

Hepatitis E Virus: Epidemiology and Burden

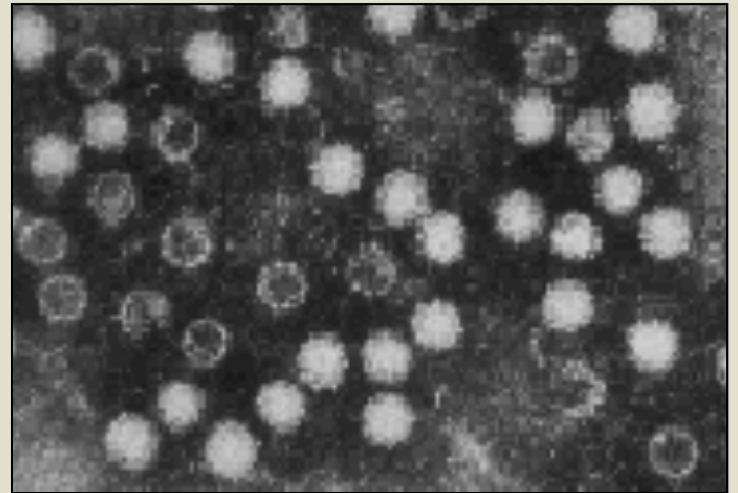
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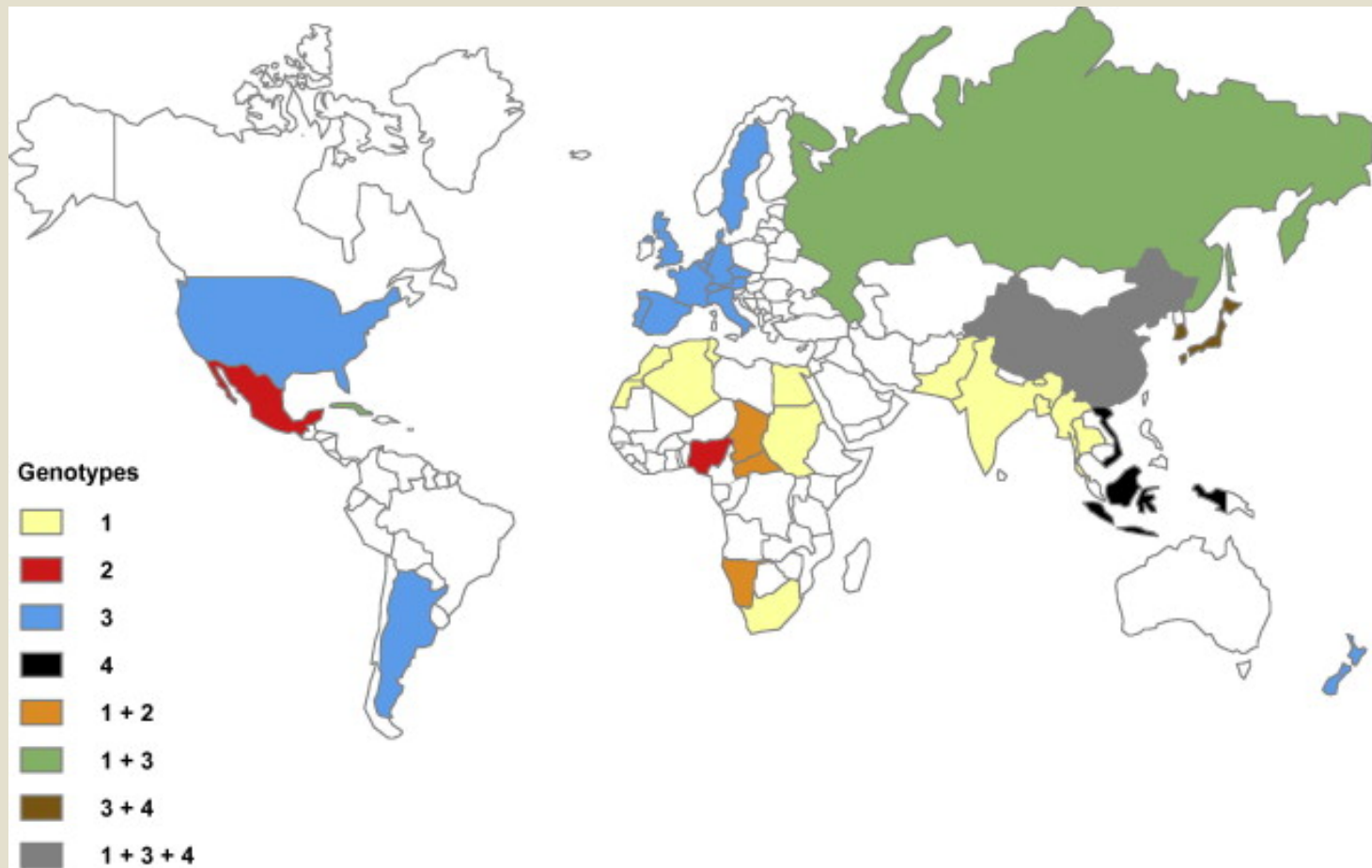
Hepatitis E

