Autochthonous hepatitis E (aHEV) in SW England

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- Stable population, <0.5% immigrants
- Cenrtalised 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 112цmol/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

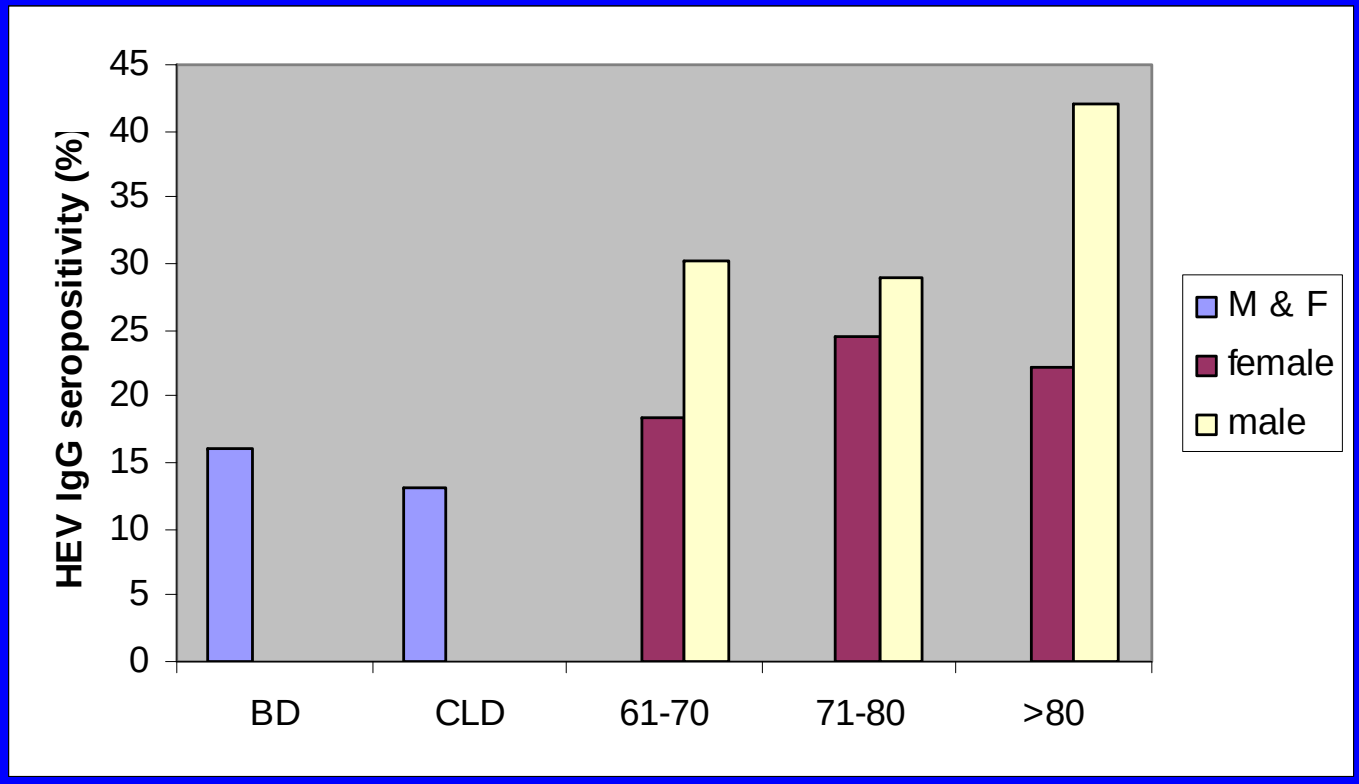
aHEV vs HAV
Devon and Cornwall 2005-6

	aHEV	HAV
• Tests	838	4503
• Cases	28	20
• Age*	65 (35-86)	41 (8-74)
• M:F	4.6	1.6
• Complications	n=5	n=0
• Death	n=2	n=0

