

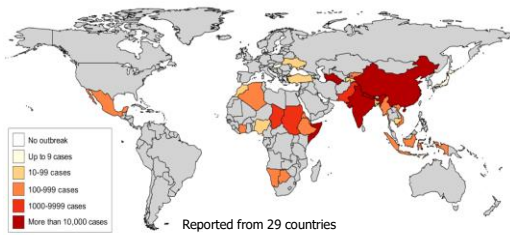
Hepatitis E in developing countries

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Hepatitis E in developing countries

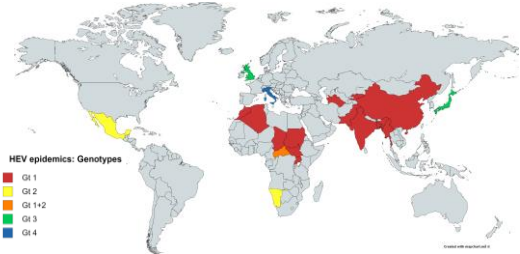
- Forms
 - Epidemic
 - Sporadic
- Transmission
 - Water-borne
 - Human-to-human
- Genotypes
 - Genotype 1
 - Genotype 2
- Clinical forms
 - Asymptomatic
 - Acute hepatitis
 - Acute liver failure
- Transmission
 - Water-borne
 - Human-to-human
- Special situations
 - During pregnancy
 - In persons with chronic liver disease

Hepatitis E: Outbreaks (1980-2007)

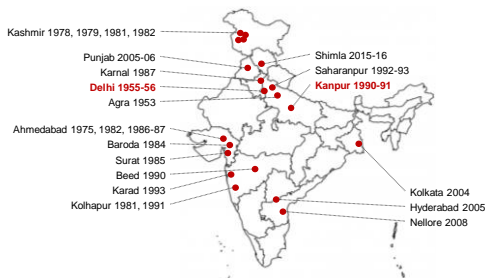


Aggarwal R. http://whqlibdoc.who.int/hq/2010/WHO_IVB_10.14_eng.pdf

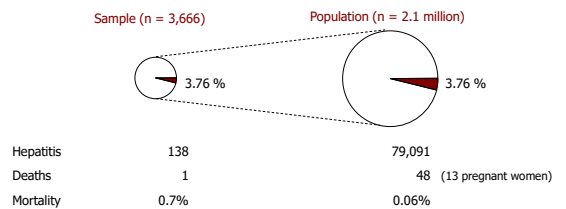
Hepatitis E outbreaks: HEV genotypes



Hepatitis E: Outbreaks in India affecting >1000 persons

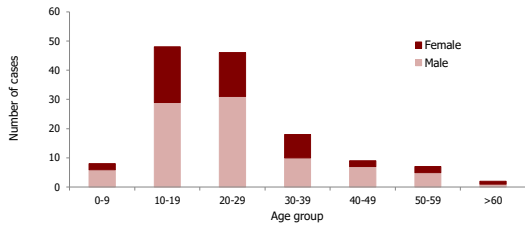


Hepatitis E epidemic: Kanpur, India, 1991



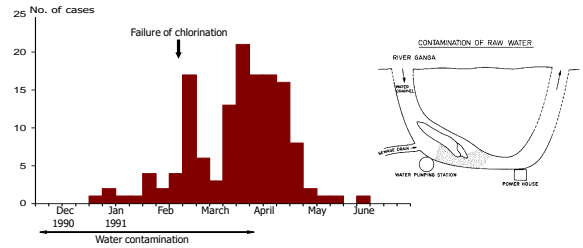
Naik SR, et al. *Bull WHO* 1992; 70: 597-604; Ray R, et al. *Lancet* 1991; 338: 783-4.

Hepatitis E epidemic: Kanpur, India, 1991



Naik SR, et al. Bull WHO 1992; 70: 597-604.

Hepatitis E epidemic, Kanpur, 1991: Time course

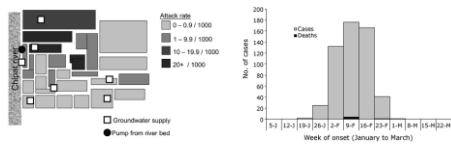


Naik SR, et al. Bull WHO 1992; 70: 597-604.

Another hepatitis E outbreak in India

A hepatitis E outbreak caused by a temporary interruption in a municipal water treatment system, Baripada, Orissa, India, 2004

Susanta K. Swain^a, Prameela Baral^b, Yvan J. Hutin^c, T. Venkat Rao^a, Manoj Murhekar^{a,c}, Mohan D. Gupte^a



Swain SK et al. Trans R Soc Trop Med Hyg 2010; 104: 66-69.