- Caused by hepatitis E virus
- Small (27-34 nm) icosahedral, single stranded, non-enveloped virions
- Three overlapping open reading frames
- Genus *Hepevirus*, Family *Hepeviridae*
 - 4 genotypes
 - At least 24 subtypes



Immune electron microscopy

Geographic Distribution of HEV Genotypes 1–4



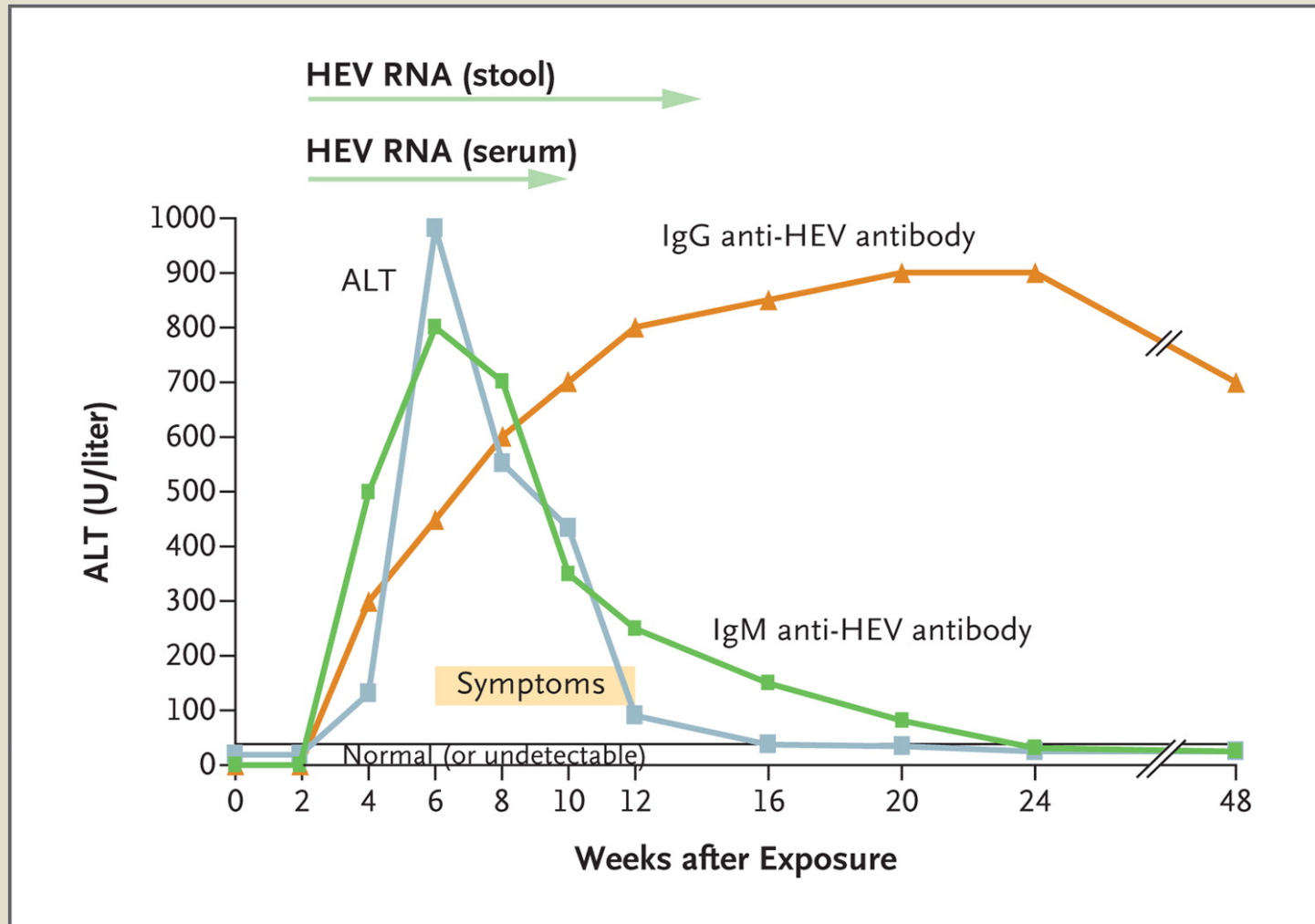
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Hepatitis E: Two Faces

