

# Hepatitis C and pregnancy

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## Disclosures

- Board: Gilead, Bristol-Myers Squibb
- Workshop or meeting invitation: Gilead, Bristol-Myers Squibb, Schering-Plough / MSD, Roche, Janssen, Mayoly-Spindler

# HCV in pregnancy

- The seroprevalence of HCV in pregnant women is estimated between 0.15 and 2.4% in European countries and U.S.
- Mother-to-child transmission of HCV is the leading cause of HCV infection in children in developed countries
- Most perinatal HCV infections are silent with long-term complications that present later in adulthood
- HCV is an underestimated childhood disease with a significant economic and health burden on society

# Plan

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1. Antenatal HCV screening
2. Mother-to-infant HCV transmission and associated factors
3. Effect of HCV on pregnancy and pregnancy on HCV

# Plan

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## 1. Antenatal HCV screening

2. Mother-to-infant HCV transmission and associated factors

3. Effect of HCV on pregnancy and pregnancy on HCV

# QUESTION 1

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# Antenatal HCV screening

- Usually not systematic but based on maternal risk factors
- Different from HIV or HBV for which screening is systematically recommended during pregnancy
- In fact depends on medical structures (at least in France...)

- 40 to 70% of HCV-infected pregnant women do not initially report major risk factors<sup>1,2</sup>
- 85 to 95% of HCV-infected children in the U.S. have not been identified due in part to the failure to identify most maternal infections<sup>3</sup>

<sup>1</sup>Conte D et al. Hepatology 2000; <sup>2</sup>Ward C et al. Gut 2000;

<sup>3</sup>Delgado-Borrego A et al. J Pediatr 2012

# Antenatal HCV screening

## Favor “risk factors”

- Economic reason
- No modification of delivery or breast-feeding
- No antiHCV treatment during pregnancy

## Favor “systematic screening”

- Missed opportunities
- No identifiable risk factors
- Screening is recommended for infants born from HCV infected mothers
- Identified HCV women to propose counseling (risk reduction...)
- Discussion about a negative impact of HCV on maternal and fetal outcomes
- In next future, new treatment options in post-partum

Its time to move toward an universal screening for HCV in pregnancy (as for HBV and HIV) even in low endemic countries



# Plan

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1. Antenatal HCV screening
- 2. Mother-to-infant HCV transmission and associated factors**
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## QUESTION 2

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# Mother-to-infant HCV transmission

## Virologic factors

- Only if antiHCV + **AND** HCV-RNA +
- Usually comprised between 3 – 5%
- Risk of transmission associated with:
  - HCV viral load (but no threshold)
  - HIV co-infection (increased risk  $\times \approx 2$ )  
(↘ if optimal control of HIV?)
- No relation with:
  - HCV genotype
  - Severity of liver disease (ALT)
  - Mode of contamination

# Mother-to-infant HCV transmission

## Obstetrical factors

Risk factors	Tested factors	Studies	N	p
Mode of delivery	Elective cesarean vs. vaginal delivery or emergent cesarean	4	2080	NS
	Elective or emergent cesarean vs. vaginal delivery	11	2308	NS
Internal fetal monitoring	Yes vs. No	3	928	NS
Rupture of membranes	Prolonged vs. less prolonged	2	245	NS
Breastfeeding vs. no breastfeeding		14	2971	NS

