Hepatitis E Prevalence in North American Blood Donors

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HÉMA-QUÉBEC

American Red Cross

Roche

Sanquin

Canadian Blood Services
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Disclosures

- Funding for all laboratory support and reagents provided by:
  - Roche Molecular Diagnostics
  - National Microbiology Laboratory (NML), Public Health Agency of Canada (Canadian Study #1)
- Testing performed by:
  - Screening: American Red Cross Scientific Affairs
  - Confirmatory: Sanquin, The Netherlands
  - Sub-population antibody screening: CDC
  - NML (Canadian Study #1)
- Samples provided by
  - American Red Cross
  - Hema-Quebec and Canadian Blood Services

Public Health Agency of Canada

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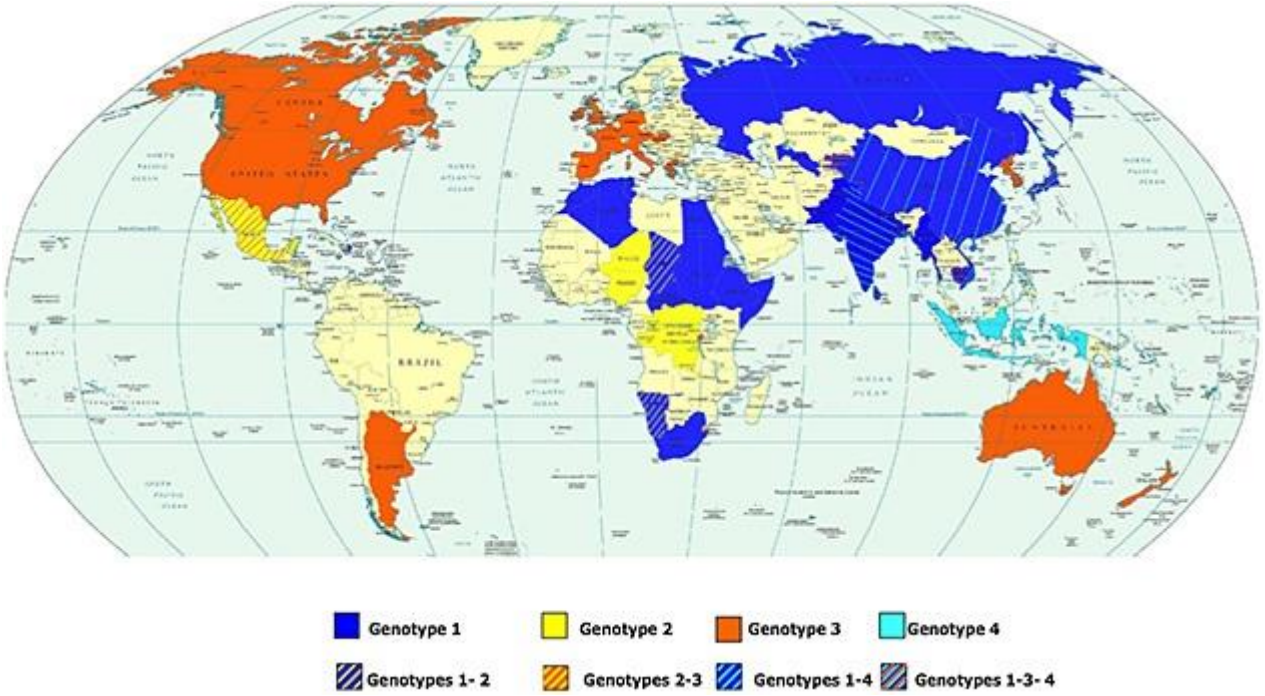
Hepatitis E Prevalence

Geographical Distribution of Hepatitis E virus Genotypes



Hepatitis E: Current Status Perez-Gracia et al. Reviews in Medical Virology 2013;23(6)

> 3 million cases/year, mainly in developing countries
Seroprevalence 2 – 50% in developed countries

Clinical Presentation

Most cases asymptomatic

- **Acute hepatitis**
  - more common in males > 65 yrs. and in pregnant women
  - Incubation period 2 weeks – 2 months
  - Jaundice, fever, malaise, anorexia
  - Viremia is transitory – disappears with symptom onset
- **Chronic hepatitis**
  - Chronic HEV infection reported in liver and kidney transplant recipients (SOT), those with non-Hodgkins lymphoma, in HIV/AIDS patients, stem-cell transplant (SCT) patients. (all immunosuppressed patients)
  - Almost all cases represent autochthonous HEV gt3
  - Persistent viremia with titers 10^5-10^7 IU/mL
  - Evolution to cirrhosis occurs in up to 50%; liver failure

Risk Profile of Hepatitis E Virus from Pigs or Pork in Canada.