Characteristic	Developing countries	Industrialized countries
Virus genotype	1, 2, (4)	3, (4)
Outbreaks	Small to very large	None to small
HEV as % of hepatitis	Common	Infrequent
Age distribution	Young	Old
Pregnant women	High mortality	No data
Co-existent diseases	Infrequent	Common
Chronic infection	No	Yes (immunosuppressed)
Transmission	Waterborne, ? food	food (animal meat)
Reservoir	Human	Animal

Course of Acute HEV Infection



Diagnosis of HEV Infection

Detection of specific immune response

- Antibody isotype
 - IgM Recent infection
 - IgG Recent/past exposure

Detection of HEV components

- Viral nucleic acid (HEV RNA)
 - Reverse transcription-PCR
- Viral protein (HEV antigen)
 - Enzyme immunoassay (EIA)

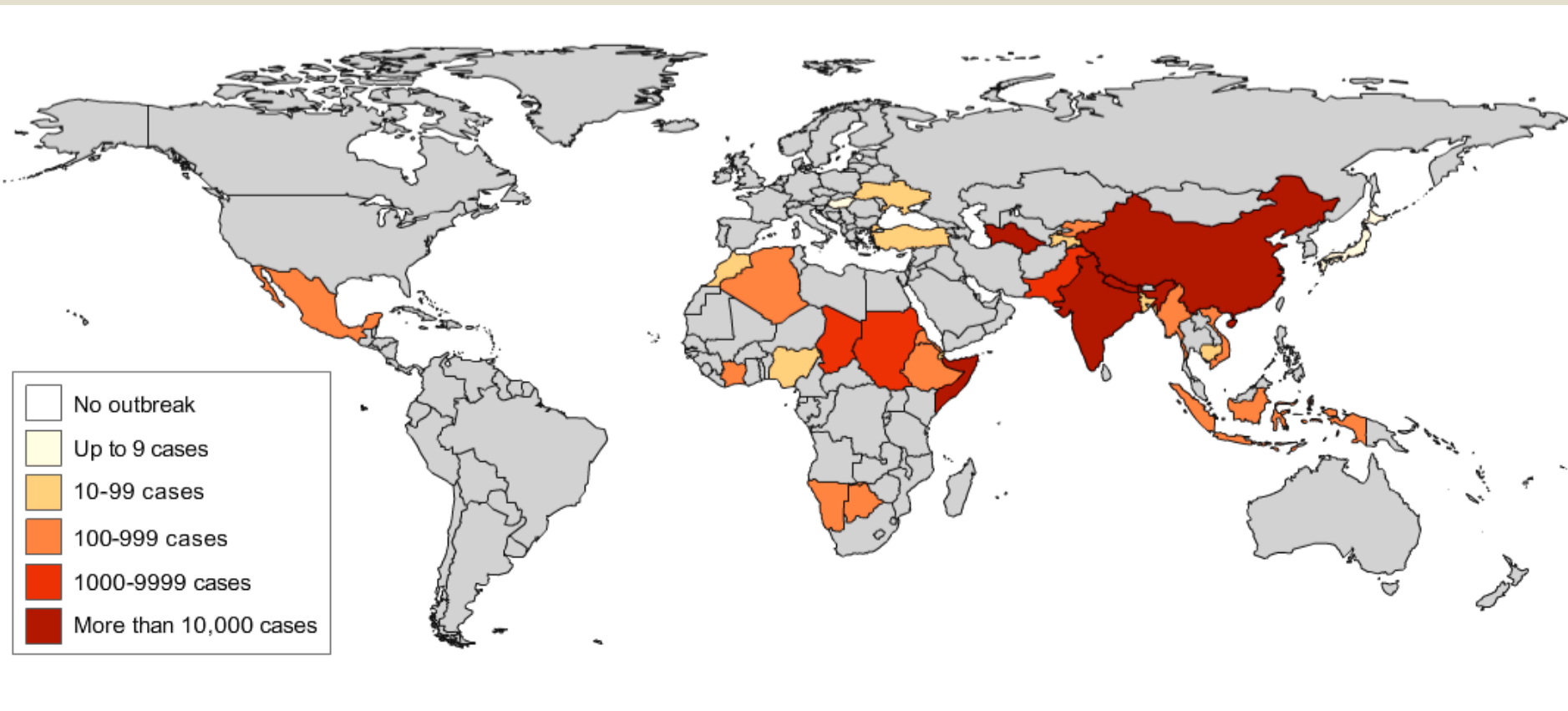