*$p<0.05$

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

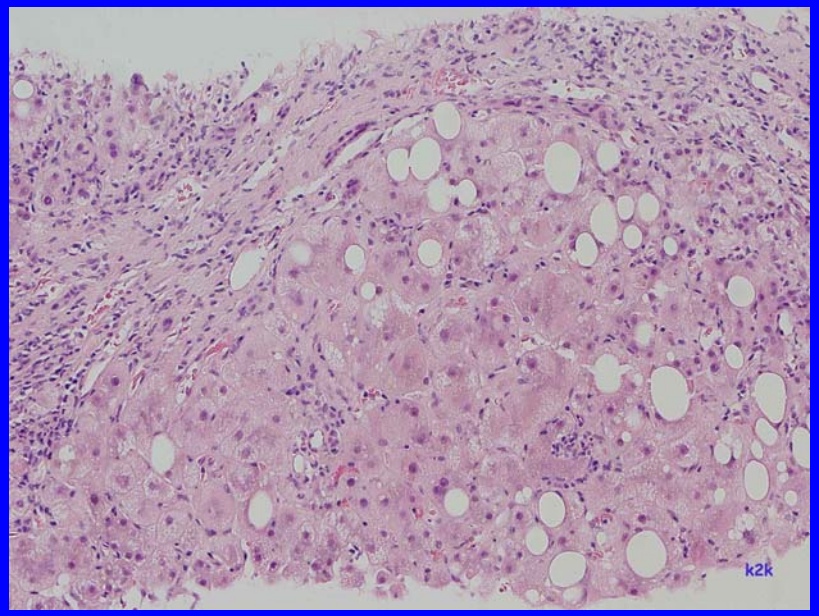
Dalton et al APharmTherap 2007

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’



aHEV

Received wisdom

- Rare in developed countries
- Mainly seen in travellers
- v. rare in non-travellers
- Of little relevance in developed countries

aHEV

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Conjecture

- Commonest cause of acute viral hepatitis
- Significant morbidity & mortality
- Prognosis poor in chronic liver disease
- Causes up to 26,000 deaths per year in developed countries