Wilhelm B[1], Fazil A[2], Rajić A[1], Houde A[3], McEwen SA[1].

Send to

Transbound Emerg Dis. 2017 Dec;64(6):1694-1708. doi: 10.1111/tbed.12582. Epub 2016 Oct.7

Survey of Canadian retail pork chops and pork livers for detection of hepatitis E virus, norovirus, and rotavirus using real time RT-PCR.

Wilhelm B[1], Leblanc D[2], Houde A[2], Brassard J[2], Gagné MJ[2], Plante D[3], Bellon-Gagnon P[3], Jones TH[4], Muehlhauser V[4], Janecko N[5], Avery B[6], Rajić A[7], McEwen SA[7].

Int J Food Microbiol. 2014 Aug 18;185:33-40. doi: 10.1016/j.ijfoodmicro.2014.05.006. Epub 2014 May 14

USDA

PIGS, PEOPLE AND HEPATITIS E

Residue Chemistry and Predictive Microbiology Research: Wyndmoor, PA

Hepatitis E and Transfusion Transmission

- Over 30 cases of reported cases of transfusion transmission.
- Cases reported in Japan, U.K., France, Saudi Arabia.
- To date, no reported cases of TT HEV in North America

Canadian Blood Services
it's in you to give

North American Donor Prevalence Studies 1

In 2013 **CBS and Hema Quebec** in collaboration with the National Microbiology Lab, carried out a geographically limited HEV prevalence study on approximately 14,000 Canadian blood donors.

- Antibody prevalence of 5.8%
- 0 HEV NAT positive donors (pooled testing 48-100)

Fearon M, O'Brien S. et al Hepatitis E in Canadian Blood Donors. Transfusion 2017;57:1420-142

Also in 2013 the **American Red Cross** surveyed approximately 19,000 U.S. blood donors

- 2 HEV NAT positive donors out of 18,829 tested (ID NAT).
- Antibody prevalence of 7.7% of 4,499 tested donors.

