

24th **ECCMID**

Barcelona, Spain
10 – 13 May 2014

Educational Workshop

EW07: Viral infections in pregnancy

Arranged with the ESCMID Study Group for Viral Hepatitis (ESGVH)


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Faculty: **Resat Ozaras (Istanbul, Turkey)**
 - no handout available
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Lens - Hepatitis E in pregnancy

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ESCMID EUROPEAN SOCIETY OF CLINICAL MICROBIOLOGY AND INFECTIOUS DISEASES

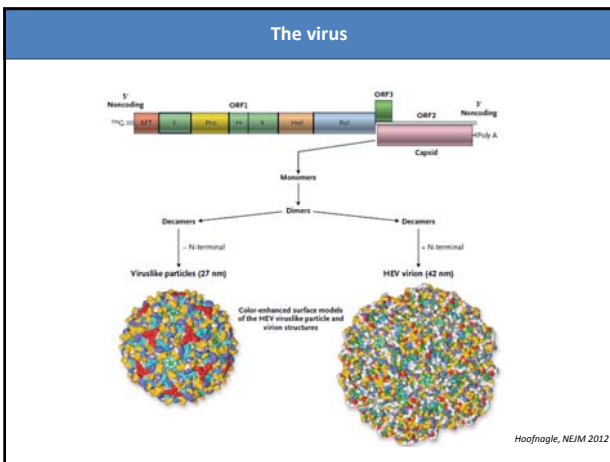


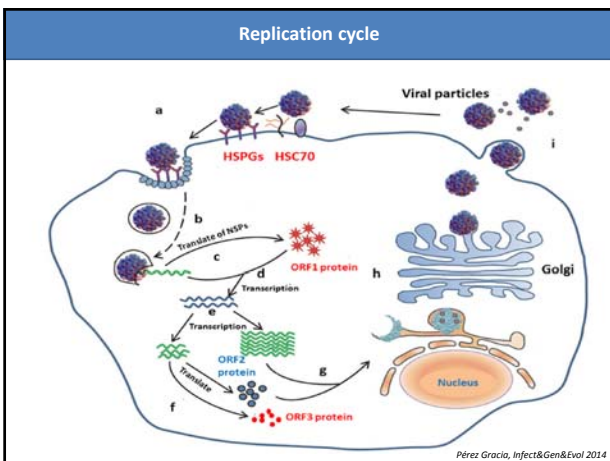
Educational Workshop

Hepatitis E in pregnancy

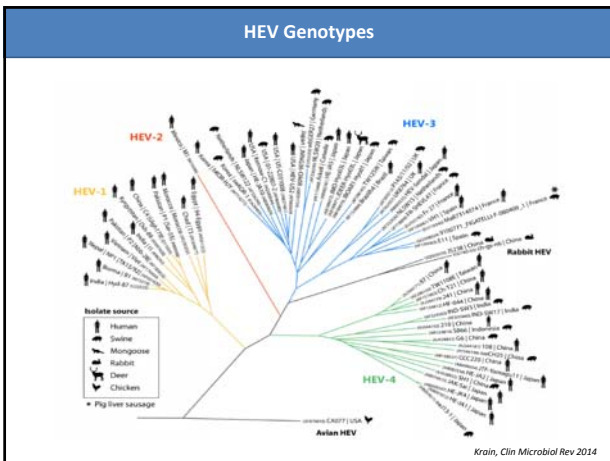
Dr. Sabela Lens
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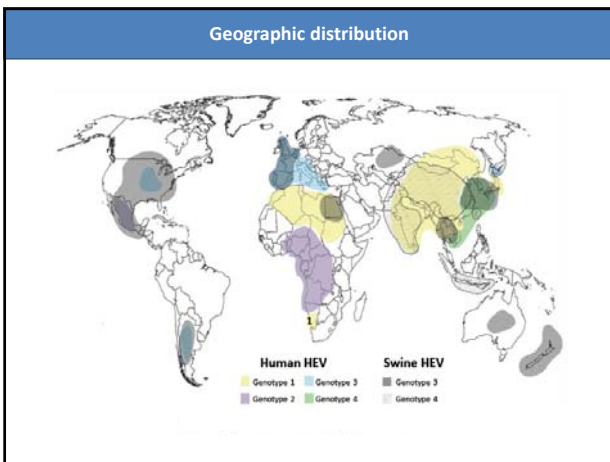
ID BAPS *Eli Lilly* **CLÍNICA BARCELONA**