Epidemic hepatitis E: Transmission

- Fecal-oral transmission, often via contaminated water supply systems
- Person-to-person transmission rare
- Food borne ?
- Vertical transmission ✗
- Transmission through blood transfusions ✗
- Zoonotic transmission ? ✗

HEV outbreaks: Associated factors

- Flooding, heavy rainfall
- Failure of water treatment systems
- Use of untreated water from river or spring
- Hot summer >> reduced river water >> increased contaminants
- Leaking water pipes, with interrupted water supply
- Leakage of sewage pipes

HEV outbreaks: Control measures

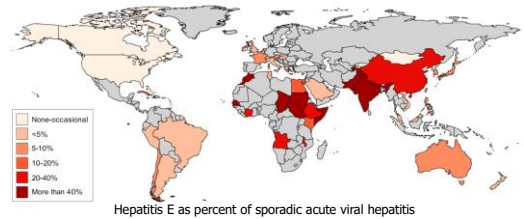
- Chlorination of water
- Water boiling
- Repair of water pipelines
- Alternative safer water supply
- Improving hygiene (e.g. handwashing practices)
- Improving sewage disposal

Africa: Outbreaks in humanitarian emergencies

- Outbreaks: In refugee camps (humanitarian emergency/conflict zones)
Waterborne infection
Large, affecting several persons
Mainly adults
Pregnant women particularly affected
- Special features: High disease attack rates
Prolonged, lasting several months
? Person-to-person (intra-familial) transmission

CDC. MMWR Morb Mortal Wkly Rep 2013; 62: 581-6.
Howard GM, et al. Am J Trop Med Hyg 2010; 83: 1170-3

Sporadic hepatitis E (1980-2007)



Aggarwal R. http://whqlibdoc.who.int/hq/2010/WHO_IVB_10.14_eng.pdf

Sporadic hepatitis E in endemic areas

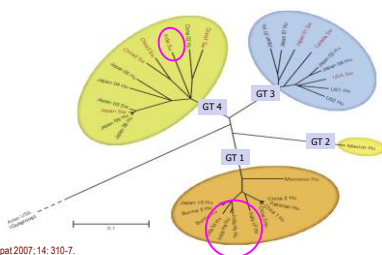
- Cases with acute hepatitis E in the absence of outbreak
- Similar to epidemic hepatitis E in
 - Epidemiologic features
 - Age, gender distribution
 - Exposure to unclean water
 - Relationship with pregnancy
 - Seasonal occurrence
 - Clinical features
 - Outcomes
- ? Micro-outbreaks – not recognized as outbreaks

Animal HEV infection in India

Animal species	n	Number (%) of animals testing positive for IgG anti-HEV	
		Modified Genelabs assay	ORF 2.1 assay
Pig	200	193 (97)	195 (98)
Goat	98	98 (100)	98 (100)
Chicken	86	84 (98)	84 (98)
Sheep	58	58 (100)	45 (78)
Buffalo	30	30 (100)	30 (100)

Shukla P. et al. J Viral Hepat 2007; 14: 310-7.

Animal and human HEV in India

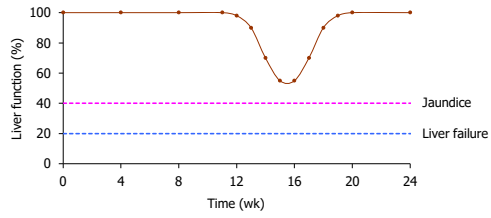


Shukla P. et al. J Viral Hepat 2007; 14: 310-7.
Aggarwal et al. J Gastroenterol Hepatol 2009; 24: 1484-93.

Epidemic hepatitis E: Clinical spectrum

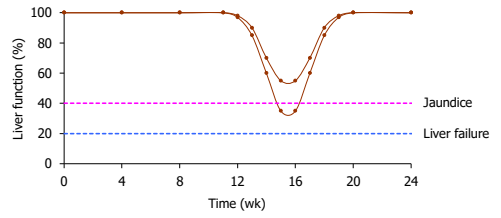
- Acute icteric viral hepatitis
- Asymptomatic infection
- Anicteric hepatitis
- Fulminant hepatic failure
- Acute worsening of chronic liver disease

Asymptomatic infection



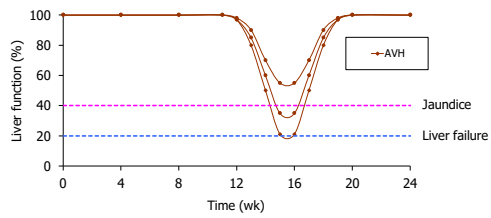
Anicteric hepatitis

Acute hepatitis (Jaundice)



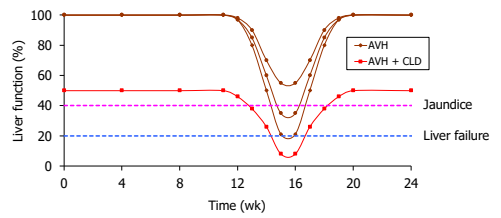
Icteric hepatitis

Acute liver failure



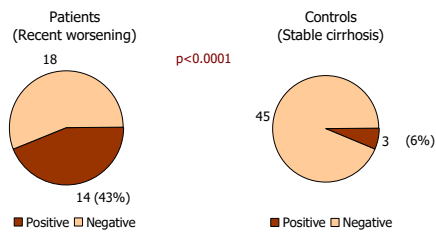
Acute liver failure

HEV superinfection in cirrhosis



HEV infection in cirrhosis: More often, more severe, longer duration

HEV superinfection in cirrhosis



Kumar et al. Indian J Gastroenterol 2004; 23: 59-62.