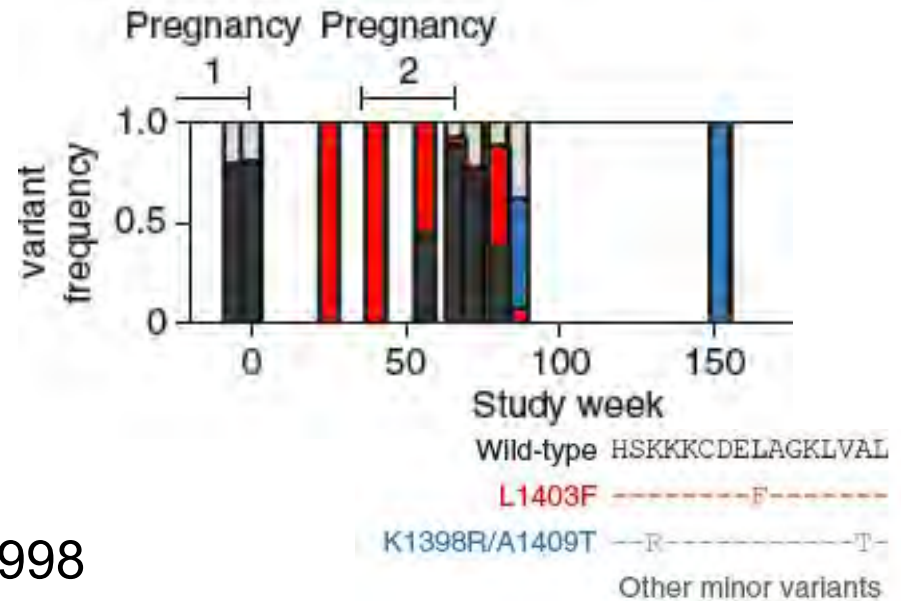
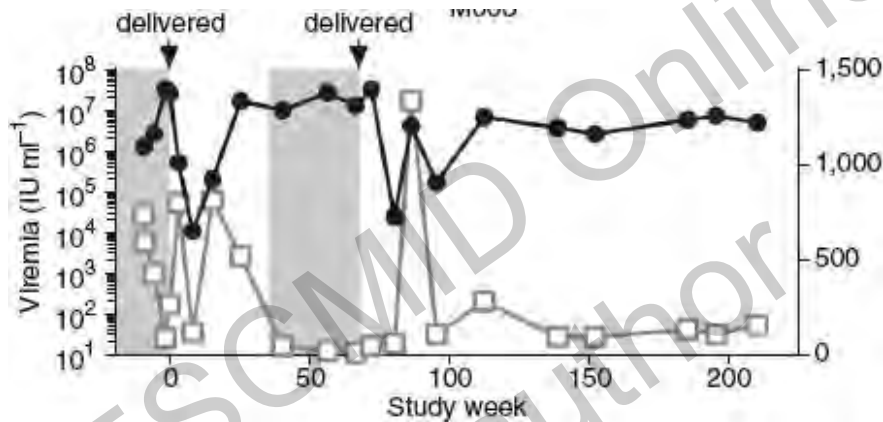
# Plan

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1. Antenatal HCV screening
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# Effect of pregnancy on HCV

- During pregnancy ↗ HCV-RNA and ↘ ALT level<sup>1,2</sup>
- Characterization of circulating viral quasispecies during and after consecutive pregnancies: loss of some escape mutations in HLA class I epitopes associated with emergence of more fit viruses<sup>3</sup>