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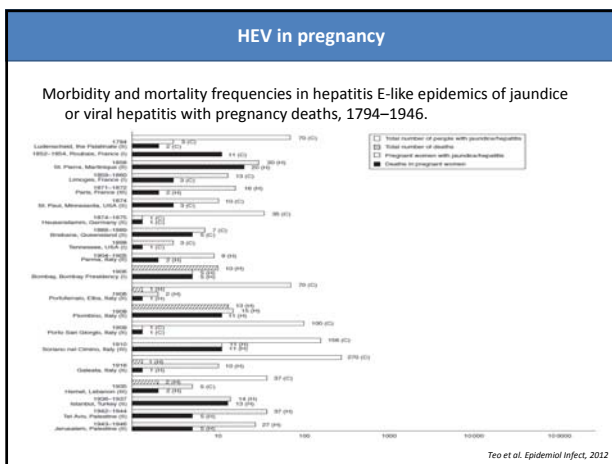
HEV: not only geographic differences among genotypes

Characteristics	Genotypes 1 and 2	Genotypes 3 and 4
Geographic distribution	Developing countries only	Both developing and developed
Pattern of spread	Epidemic/Sporadic	Sporadic
Species specificity	Human	Swine, human
Major mode of spread	Fecal-oral, waterborne	Foodborne
Age	Adolescents and young adults	Disease rates higher among older adults
Sex	Similar	Men
Mortality	High in pregnant women	High among older adults
Extrahepatic features	No	Yes
Chronic infection	No	Immunosuppressed
Therapy	None known (vaccine)	RBV, IFN

Hoofnagle NEJM 2012

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HEV in pregnancy



HEV in pregnancy

Seroprevalence of IgG antibodies to HEV among asymptomatic pregnant woman:

Study location	Time	Seroprevalence n/N (%)	Risk factors
Egypt	(1997-2003)	2046/2428 (84.3%)	Older age, village, unwashed food
India	(2006-2007)	101/300 (33.7%)	Lower education / economic status
Bah	(2003)	501/810 (61.4%)	District of residence
Gabon	(2005)	119/840 (14%)	Urban-rural
Turkey	(2002-2002)	31/245 (12.6%)	Older age
Tunisia	(2006)	49/404 (12%)	Older age, high parity
China	(2012)	30/293 (10.2%)	Not described
Spain	(2004)	2/365 (0.6%)	Not described

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Undeveloped countries & Genotype 1-2

¿Host related factors or viral factors?

- Genotype / viral load
- Coinfection
- Nutritional status
- Environment: seasonal rainfall patterns, sanitation systems, animal exposures

Mother:

- High incidence of fatal outcomes
- Peripartum Haemorrhage

Fetus:

- Miscarriage
- Stillbirth
- Premature delivery
- Neonatal jaundice

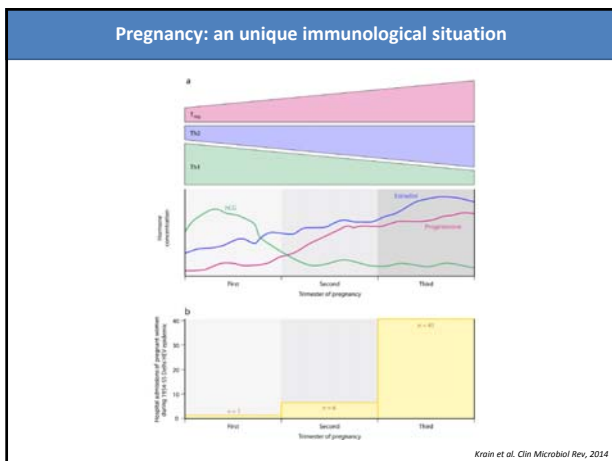
Maternal response to infection
Vertically transmitted infection

