Hepatitis E Virus:
A new understanding of an old disease

Samreen Ijaz
Blood Borne Virus Unit (BBVU)
Virus Reference Department

01 June 2011
Hepatitis E virus

• Hepatitis E was not recognised as a separate clinical entity until the 1980s
• HEV endemic through the developing world where it is enterically transmitted
  • large waterborne outbreaks
  • sporadic infections
• Disease is self-limited and not all infections are clinically apparent
  1% mortality rate in general population
  20% mortality rate in pregnant women
• Primary cause of enterically transmitted non-A non-B hepatitis worldwide and is responsible for over 50% of acute viral hepatitis in endemic countries
HEV in the developed world

- In the UK, hepatitis E disease traditionally associated with imported infections

- HEV infections occur in non-endemic countries
  - no travel history
  - no recognised risk factors for HEV

- HEV can be acquired in industrialised countries (indigenous HEV infections)
Indigenous HEV cases

Enhanced surveillance of indigenous HEV cases in England and Wales

GENDER

MOLECULAR ANALYSIS

AGE

Genotype 3
UK strains

Genotype 1 & 2
Endemic strains

Male
Female

< 40 yrs
41 - 59 yrs
> 60 yrs

< 40 yrs
41 - 59 yrs
> 60 yrs
HEV Seroprevalence in England

Overall seroprevalence of ~13%
The detection of HEV Abs and RNA in swine and other animals has led to suggestions of a potential zoonosis with animals acting as reservoirs for HEV infection in humans.

- 85% of UK pigs are anti-HEV pos.

The UK genotype 3 sequences, whilst unique are closely related to those from British pig sequences.

Recommended that indigenous HEV be considered a level 2 zoonosis (potential zoonosis), thus requiring enhanced surveillance in the UK.
Evidence of transmission through food products

• Studies from Japan where individuals became infected after consuming raw/undercooked deer or boar meat

• Consumption of figatellu (traditional Corsican pig liver sausage, eaten raw) linked to 3 separate outbreaks
  • Study led to authorities recommending the product be cooked

• French study – questionnaire on confirmed cases
  • Consumption of game meat
  • Consumption of processed pork
  • Consumption of mussels
Faecal-oral route
Endemic regions
Human strains

Zoonosis?
Non-Endemic regions
Human & animal strains
Parenteral transmission of HEV

- Reports of higher HEV antibody levels in:
  - paid blood donors positive for other blood borne viruses
  - repeatedly transfused haemodialysis patients

- Subsequent reports of transfusion transmitted HEV from France, Japan, and Saudi Arabia

- 2006 reported the first PTH linked to HEV in England
Risk of HEV related PTH

Studies from Japan have demonstrated that a small but significant proportion of their blood donors were viraemic and potentially able to cause transfusion-associated HEV in the absence of signs or symptoms of hepatitis.

Seroprevalence studies

- European blood donors – 3.2% to 20%
- SE Asian blood donors – 3.4% to 33%
• Incidence estimates between 1991 and 2004 indicate that ~62 000 cases of HEV occurred per year in England

• Suggests that there are a significant number of subclinical HEV infections

• Occurring in blood donors this would give an opportunity for donors to infect recipients.
Seroprevalence data

- IgG – 11%
- IgM – 0.7%

Testing of mini-pools for HEV RNA

Tested 880 mini-pools (pools of 48, >42 000 donors)

- 6/880 (0.7%) mini-pools were RNA positive

EVIDENCE OF HEV INFECTION IN DONOR POPULATION
Blood Safety

• Post transfusion hepatitis in the UK is now a relatively rare event

• Speculate that transmissions are occurring but result in asymptomatic infections

• Suggestion that genotype 3&4 (animal viruses) less virulent than genotypes 1&2 which are human viruses

• Data showing that HEV is not a trivial infection in immunosuppressed patients
Chronic Hepatitis E Virus

- HEV infection associated with an acute infection
- Chronic HEV infection reported in immunosuppressed patients
  - Persistent viraemia
  - Persistently raised transaminases
  - Histological features associated with chronic hepatitis
  - Evidence of cirrhosis
Persistent HEV Infections in the transplant setting
Toulouse University Hospital data

- 2008 NEJM – SOT patients with abnormal LFTs
  - 14/217 HEV RNA pos; 8/14 developed chronic hepatitis
- 2010 Transplantation – 33 cases of HEV in SOT patients
  - 27 cases followed up of which 16 (60%) evolved to chronic hepatitis
- 2011 EID – 808 kidney or liver transplant patients
  - 14% seropositive prior to transplant
    - none infected, no reactivation post transplant
  - Of those with no HEV antibodies prior to transplant
    - 6% had de novo HEV infections
    - 47% of whom evolved chronic hepatitis
Outcome for chronic HEV infections

- No treatment available for HEV

- Reduction of immunosuppression leads to viral clearance in 30% of cases

- Pegylated α-interferon has been shown to effectively treat chronic HEV (liver and kidney transplant patients)

- 3 months of Ribavirin monotherapy also shown to effectively inhibit HEV RNA replication in kidney transplant patients
Implication of hepatitis E virus carriage in HIV infection

- Male diagnosed with HIV in 2001 whilst living abroad
- Jan 2007 – returned to UK
  - CD4 count low, HIV VL high, commenced on HAART
  - HIV viral load became undetected
  - CD4 counts remained depressed at ~120 cells/mm
  - ALT raised (58 iu/l – 195iu/l)
  - No evidence of HBV, HCV, CMV or syphilis
Implication of hepatitis E virus carriage in HIV infection (cont.....)

• January 2009: further hepatological assessment & tested for HEV markers
  • HEV IgM, IgG, RNA pos (genotype 3)
• Retrospective testing from Jan 2007 – Jan 2009
  • All serum samples were HEV antibody and RNA pos
• Biopsy showed evidence of cirrhosis; danger of liver failure
• Options limited for this individual
• Should we try and treat?
HEV/HIV co-infected case

- Patient started on Interferon
- Viral load in plasma and stool dropped initially but then plateaued out
- At 6 months, ribavirin was added to treatment protocol
- Ribavirin for 12 weeks, virus became undetectable in both plasma and stool
- Treatment stopped in July 2010 – virus remains undetectable in plasma and stool
How common are persistent HEV infections in the UK?

• No comprehensive data
• Two more cases in HIV infected individuals
  • Case 1 successfully cleared virus whilst on treatment
  • Case 2 developed ascities, died
• Study to look at HIV infected individuals with abnormal LFTs
• Study of HEV in the transplant setting
Indigenous HEV infections

Questions?

• Blood safety?
  • 75% of blood products are given to immunosuppressed individuals
  • Persistent HEV infections are not trivial
  • More comprehensive studies in both blood donors and in the immunosuppressed need to be undertaken

• Is there adequate testing for HEV being undertaken?
  • Probably not enough
  • Essential in the immunosuppressed
  • Treatment options are now available.
Acknowledgements

MS-Colindale, HPA
Richard Tedder
Dilys Morgan
David Brown
Renata Szypulska
Mathew Beale

Royal Cornwall Hospital
Richard Bendall
Harry Dalton

NTMRL, NHSBT, Colindale
Alan Kitchen

Funding
NHS Blood and Transplant & Health Protection Agency