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

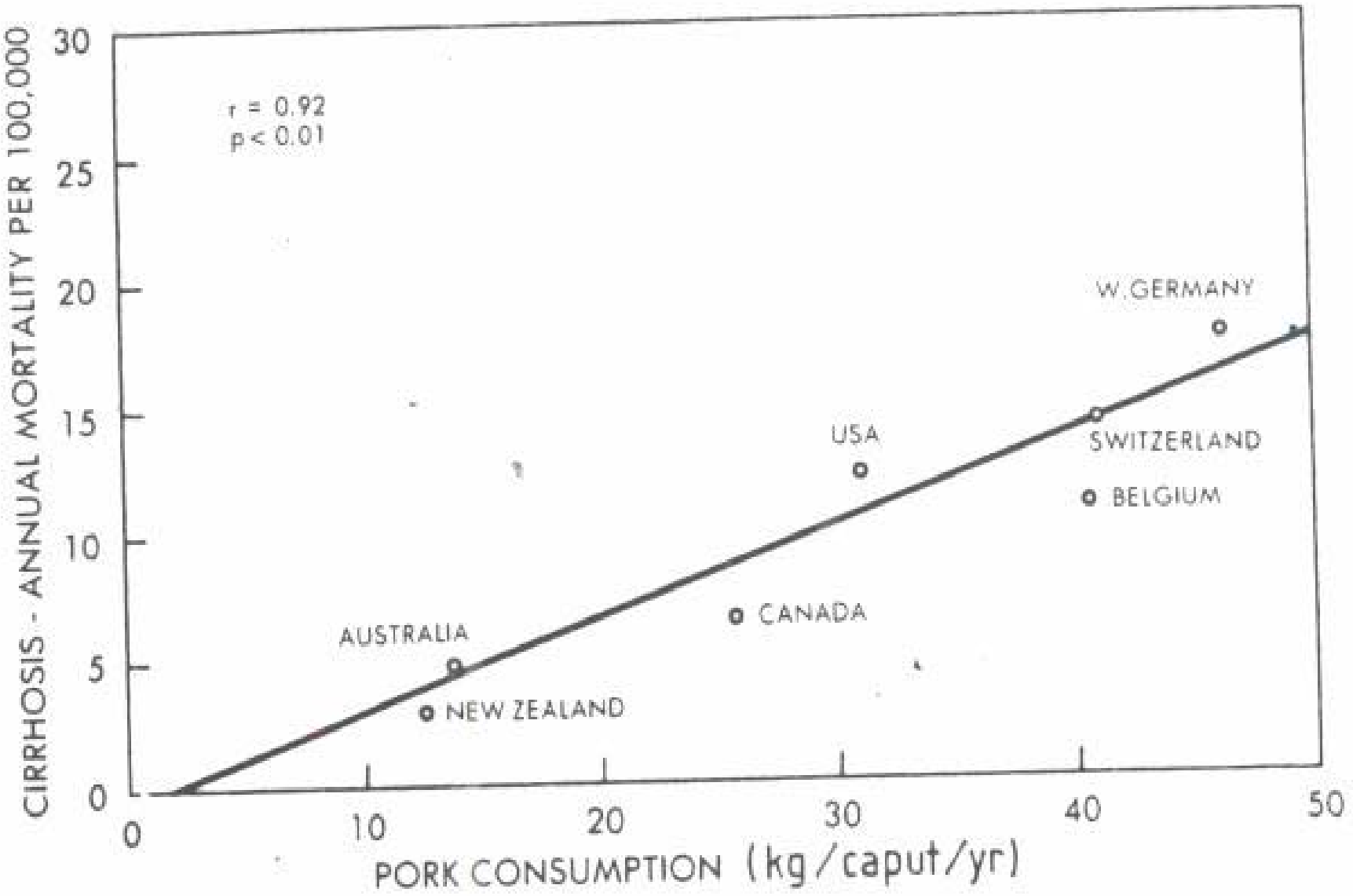
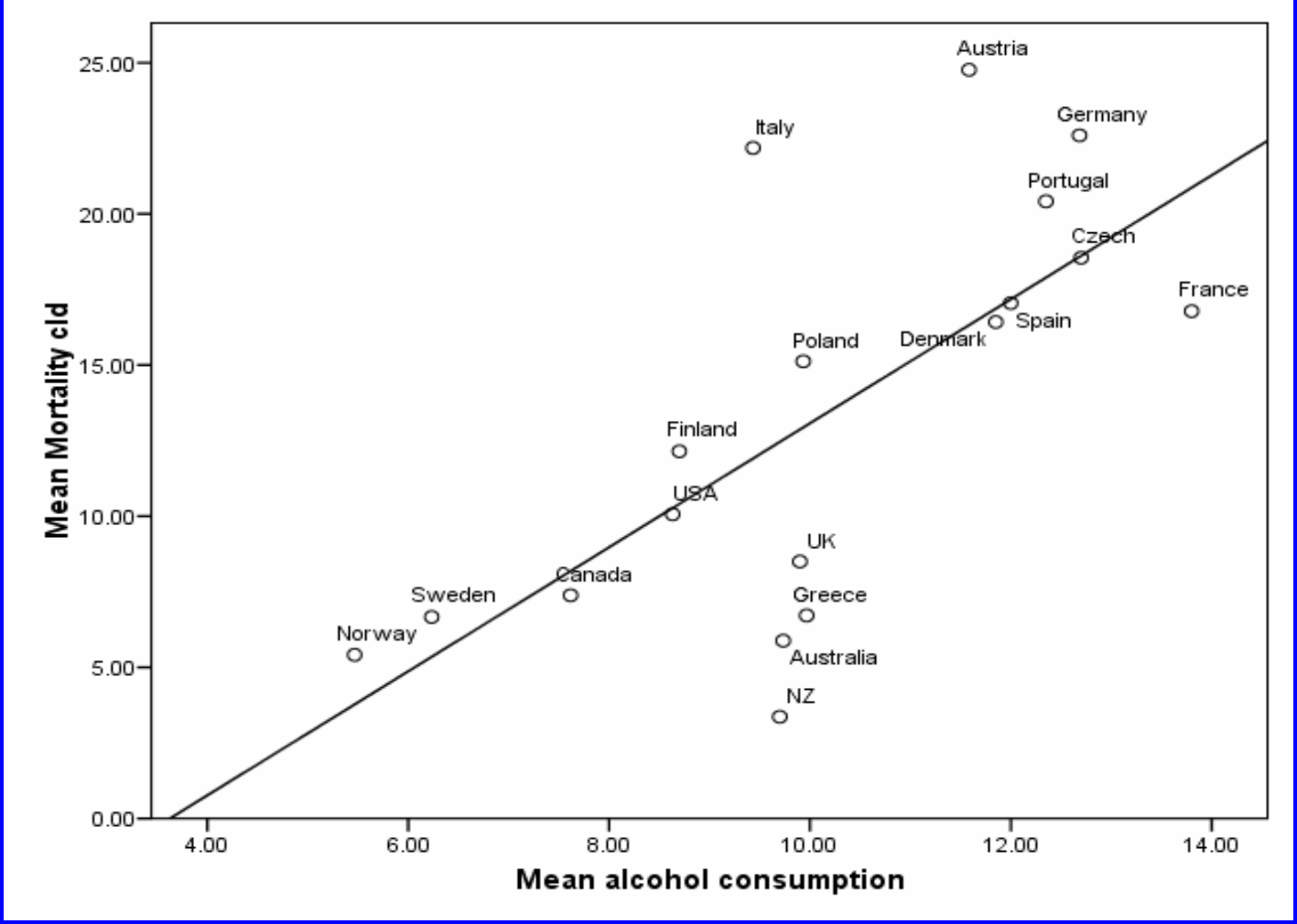


