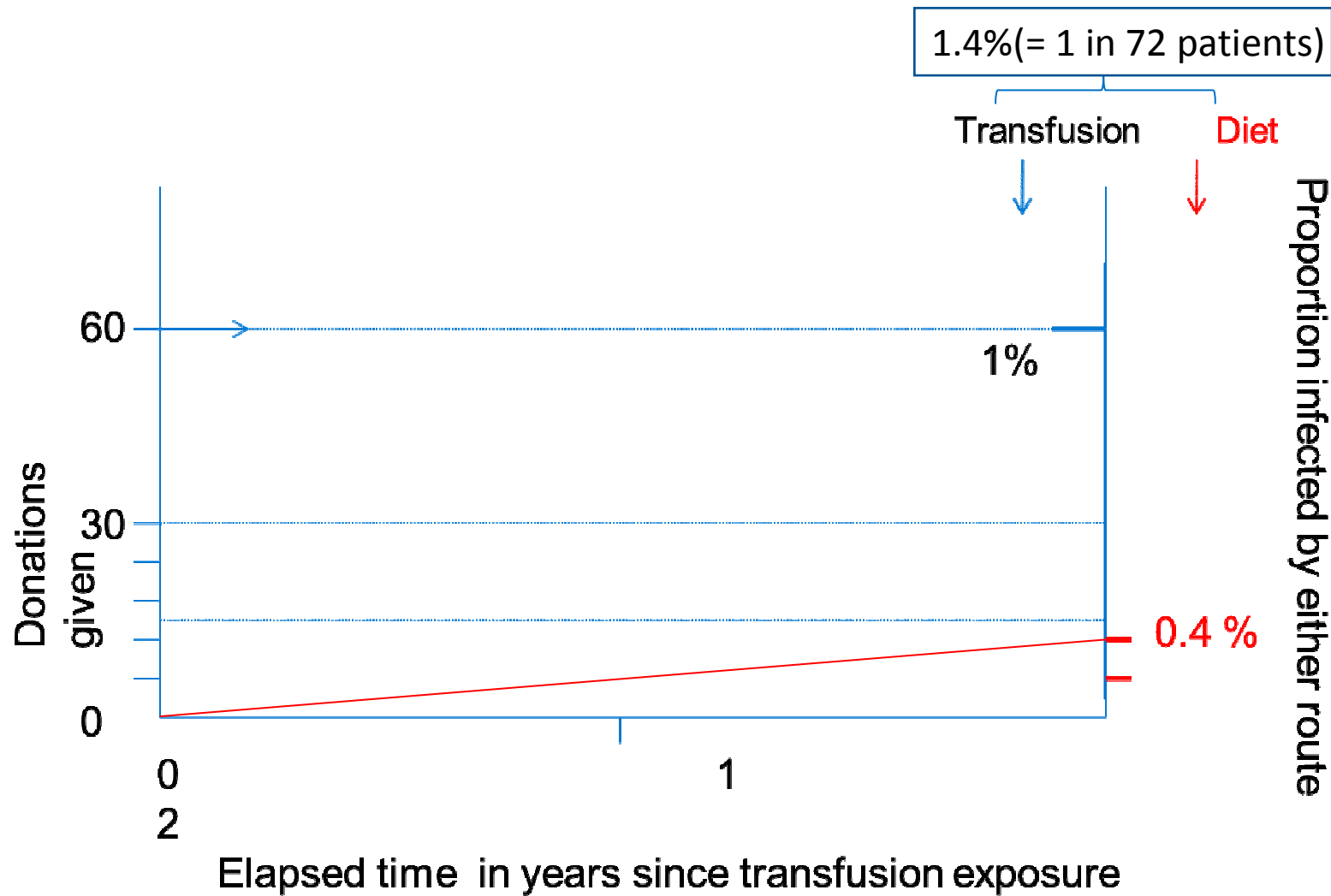
- HEV genotype 3 infections - widespread in English population and in blood donors (higher in parts of Europe)
- Transfusion-transmitted infection varies by component (greater transmission by plasma & platelets than red cells); rarely causes acute morbidity; but some immunosuppressed patients, infection is persistent (potential cirrhosis in 3-5 yrs)

## Dietary Considerations:

- Strong association between genotype 3 and pork/pork products (pork pies, sausages, ham)
- Is the risk of transmission from food higher than that of transmission via blood components or transplant?

# GIVENS

Donor annual seroconversion rate 0.2%  
60 donor exposures  
two years after procedure





# SaBTO Recommendations

- Advisory Committee for Safety of Blood, Tissues & Organs – Aug15.