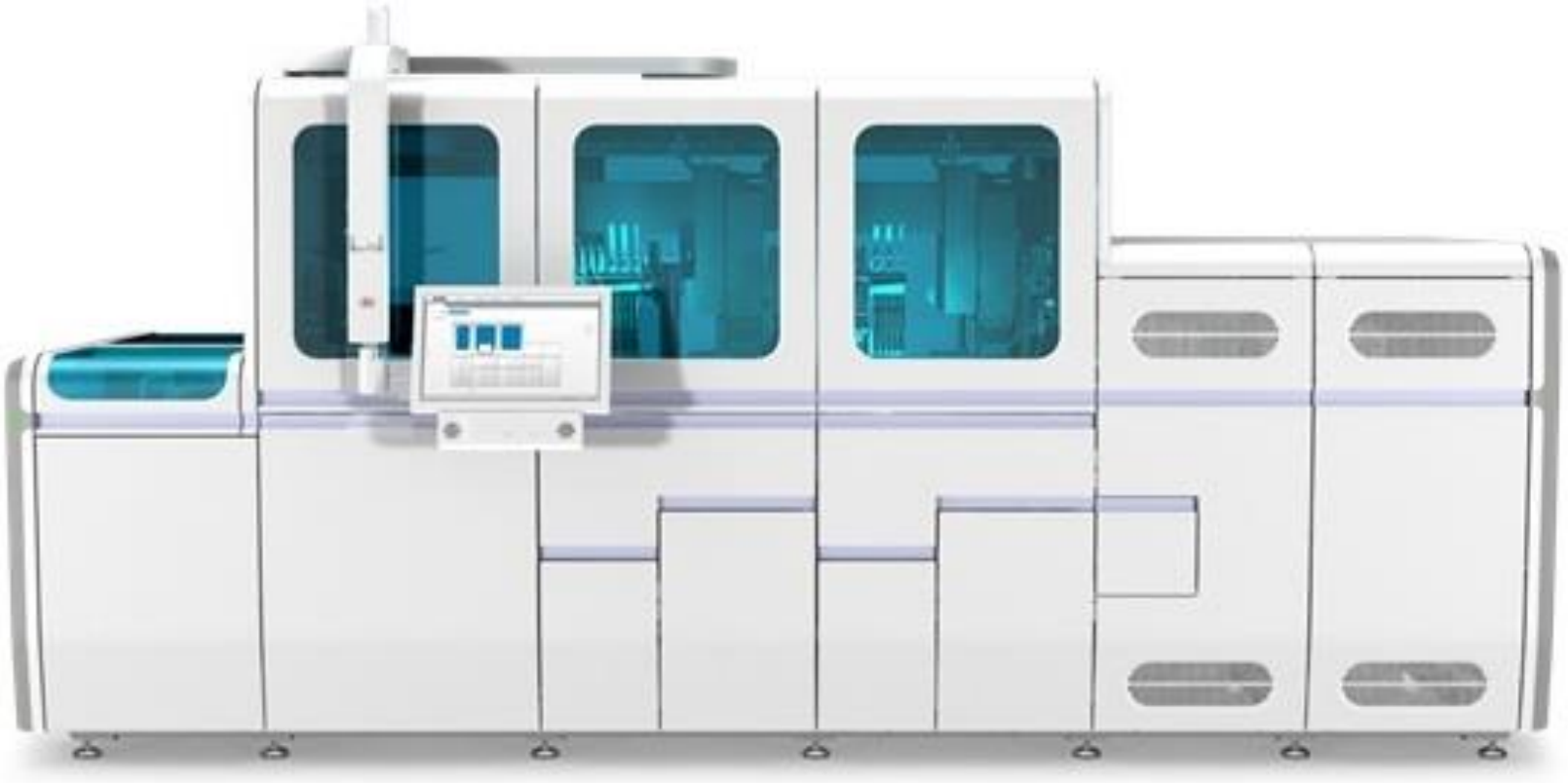
Stramer S, Moritz E.et al. Hepatitis E virus:seroprevalence and frequency of viral RNA detection among US blood donors. Transfusion 2016;56:481-488

Canadian Blood Services
it's in you to give

North American Donor Prevalence Studies 2

- Two independent RNA prevalence studies – target 100,000 donations total
  - US – between Feb 2015 - Feb 2016
  - Canadian - between October 2016 - June 2017
- **50,000 US (ARC)** donations throughout US but focus in Midwest
  - Unlinked
- **50,000 (30,000 CBS and 20,000 HQ)** donations from every province
  - Linked, tested following product release
- Donations tested for HEV RNA by ID-NAT at the ARC, using the Roche **cobas®** HEV test, and the **cobas®** 6800/8800 System (assay not approved for use in the US or Canada)
  - Hemi-nested PCR from amp/detection plates at Roche
- Additional testing on reactive samples performed at Sanquin and included
  - HEV RNA quantitative PCR (74 bp ORF-3; LOD 10.3 IU/mL)
  - HEV genotyping (ORF-1, ORF-2)
  - HEV antibody testing (Wantai)
- Comparative antibody studies done on a subset of US samples at CDC

Testing System



HEV Analytic Sensitivity	
50% LOD (IU/mL) (95% CI)	**3.9 (3.4 - 4.3)**
95% LOD (IU/mL) (95% CI)	**18.6 (15.9 – 22.6)**

The **cobas®** HEV test is not approved in the US or Canada but is available in countries that accept the CE mark.

US Results

3 positives/50,724 valid results

1:16,908 (95% CI: 1:5786-1:81,987)

Sex	Age	State	cobas® HEV Test (Ct value; max = 50)	hn-PCR (Roche)	Viral Load (IU/mL) 2 reps	Geno-type	IgM (S/CO)	IgG (S/CO)
Male	65	IN	38.54	Pos	15, 30	3a	0.02	0.02
Male	21	CA	37.38	Pos	13, 58	3b	0.02	0.02
Female	55	KY	34.42	Pos	1440, 1400	n/a	11.03	>15

Prior published US study (Stramer et al. Transfusion 2016):