<sup>1</sup>Gervais A et al. J Hepatol 2000

<sup>2</sup>Wejstal R et al. Scand J Infect Dis 1998

<sup>3</sup>Honegger JR et al. Nat Med 2013

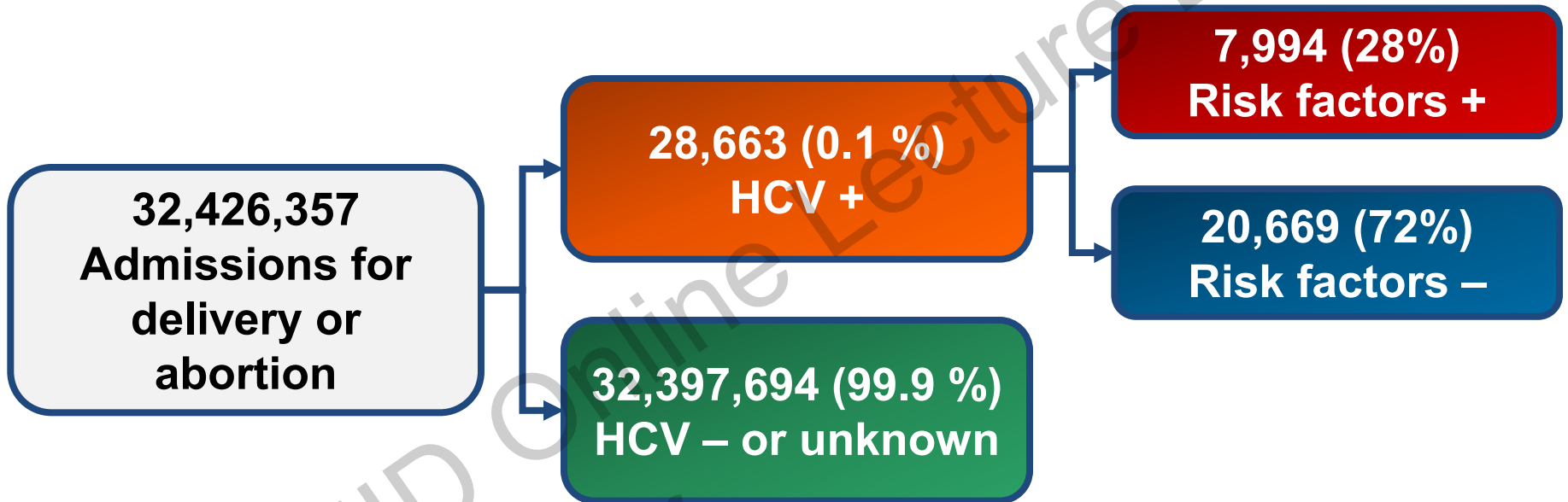
# Effect of HCV on pregnancy outcome

- Swedish Birth Medical Registry (birth after 1996)
- Women with Intrahepatic cholestasis of pregnancy have ↗ risk for later hepatobiliary disease (including hepatitis C)
- Women with hepatobiliary diseases have ↗ risk of later Intrahepatic cholestasis of pregnancy (ICP)

Diseases	Controls N=66,651	ICP N=6,667	OR [95% CI]	p
Hepatitis B	0.2 %	0.3 %	0.87 [0.06 – 13.55]	ns
Hepatitis C	0.2 %	1.0 %	5.76 [1.30 – 25.44]	0.02

# Effect of HCV on pregnancy outcome

National U.S. survey on delivery and abortion (2003 – 2010)



In multivariate analysis (adjusted) in HCV + women:

- ↗ maternal outcomes: anemia, thyroid, pulmonary embolism
- ↗ fetal outcomes: premature labor, hemorrhage, low birth weight

Direct or indirect role? More risk factors in HCV + women?