Evaluation of IgM anti-HEV Assays

Assay	Analytic Sensitivity WRU/mL	Clinical Sensitivity (N=51; GT1-4)	Specificity (N=228)
I - 56kD (NIH)	NT	98%	78.5%
II - p166 (CDC)	NT	98%	93.4%
III - IID	120	82%	92.1%
IV - MP	250	72%	93%
V – DSI	10	98%	95.2%
VI - Mikrogen	50	90%	95.6%

Global burden of viral hepatitis

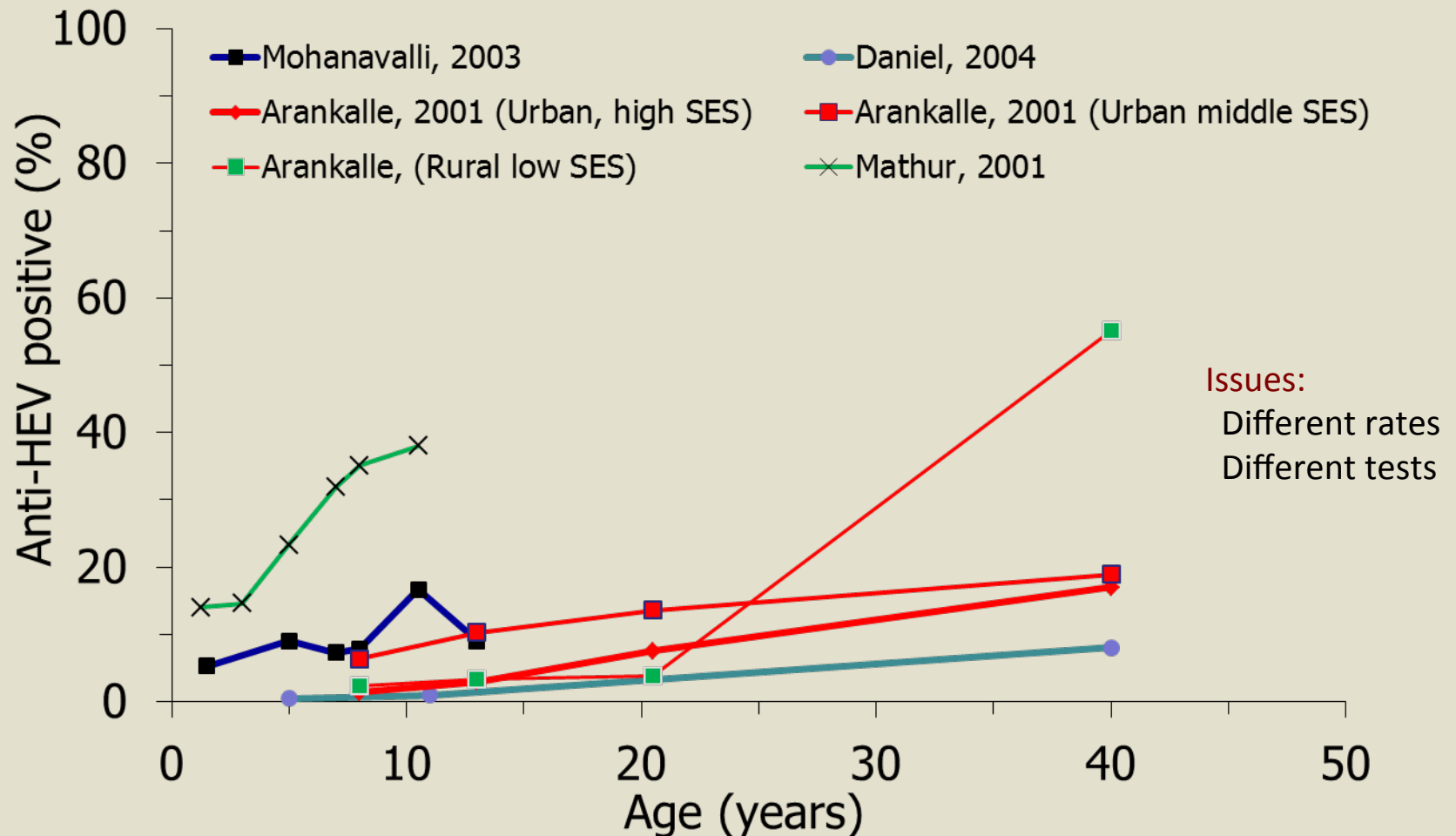
	Hep A	Hep E	Hep B+D	Hep C
Mode of transmission	Contaminated water and food		Blood or blood products, sex, mother-to-child	
Number of infections per year		20 million		3-4 million
Number of acute cases per year	1.4 million	3.3 million	4 million	---
Number of cases with chronic infection	---	Very few	~240 million	150-170 million
Number of deaths per year	103,000	70,000	786,000	499,000