Hepatitis E and pregnancy

Group	Sample	Hepatitis, n (%)	Acute liver failure, n (%)
Men	3,822	107 (2.8%)	3/107 (2.8%)
Non-pregnant women	3,350	71 (2.1%)	0/71 (0%)
Pregnant women	208	36 (17.3%)	8/36 (22.2%)

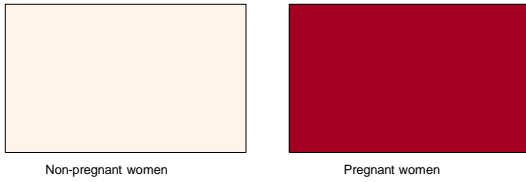
Pregnancy associated with

- Higher disease attack rate
- More often severe disease
- Mortality: 15-25%

Trimester	Hepatitis, n (%)
I:	8.8%
II:	19.4%
III:	18.6%

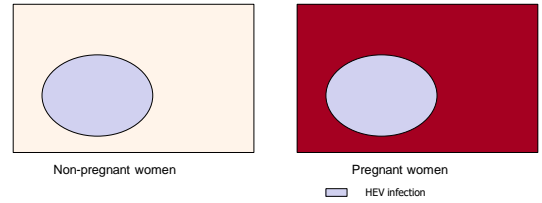
Khuroo et al. Am J Med 1981; 70: 252-5

Hepatitis E and pregnancy



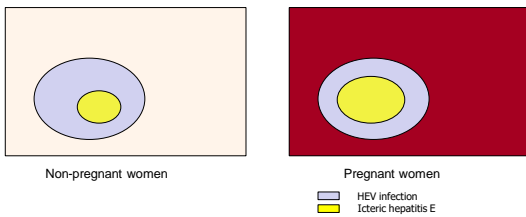
Aggarwal R. Virus Res 2011; 161: 15-22.

Hepatitis E and pregnancy



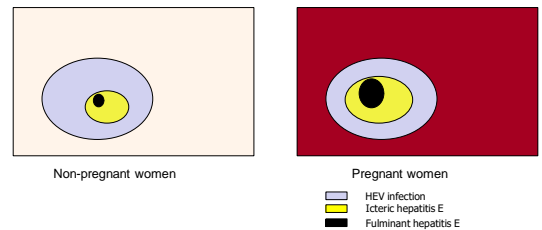
Aggarwal R. Virus Res 2011; 161: 15-22.

Hepatitis E and pregnancy



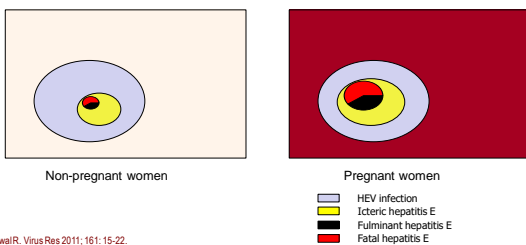
Aggarwal R. Virus Res 2011; 161: 15-22.

Hepatitis E and pregnancy



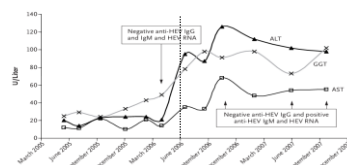
Aggarwal R. Virus Res 2011; 161: 15-22.

Hepatitis E and pregnancy



Aggarwal R. Virus Res 2011; 161: 15-22.

Chronic hepatitis E: not in endemic areas of Asia and Africa



Lack of evidence of hepatitis E virus infection among renal transplant recipients in a disease-endemic area

A. Naik,¹ N. Gupta,² D. Goel,¹ S. K. Ippagunta,¹ R. K. Sharma² and R. Aggarwal¹ Department of Gastroenterology and ²Department of Nephrology, Sangli Gandhi Postgraduate Institute of Medical Sciences, Lucknow, India

Naik et al. J Viral Hepatitis 2013; 20: e138-e140.

Hepatitis E: Two different faces

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

Hepatitis E in Asia and Africa: Estimated disease burden

- Based on seroprevalence data
- Assumptions:
 - 19.8% of infections are symptomatic
 - 1.9% of non-pregnant and 19.8% of pregnant women with disease die

Outcome	Mid-estimate	95% credible interval	Upper/lower bound ratio
Infections	20.1 million	2.8 – 37.0 million	13.3
Symptomatic cases	3.3 million	0.47 – 6.50 million	13.9
Deaths	69,622	12,400 – 132,732	10.7
Stillbirths	3,019	982 – 4,424	2.3

Rein D. Hepatology 2012; 55: 988-97.

Hepatitis E in developing countries: Take-home summary

- Outbreaks, frequent sporadic cases with acute infection
 - Mainly waterborne, possibly food
 - Affects young people
 - Pregnant women have severe disease with frequent fatal outcome
 - Severe disease also among persons with pre-existing liver disease
- Caused by genotype 1 or 2 virus
 - Very little or no zoonotic transmission
 - No chronic infection
- Cause significant preventable human morbidity