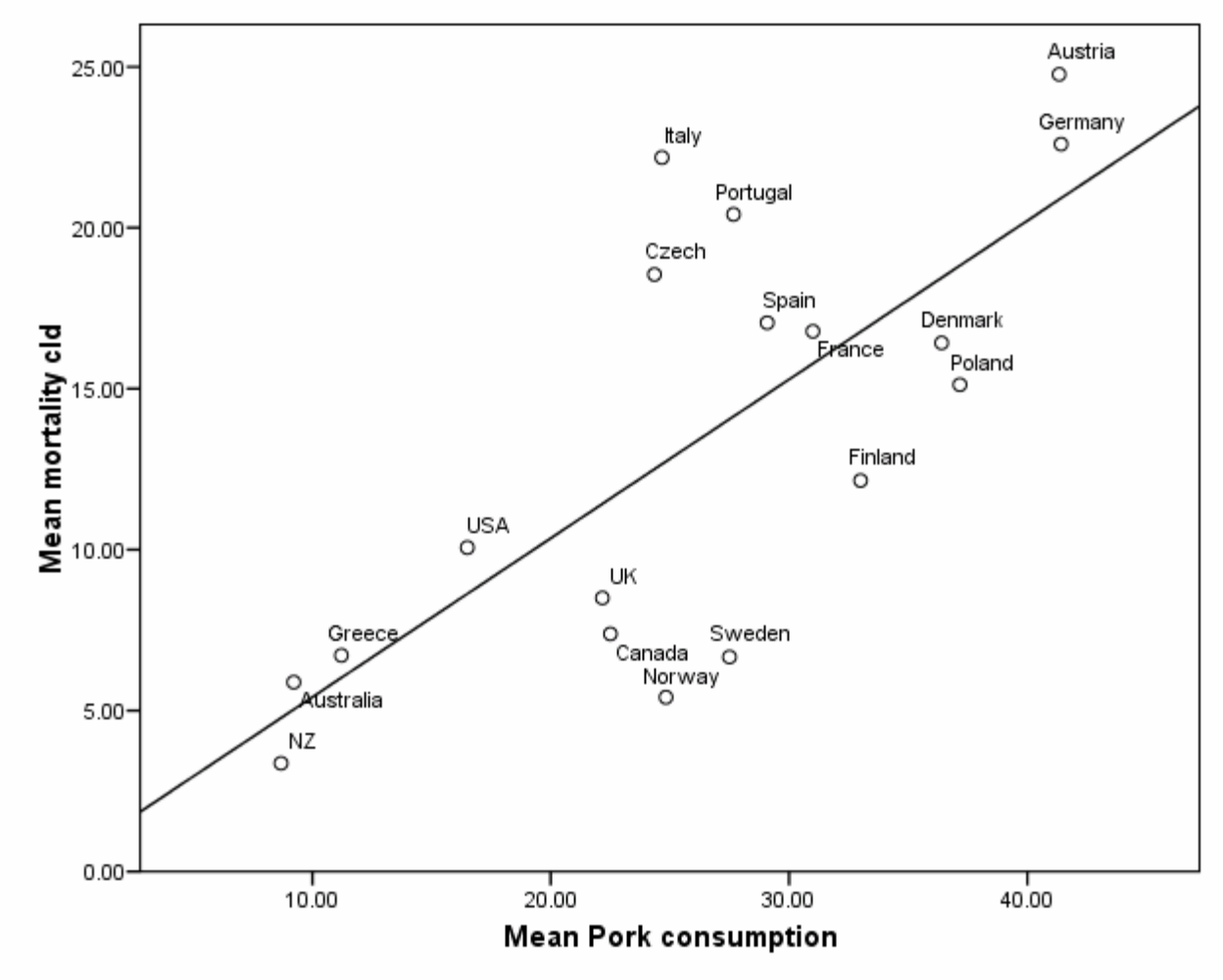
Fig 3—Relationship between cirrhosis mortality and pork consumption.