Hepatitis E: Outbreaks (1980-2007)

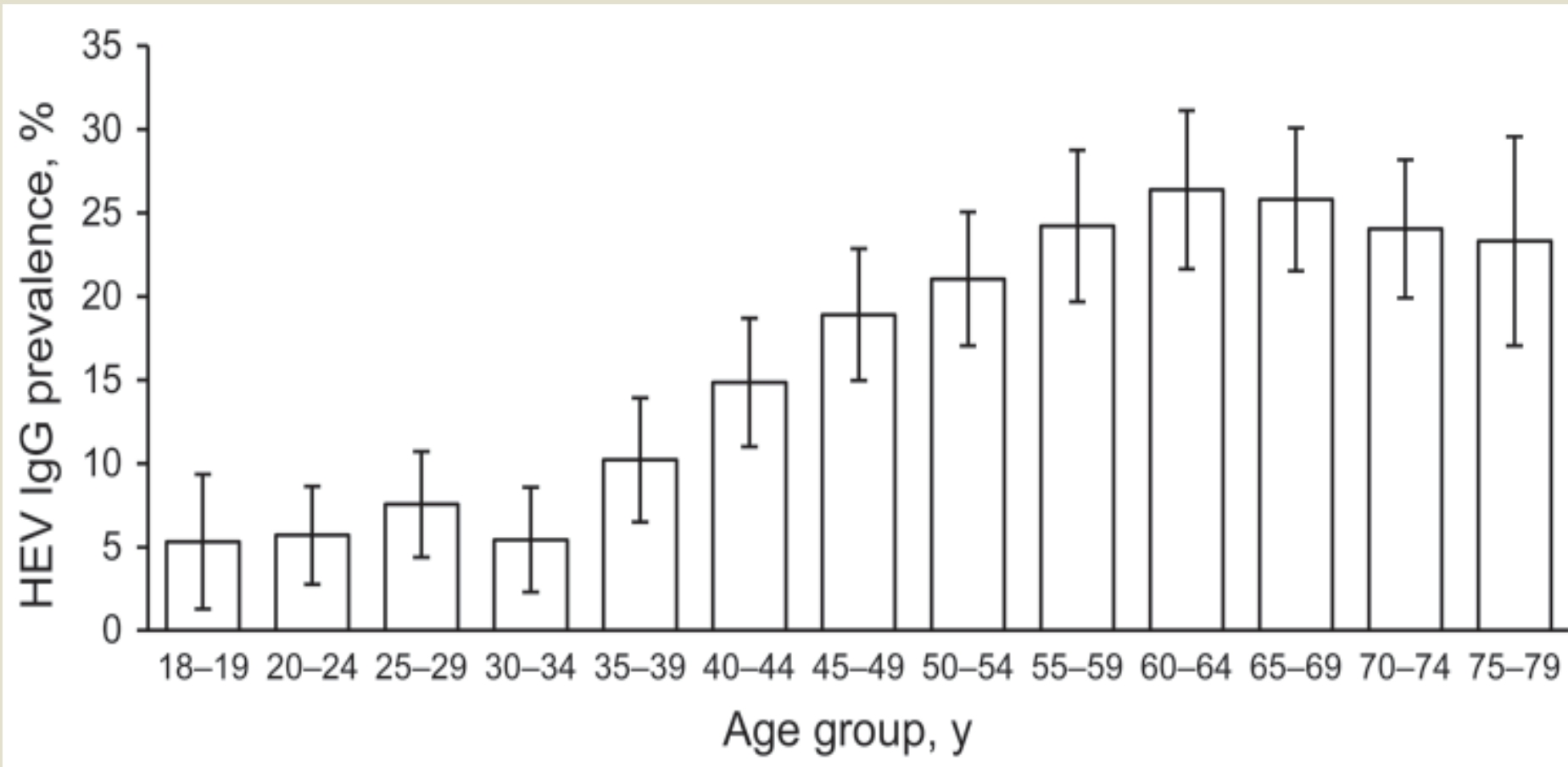


Reported from 29 countries

HEV Seroprevalence in India



Anti-HEV Prevalence, Germany, 2010



Special Populations

- Pregnant women
- Persons with pre-existing chronic liver disease
- Persons with immunosuppression
 - Solid organ transplant recipients
 - HIV