# In practice (1)

**Woman  
before  
pregnancy**

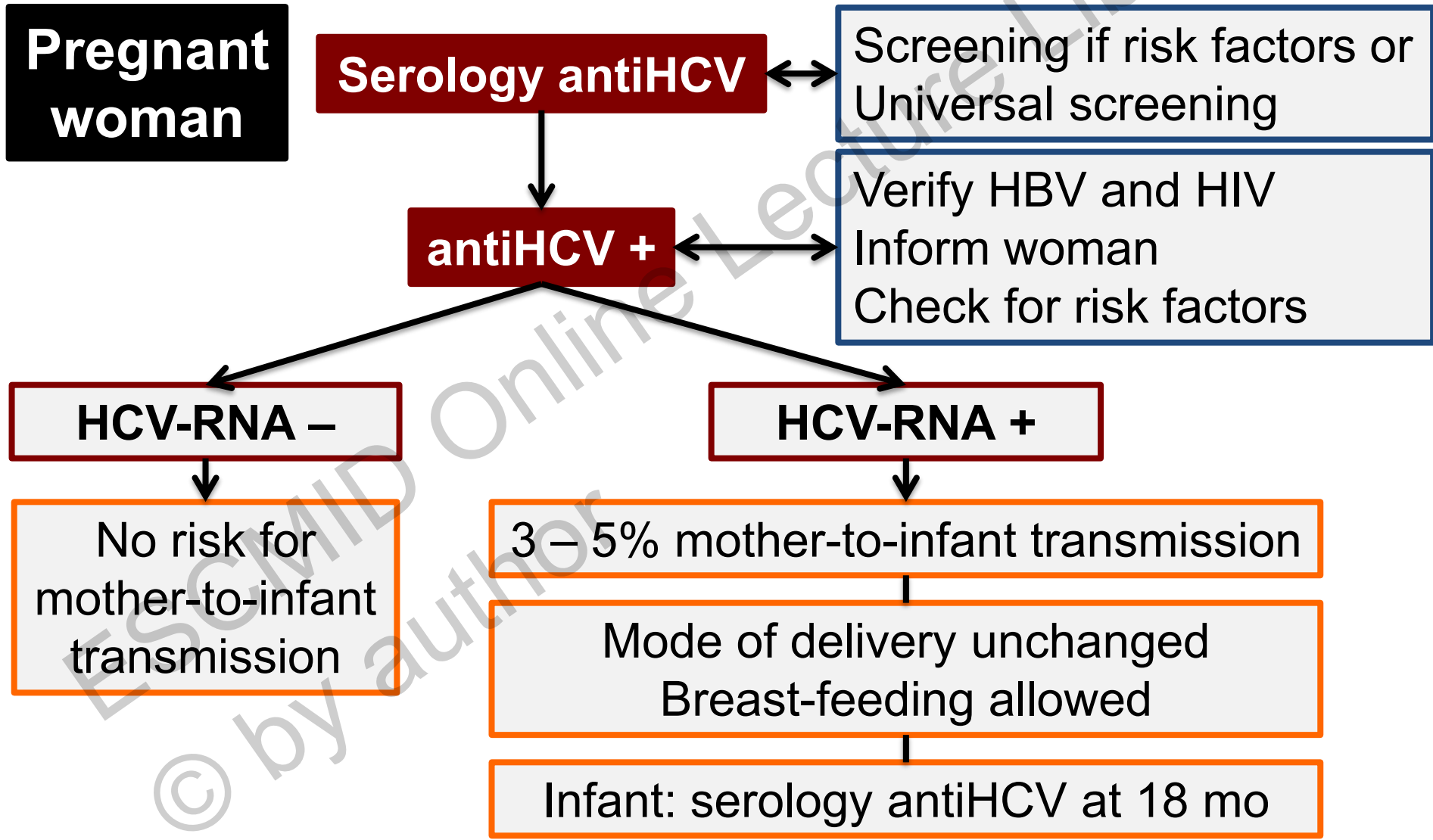
**Diagnosis of a  
chronic hepatitis C**

Information  
including pregnancy, delivery  
and breast-feeding

Evaluation of liver disease and  
extra-hepatic manifestation  
Discussion for a treatment  
before pregnancy

- Pregnancy is not allowed during antiHCV treatment and 7 months after the end of ribavirin
- In case of Sustained Virologic Response after antiHCV treatment, the risk of HCV mother-to-infant transmission is null

# In practice (2)



# Unresolved issues

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1. Final demonstration that systematic antenatal screening is cost-effective in term of public health? – Depending on prevalence, on health-care system...
2. Is still an increasing risk of HCV mother-to-infant transmission in case of HIV co-infection when HIV is efficiently controlled?
3. In clinical practice, is amniocentesis increased the risk for HCV mother-to-infant transmission?
4. is HCV infection in pregnant women is at risk for maternal and fetal outcomes?

# Many thanks!

## Group “Viral Hepatitis & Pregnancy”

### *In French Hepatitis Report – 2014 (Prof D. Dhumeaux)*

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