2 positives/18,829 valid results

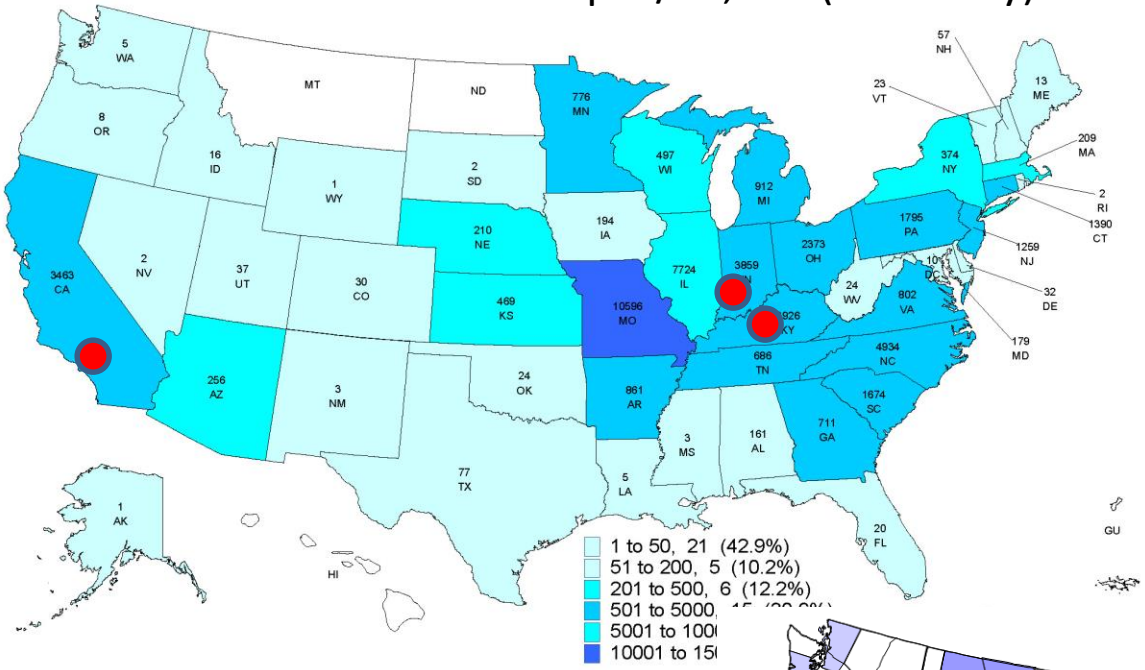
1:9500 (95%CI: 1:2580-1:56,180)

66 yo Male, IA (n/a IU/mL, Ab pos)

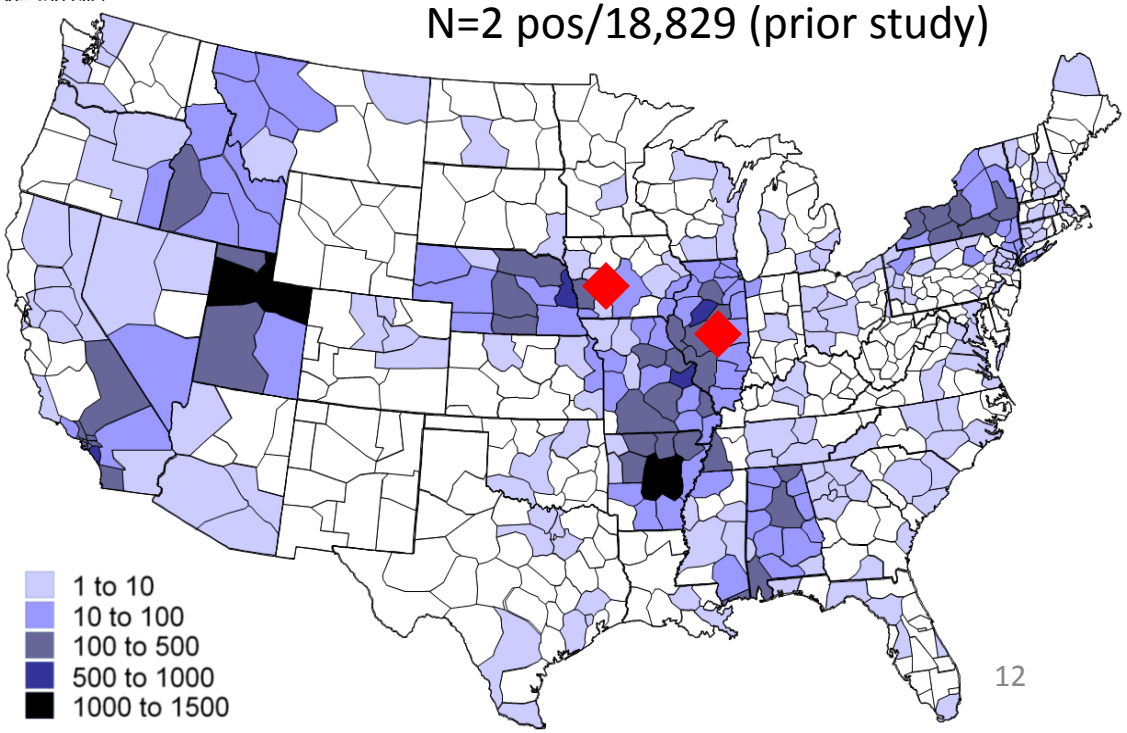
71 yo Male, IL (14 IU/mL, Ab neg)