- Displaced persons/refugees
- International travelers

Hepatitis E among pregnant women

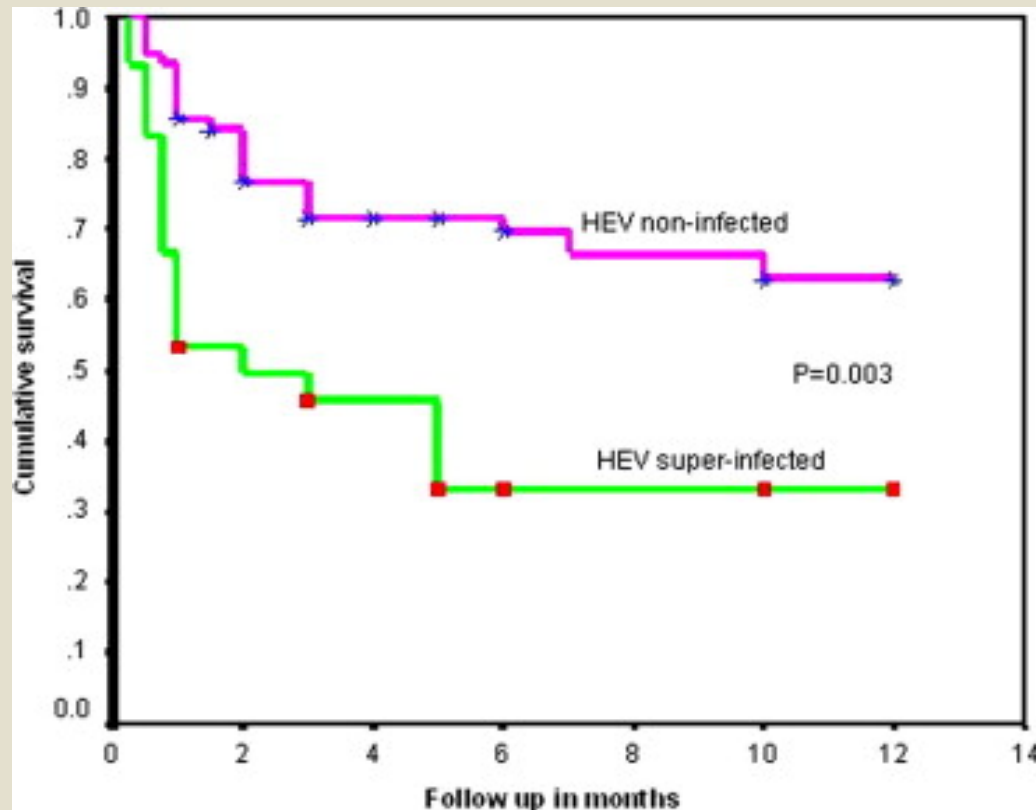
- Pregnancy: higher attack rate with acute hepatitis E, RR=9.7 (6.3-14.8)

• Men	107/3822	2.8%
• Non-pregnant women	71/3350	2.1%
• Pregnant women	36/208	17.3%

- Pregnancy: Higher frequency of hepatic failure, RR= 8.2 (5.6-11.9)

