Autochthonous hepatitis E (aHEV) in SW England
Autochthonous hepatitis E (aHEV) in SW England

- Stable population, <0.5% immigrants
- Centralised rapid-access jaundice clinic
HEV in Cornwall

• 51 cases HEV
  • 2/51 travelled to endemic area (India & China)
• 49 cases of aHEV
  • 45/49 HEV IgM +ve
  • 34/49 HEV PCR +ve, all genotype 3
• M:F = 3:1
• All Caucasian
• Median age 64 years (range 35-86)
Symptoms: 49 cases of aHEV

- Jaundice (n=36)
- Anorexia (n=20)
- Lethargy (n=20)
- Abdominal pain (n=19)
- Nausea (n=18)
- Vomiting (n=9)
- Fever (n=10)
- Myalgia (n=8)
- Pruritis (n=5)
- Weight loss (n=4)
- Headaches (n=4)
- Arthralgia (n=3)
- Back pain (n=2)
- Rash (n=1)
- Paraesthesiae (n=3)
- No symptoms (n=2)
Cornish aHEV: Spectrum of severity

- Asymptomatic – mild hepatitis – liver failure
- Median bilirubin 112 µmol/l (range 3-417)
- Median ALT 1412 IU/L
- 46/49 recovered (usually in 4 – 6 weeks)
- 3 patients died
  - Liver failure n=2, unrelated cause n=1
Hepatic complications (n=3)

- All had pre-existing cirrhosis
- Self-limiting encephalopathy (n=1): survived
- Sub-acute liver failure (n=2): died at 4 and 5 months
  *Dalton et al Lancet 2007*

- 70% mortality in HEV superinfection in CLD
  *Kumar Acharya et al J Hepatol 2007*
# aHEV vs HAV

Devon and Cornwall 2005-6

<table>
<thead>
<tr>
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<th>aHEV</th>
<th>HAV</th>
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<tbody>
<tr>
<td>Tests</td>
<td>838</td>
<td>4503</td>
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<tr>
<td>Cases</td>
<td>28</td>
<td>20</td>
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<tr>
<td>Age*</td>
<td>65 (35-86)</td>
<td>41 (8-74)</td>
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<tr>
<td>M:F</td>
<td>4.6</td>
<td>1.6</td>
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<tr>
<td>Complications</td>
<td>n=5</td>
<td>n=0</td>
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<tr>
<td>Death</td>
<td>n=2</td>
<td>n=0</td>
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*p<0.05

_Dalton et al EurJClinMicro 2008_
HEV IgG seroprevalence: SW England

Dalton et al EuroJGastroHep 2008
Seroprevalence 16% why so high???

• ? Inaccurate HEV IgG ELISA
  • ELISA used validated against convalescent sera (n=50), from HEV3 PCR +ve cases (n=18)

• ? Sub-clinical infection

• ? Unrecognised infection
Unrecognised infection (1): Drug-induced liver injury (DILI)

- 20% of patients with DILI have aHEV

- Diagnosis of DILI not secure without testing for HEV

Dalton et al
APHarmTherap
2007
Unrecognised infection (2):
Inflammatory polyradiculopathy

• 3 cases (males, age 40-50yrs)
• Inflammation of peripheral nervous system
  • Not jaundiced
  • ALT 100-1000
  • Spontaneous resolution n=1 (3 months)
  • On-going symptoms n=2
• Minnesota pig factory
Unrecognised infection (3): in chronic liver disease

- 76 yr old male
- Alcohol 35U/week
  - Bilirubin 86
  - ALT 2286
- Decompensated +++
- Transferred to another hospital
- Died at 4 months:
- ‘Alcoholic hepatitis & alcoholic liver disease’
Received wisdom

- Rare in developed countries
- Mainly seen in travellers
- v. rare in non-travellers
- Of little relevance in developed countries
<table>
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<th>Received wisdom</th>
<th>Conjecture</th>
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<tr>
<td>• Rare in developed countries</td>
<td>• Commonest cause of acute viral hepatitis</td>
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<tr>
<td>• Mainly seen in travellers</td>
<td>• Significant morbidity &amp; mortality</td>
</tr>
<tr>
<td>• v. rare in non-travellers</td>
<td>• Prognosis poor in chronic liver disease</td>
</tr>
<tr>
<td>• Of little relevance in developed countries</td>
<td>• Causes up to 26,000 deaths per year in developed countries</td>
</tr>
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</table>
Pork consumption and mortality from liver cirrhosis

- Deaths from cirrhosis vs ethanol consumption and pork consumption
  - in developed countries (1965, mid 1970’s)
  - In states of Canada (1978)

_Nanji and French, Lancet 1985_
Fig 3—Relationship between cirrhosis mortality and pork consumption.
Mortality from chronic liver disease vs alcohol consumption 1990 -2000

$R^2=0.473 \quad p=0.002$
Mortality from chronic liver disease vs pork consumption 1990 - 2000

R^2 = 0.531    p = 0.001
Multiple regression:

• Independent predictors of mortality:
  • Alcohol (p=0.005)
  • Pig meat consumption (p<0.001)
  • HBV (p=0.037)
Possible explanations:

• Epiphenomenon
• A factor in pork causes cirrhosis
• **A factor in pork causes death in patients with pre-existing cirrhosis? aHEV**
  - HEV found in retail pig meat
    - USA, Holland, Japan, and Cornwall
  - HEV survives cooking at 56C & can be transmitted by eating infected meat
  - aHEV mortality in CLD = 70%
aHEV: potential mortality in developed countries

- Assuming:
  - Prevalence of chronic liver disease = 0.5 - 1%
  - Mortality aHEV in chronic liver disease = 70%
  - Population of USA, Canada, EU, Japan, Australia & NZ = 931 million
  - Annual aHEV seroconversion rate = 0.4%

- 13,000 – 26,000 deaths/annum attributable to aHEV infection in patients with chronic liver disease
HEV IgG in patients with chronic liver disease

HEV IgG status in stable chronic alcoholic liver disease (ALD)

- HEV IgG -ve
- HEV IgG +ve

ALD
Non-ALD
aHEV: research collaborators

• **Colleagues in Devon and Cornwall:**
  - Dr Richard Bendall (virologist)

• **UK, national:**
  - Veterinary Laboratory Association (Surrey)
    - Dr Malcolm Banks
  - Health Protection Agency (London)
    - Prof Richard Tedder
    - Dr Samreen Ijaz

• **International:**
  - Centres for Disease Control (CDC), Atlanta, Georgia