HEV RNA Positive Donations By Donor Residence

N=3 pos/50,724 (this study)



N=2 pos/18,829 (prior study)



Canadian Results

11 positives/50,765 valid results

Total: 1:4615 (95% CI: 1:2579-1:9244)

HQ: 1:2920 (95% CI: 1:1417-1:7262)

CBS: 1:7582 (95% CI: 1:2961-1:27,825)

Follow-up

Site	Sex	Age	Province	cobas® HEV Test (Ct value; max = 50)	Viral load (IU/mL)	IgM (S/CO)	IgG (S/CO)	IgM (S/CO)	IgG (S/CO)
HQ	M	34	Quebec	**36.86**	**68**	0.04	0.28	0.05	**13.55**
HQ	M	60	Quebec	**38.92**	<10	0.05	**1.21**	0.1	**41.4**
HQ	M	59	Quebec	**38.89**	**55**	0.01	0.04	0.25	**14.62**
HQ	M	70	Quebec	**38.89**	<10	0.47	**>15**	0.05	**276**
HQ	F	21	Quebec	**34.55**	**151**	**2.21**	**5.87**	**2.17**	**31.1**
HQ	M	39	Quebec	**40.41**	**28**	**9.33**	**14.98**	0.91	**87.8**
HQ	F	41	Quebec	**38.29**	**20**	0.01	0.26	**2.02**	**92.4**
CBS	M	62	N.S.	**37.94**	**32**	0.02	0.03	**2.33**	**147.3**
CBS	M	56	Alberta	**38.97**	**43**	0.38	0.02	0.76	**50.4**
CBS	M	17	Alberta	**32.35**	**3080***	0.01	0	0.56	**14.91**
CBS	M	53	Ontario	**39.41**	<10	0	0.02	0.1	**26.3**