• Men	3/107	2.8%
• Non-pregnant women	0/71	-
• Pregnant women	8/36	22.2%

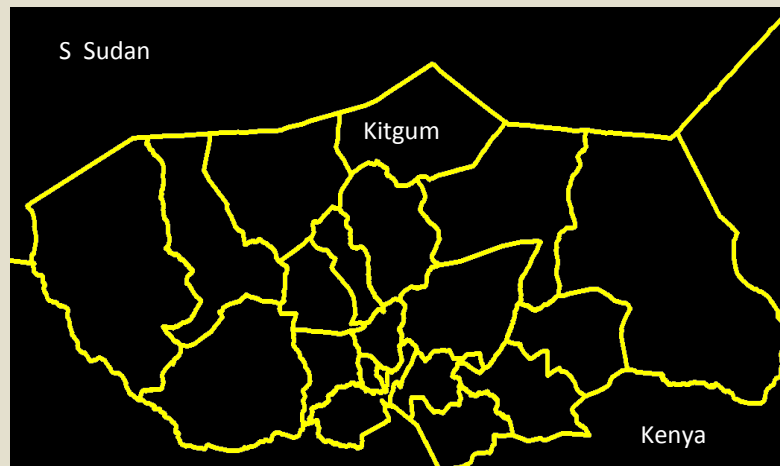
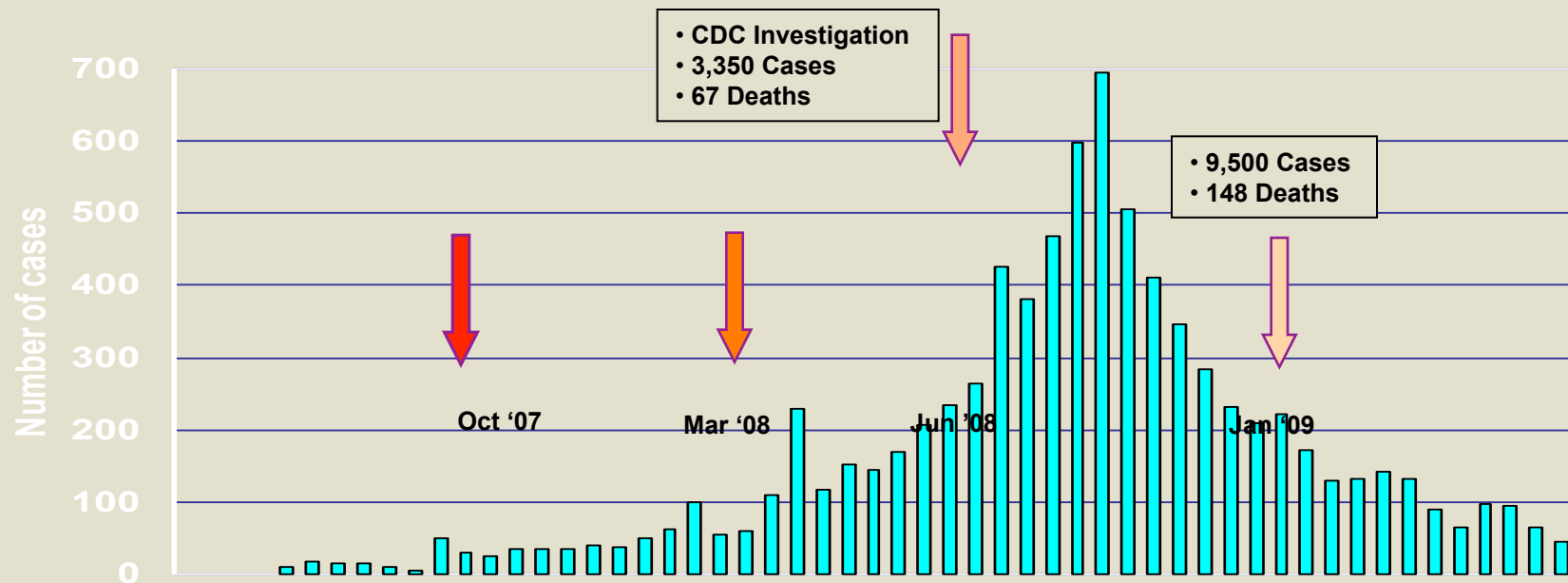
Hepatitis E in persons with pre-existing chronic liver disease



Hepatitis E among Solid-organ Transplant Recipients

- General characteristics of cases reported:
 - Progress to chronic infection in up to 60%
 - Risk factors for chronicity are related to
 - heavy immunosuppression,
 - reflected by lower CD2, CD3, CD4 and TLC
 - tacrolimus versus a cyclosporine regimen.
- Antibodies often not found during or after an HEV infection.