HEV in pregnancy

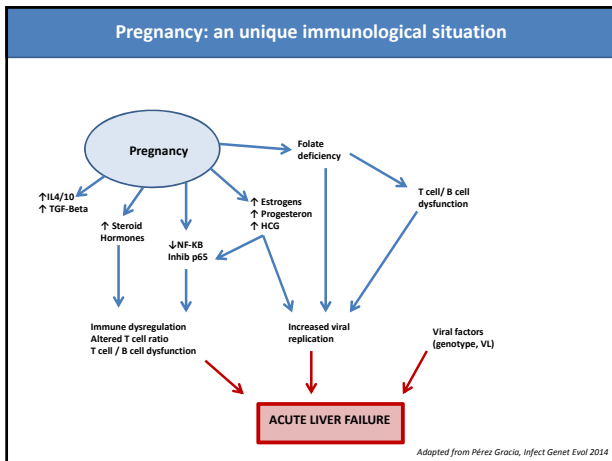
Vertically transmitted HEV infection, morbidity and mortality in live-born infants of mothers with laboratory confirmed antenatal HEV infection

Location	Mothers with AVH/FHF	Live births	HEV infections in neonates (% of live births)	HEV cases in neonates (% of live births)	Icteric HEV cases in neonates (% of live births)	Neonatal deaths (% of live births)
India ¹	20/16	33	22 (67%)	22 (67%)	20 (61%)	11 (33%)
India ^{2,3}	19/9	18	6 (33%)	No data	No data	No data
India ⁴	8/14	6	3 (50%)	1 (17%)	1 (17%)	0 (0%)
Ghana ⁵	1/2	1	1 (100%)	1 (100%)	1 (100%)	0 (0%)

¹ Khuroo et al, JK Pract 2006; ² Kumar et al, Int J Gynaecol Obstet 2004; ³ Dahiya et al, Indian Gastroenterol 2005; ⁴ Singh et al, Indian J Pediatr 2003; ⁵ Bonney et al, BMC Res Notes 2012



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HEV in pregnancy: coagulopathy

Post-partum haemorrhage (PPH) is the leading proximal cause of maternal death in developing countries

Variable	HEV-infected Women (n = 132), n/n (%)	Non-HEV-infected Women (n = 88), n/n (%)	Relative Risk (95% CI)	P Value
Maternal mortality rate				
Overall	54/132 (41)	6/88 (7)	6.0 (2.7-13.3)	<0.001
Patients with fulminant hepatic failure	54/73 (74)	6/19 (33)	2.3 (1.1-4.3)	0.001
Serum bilirubin	182/186	5/7 (6)	=	0.002
Third trimester	36/46 (78)	6/11 (54)	1.4 (0.9-2.1)	0.11
Patients without fulminant hepatic failure	0/59 (0)	0/70 (0)	=	1.00
Medical complications				
Coagulopathy defined	104/132 (79)	32/88 (37)	2.2 (1.6-2.9)	<0.001
Nasal or gastrointestinal hemorrhage	27/132 (21)	4/88 (5)	4.2 (1.5-11.4)	0.002
Leucocyte count $\geq 11 \times 10^9$ cells/L	86/132 (65)	31/88 (35)	1.8 (1.4-2.5)	<0.001
Serum creatinine concentration $\geq 34 \mu\text{mol/L}$ ($\geq 2 \text{ mg/dL}$)	39/132 (30)	4/88 (5)	6.5 (2.4-17.5)	<0.001
Asplenia	33/132 (25)	5/88 (6)	4.4 (3.0-6.0)	<0.001
Clinical signs of increased intracranial tension	27/132 (20)	1/88 (1)	18.0 (2.5-130.1)	<0.001

Patra S, Ann Int Med 2007
Puri M, Obstet Med 2011

HEV-ORF3 may interact with several clotting related pathways:

Genp. PLoS One 2013

HEV in pregnancy: Key questions

- Can maternal vaccination prevent vertical transmission of HEV?
- What risks do early in pregnancy maternal HEV infections pose to fetal health?
- Are some delivery-associated PPH related to not diagnosed HEV infection?
- Does vertical transmission occur during labor?
- Can breastfeeding contribute to neonatal infection?
- How to treat in order to avoid fetal and neonatal morbidity and mortality?

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Additional investigation of HEV pathogenesis in pregnant women
Population-based serologic surveillance in pregnancy and follow-up of neonatal outcomes