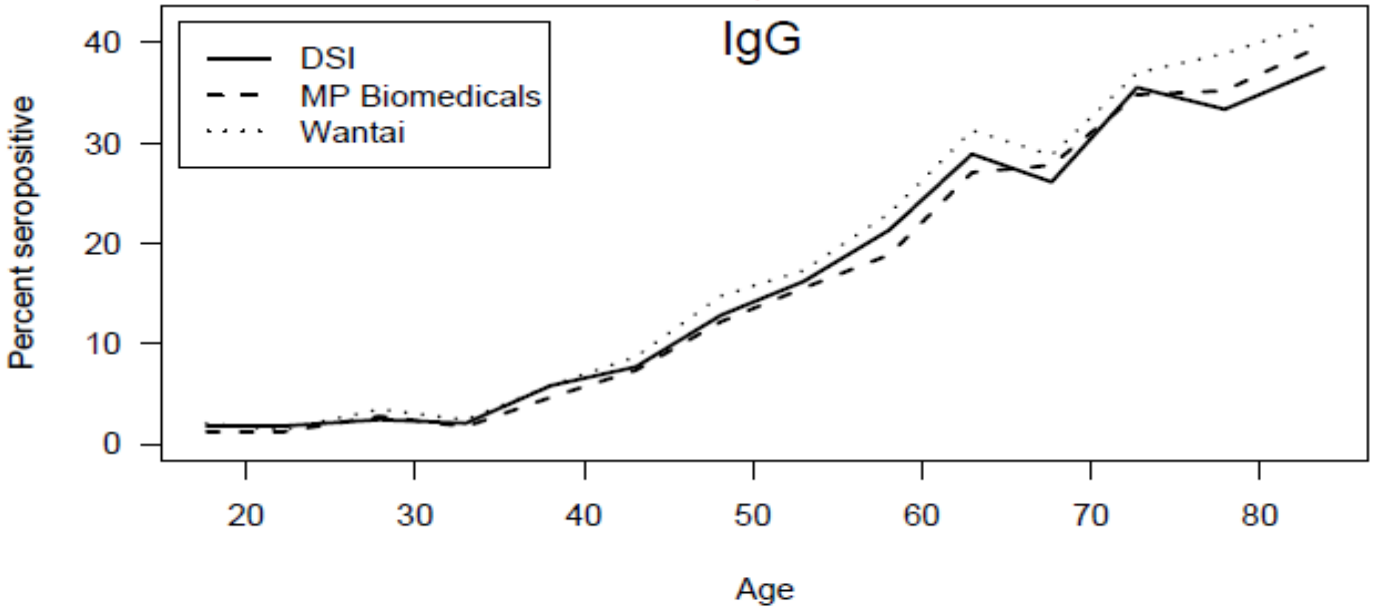
***Genotype 3 (unique)**

GREENLAND
ELLESMERE ISLAND
DEVON ISLAND
Baffin Bay
Beauton Sea
BANKS ISLAND
MELVILLE ISLAND
SOMERSET ISLAND
PRINCE OF WALES ISLAND
VICTORIA ISLAND
Davis Strait
PRINCE CHARLES ISLAND
BAFFIN ISLAND
Iqaluit
YUKON
Whitehorse
Great Bear Lake
NUNAVUT
SOUTHHAMPTON ISLAND
NORTHWEST TERRITORY
Yellowknife
Great Slave Lake
Labrador Sea
NEWFOUNDLAND and LABRADOR
St. John's
Hudson Bay
2
Lake Athabasca
7
BRITISH COLUMBIA
ALBERTA
SASKATCHEWAN
MANITOBA
James Bay
QUEBEC
Gulf of St. Lawrence
Pacific Ocean
Edmonton
Lake Winnipeg
Prince Edward Island
NEW BRUNSWICK
Fredericton
NOVA SCOTIA
VANCOUVER ISLAND
Vancouver
Victoria
Calgary
Saskatoon
Regina
Lake Winnipegosis
Winnipeg
ONTARIO
Lake Nipigon
Quebec
Saint John
Halifax
1
Thunder Bay
Lake Superior
Montreal
Ottawa
Lake Huron
Lake Ontario
Toronto
Lake Michigan
Lake Erie
1