Hepatitis E among displaced persons/refugees



	%	n/N
Attack rate	25.1%	4789/19098
Overall CFR	1.5%	72/4789
Mortality ratio: pregnant	18.1%	13/72

Hepatitis E among international travelers

Italy: 1994-2009

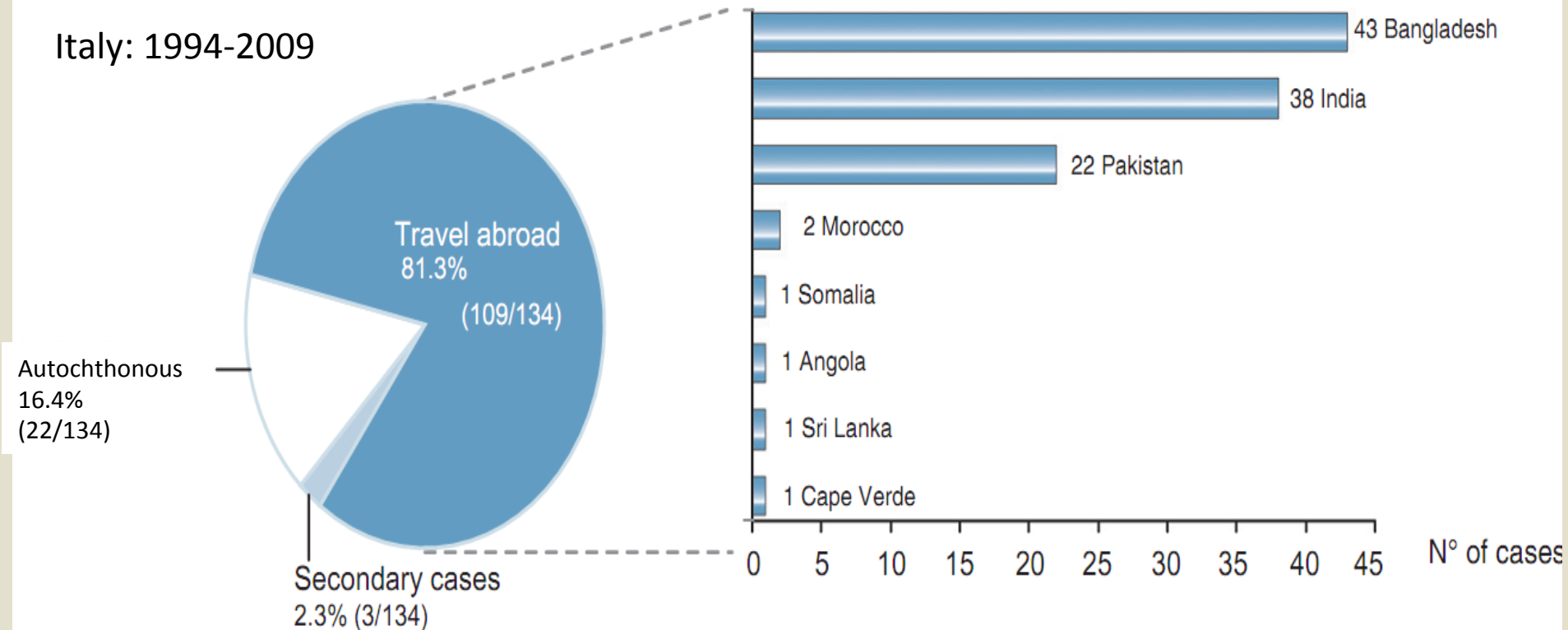


Fig. 2. Acute hepatitis E among 134 patients according to their travel history.

Gaps in Knowledge

- Impeded by lack of properly standardized serological and molecular assays
 - Transmission and propagation in outbreak setting
 - Disease incidence and burden
 - Chronicity following genotype 1 infection

Conclusion

- Approximately 3.3 million cases and 70,000 deaths occur due to hepatitis E annually
- HEV infection causes severe disease among pregnant women, persons with pre-existing chronic liver disease, and immunosuppressed organ transplant recipients
- Large waterborne outbreaks occur
 - Outbreak control efforts could be challenging

Anti-HEV Antibodies: Seroprevalence