Mortality from chronic liver disease vs alcohol consumption 1990 -2000



R^2=0.473 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)

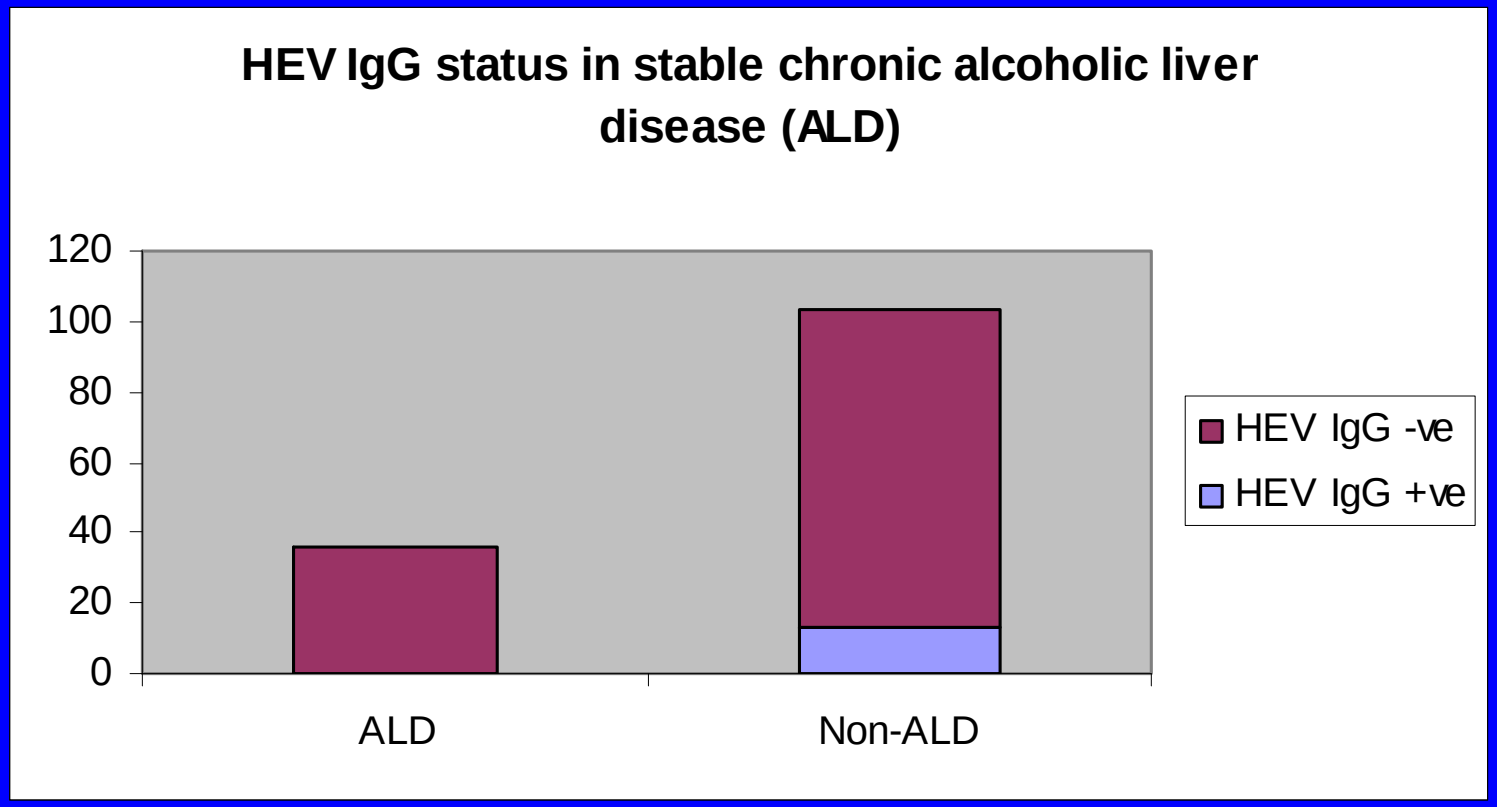
Possible explanations:

- 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 = 931million
  - 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

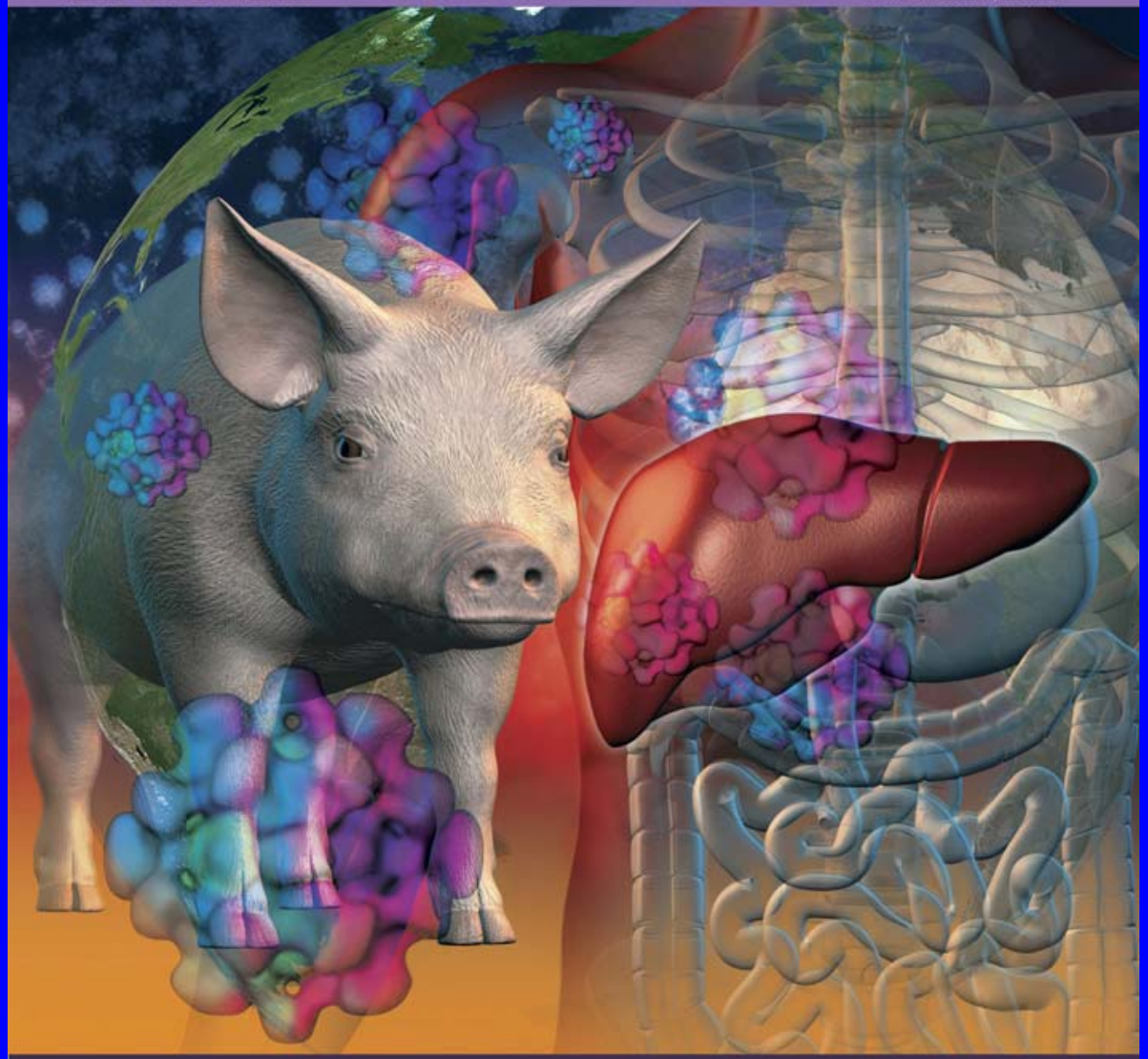


aHEV: research collaborators

- 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

THE LANCET Infectious Diseases

Volume 8 · Issue 11 · November 2008 www.thelancet.com/infection



Review

Intervening in HIV immunopathogenesis

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People, pigs, and hepatitis E

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Historical Review

Emerging infections: from ancient Greece to AIDS

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