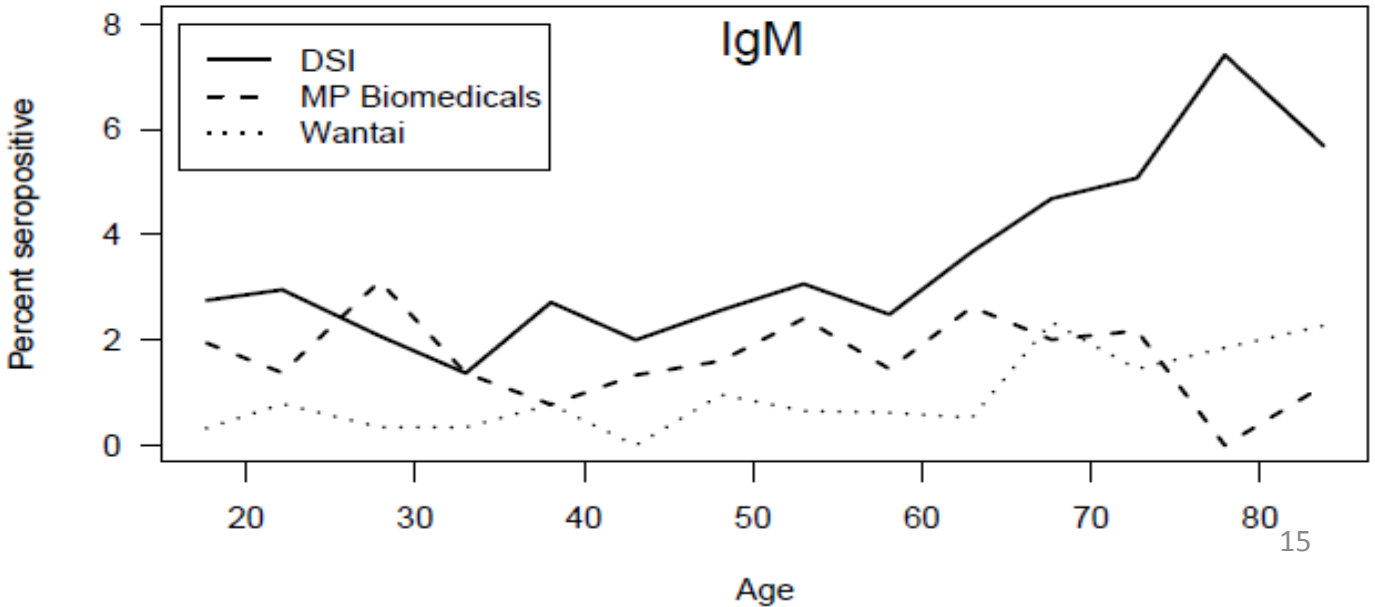
Subset of 5040 RNA-negative samples tested for IgM/IgG by 3 Commercial HEV antibody assays (CDC; submitted)

Prevalence increases with age

11.4% prevalence (range 10.65-12.28%) 84% agreement between assays



1.8% prevalence (range 0.67-2.9%) 22% agreement between assays



Summary

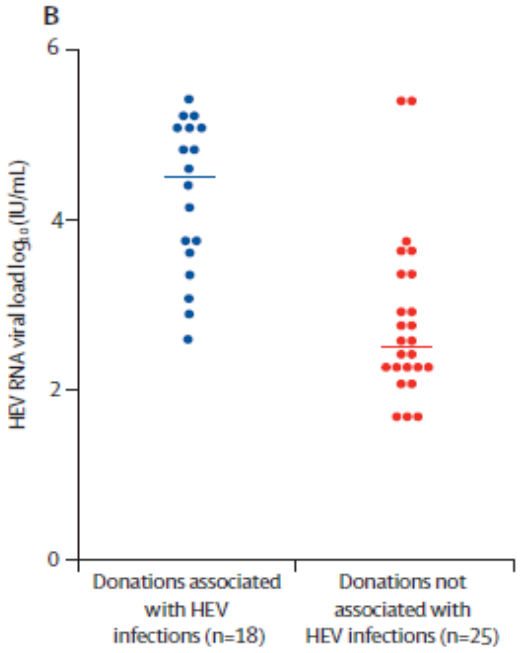
- HEV RNA is present in US and Canadian donors
  - Frequency of all ID-NAT studies (Roche/Grifols)
  - 16 pos/120,318 tested, or **1:7500**
    - Wide 95% CIs; no statistical difference amongst studies
    - Highest viral load = 3080 IU/mL; most too low to genotype @ < 100 IU/mL (all gt 3)
    - Most males (13/16)
    - High performance of ID-NAT assays
  - Ab positivity suggests higher frequencies of infection
    - IgM = 1.8% vs IgG = 11.8% => this study
    - IgM = 0.58% vs IgG = 7.7% => prior study
    - IgG = 5.9% Fearon et al; Canada; all significantly different

Summary

- Absence of TT HEV in US/Canada, but clinical disease occurs - magnitude not well understood
  - Kamar et al-chronic HEV after SOT 17-center survey, 2011*; Drobeniuc et al-CDC, surveillance 2005-2012

    ***"HEV infection causes chronic hepatitis in >60% recipients of solid organ transplants"**

  - Hewitt et al-UK; mean viral load
    - **TT = 4.53 $\log_{10}$ IU/mL** vs
    - **non-TT = 2.57 $\log_{10}$ IU/mL**; 95% CIs overlap



- Decision making underway in Canada
  - RBDM
- Should screened blood be used for:
  - Solid organ, stem cell transplant recipients?