## Key Recommendations:

- Introduce testing to provide hepatitis E neg components for patients having solid organ or allogeneic SCT (timings – later)
- Provide dietary advice to allogeneic SCT and SOT patients regarding risk of eating poorly-cooked pork or pork products.
- Screen patients for HEV PCR (3 monthly) for dietary acquisition

## Other groups:

- NHSBT also provides HEV neg components for neonates
- No evidence at present for HEV neg components in pregnancy
- Current assessment re: patients with chronic liver disease, haemoglobinopathies and other immunocompromised patients

# What does that mean?

- NHSBT started supplying HEV neg components from 14/03/2016.

## **Clinical indications for hepatitis E negative components?**

### **1. Haematopoietic Stem Cell Transplantation:**

Allogeneic SCT: definite or potential/likely allogeneic SCT recipients:

- from 3 months prior to planned SCT (time of diagnosis for acute leukaemias or AA);
- to 6 months post-SCT, or for as long as patient is immunosuppressed.

Autologous SCT: at present, no convincing evidence to support HEV-components for autologous SCT. SaBTO to review in 6 -12 months, on basis of data collected by BSBMT on patients having autologous SCT, acquiring HEV infection.

## 2. Solid Organ Transplantation

1. All post-SOT recipients, as taking immunosuppressive medication (for life).
2. Potential SOT recipients:
  - From 3 months prior to date of planned (live donor) SOT, or
  - From date of listing for cadaveric SOT, so that any HEV infection may be cleared *before* transplant.
3. Any potential SOT recipient on IS therapy before SOT.
4. Extra corporeal procedures: HEV- blood components should be used for dialysis or extra-corporeal circulatory support - **in those patients undergoing SOT / SOT patients receiving immunosuppressive medication (before or after).**

SaBTO will revisit HEV neg components decision in 2018

## Example:

# How to order HEV- components

- Yellow Form for Haematology patients: updated special requirements list, with HEV tickbox and reason;
  - a. New patients: decide if likely for allogeneic SCT? If so:
    - if acute leukaemia / AA – from diagnosis;
    - Others – from 3/12 pre-SCT;
  - b. Existing patients: all will need updated form; decide as above;
    - If patients change eg: no longer suitable for transplant (whatever reason) – let Tx Lab know (& change form); conserve HEV- supply & cost.
    - If ever acute need & can't get HEV- supply, then balance of risks – d/w Haematology StR/Consultant.

# Practical Issues:

- HEV- and CMV- components:
  - Rare patient needs both!
    1. CMV- only in pregnant women, non-emergency situation (not post-partum: baby is out);
      - (neonatal components are CMV- HEV- already).
    2. Unless hospital has not changed CMV- policy / shared care with such hospital (1 case where referring hospital thought that, but no longer true)
  - Keep separate stock: **red cells:**
    - 2x O-CMV- & 2x A-CMV- blood (rarely needed, sometimes not used before eventually use in “ordinary” patients). Usually 2 x MOH/week.

# HEV- stock: red cells

- HEV- red cells: most ordered for next delivery for specific patients (irradiated when indicated); 2x deliveries per day.
- With red cells, can order “exact blood” in advance for “patients on the go” as shelf life allows usage later in week.
- Stock: breakdown of stock with special requirements (other than CMV-):
  - ½ O+ irradiated; ½ HEV-
  - ¼ A+ irradiated; all HEV-
  - ¼ (O- & A-) irradiated; not HEV-
- If stock all HEV-CMV- & regularly re-ordered (eg: because use in patients who only needed HEV-): huge cost & supply problems: >> than SABTO balance of cost-benefit to NHS.

# Platelets:

- **Stock all A- CMV- HEV- +/- irradiated on daily basis! Unsustainable.**
- 1. Keep separate CMV- stock, if really need: not needed in pregnant women in emergency (SABTO);
- 2. HEV-.....does it really all have to be A-?
  - We stock most as A+ as:
    - 80% of recipients will be D+ anyway;
    - ½ of the D- will be male/post-menopausal females;
    - if female of childbearing age, we give anti-D (SC if necessary);
    - (40% patients will be group O.....)
- A- platelets exponential demand – means excess A- red cells as result: some hospitals won't accept substitute for A+, as precludes EI!
- Options:
  - Either waste (huge cost to NHS)! Or hospitals use in patients not suitable for EI (Abs; SCT etc); or stop over-ordering A- platelets.

# Platelets stock:

- most ordered for next delivery for specific patients (irradiated or HEV- when indicated);
- **Stock:**
  - CMV- - nil;
  - HEV- - 1x A+ irradiated, HEV-
  - Irradiated, non-HEV- - 2x A+; 1x A-; 1x O+(HT-);
  - No requirements - 1x A+; 1x B+

## Conclusion:

- Everywhere different: review requirements & where actually go
- In emergency, accept components unscreened for HEV: likelihood HEV viraemic & transmission; dietary risk in parallel & screening for HEV; treatable. MHRA aware of this rationale, as discussed before HEV screening started.