

# Herpesvirus infections in pregnancy

Dr. med. Daniela Huzly  
Dept. of Virology  
University Medical Center  
Freiburg, Germany

# Human Herpesviruses

- Enveloped double-strand DNA-Viruses
- 8 human herpesviruses known
- All herpesviruses establish latency after primary infection
- $\alpha$ -herpesvirus: HSV1+2 (HHV1+2), VZV (HHV3)
- $\beta$ -herpesvirus: CMV (HHV5), HHV6, HHV7
- $\gamma$ -herpesvirus: EBV (HHV4), HHV8

# Herpes simplex virus (HSV) 1+2

## Risk in pregnancy/at birth

- Vertical transmission
  - In utero: rare, primary infection with viremia, women <21y at risk
  - Intrapartum: during passage through the infected birth canal (Herpes genitalis); fetal-scalp electrodes
- Post natal transmission
  - contact with infected person

# Genital Herpes

- ~5% of women of childbearing age report history of genital herpes
- 20-30% have antibodies against HSV2



LAMPSON 05

# Genital Herpes



# Genital Herpes





# Herpes genitalis infection in pregnancy

- Herpes genitalis as main risk for neonatal herpes
  - 70-90% HSV2, 10-30% HSV1
- Differential management according to infection status
  - Primary
  - Non-primary first episode
  - Recurrent
  - Asymptomatic viral shedding

# Herpes genitalis primary infection

- Not always symptomatic (only 25%)
- Lesions appear 2-14 days after exposure, pain, dysuria
- Systemic symptoms
  - fever, lymphadenopathia, meningitis
- Without therapy ~20 days
- Viral shedding ~12 days
- Antibody response 3 weeks – 6 mo

# HSV non-primary first episode

- Heterologous antibodies present
  - Recurrent herpes labialis
- New genital infection with HSV2
- Partial protection from HSV1-antibodies
- Duration of lesions and shedding shorter (15d/7d)

# Recurrent HSV infection

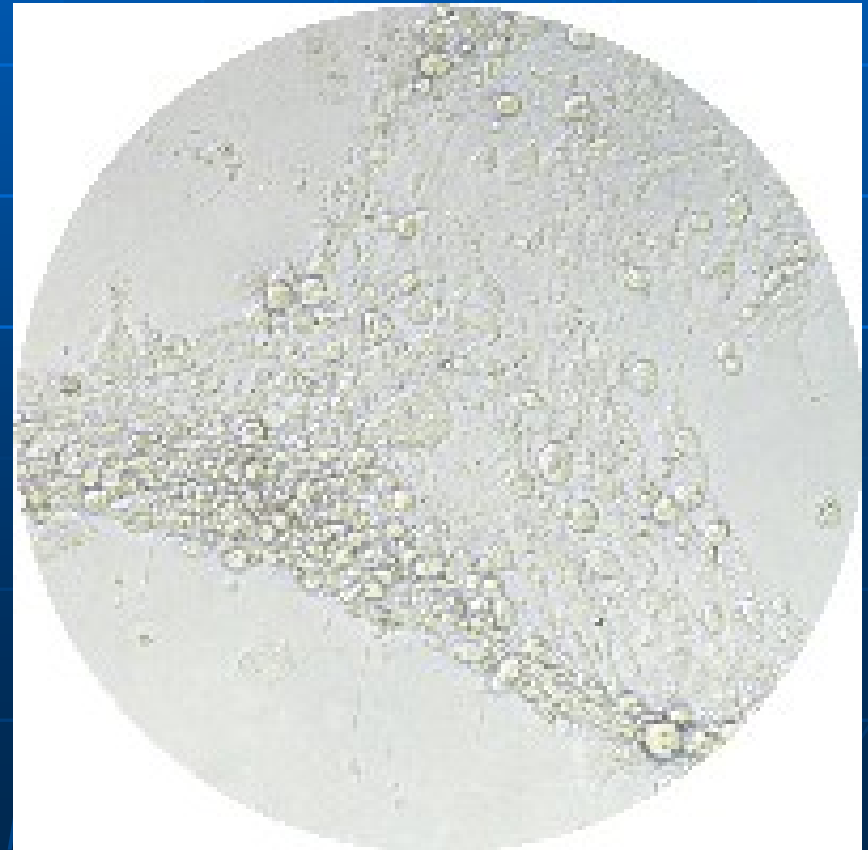
- Homologous antibodies present when symptoms appear
- Recurrent outbreaks may be symptomatic or asymptomatic
- Around 15% of pregnant women experience recurrence at delivery
- Most symptoms localized
- Symptoms/shedding 9/4 days, lower viral load

# Asymptomatic shedding

- Episodic and brief (24-48h)
- 1-2% of pregnant women with HSV history shed at delivery
- Coinfection with HIV increases asymptomatic shedding

# Diagnosis of HSV infection in pregnancy

- HSV-IgG Screening assay(HSV1+2)
- If positive, type specific serology
  - Glyccoprotein G ELISA or Westernblot
  - Lysate ELISAs not useful
- HSV-IgM not useful, no differentiation of primary-non-primary
- Virus culture and typing from swab



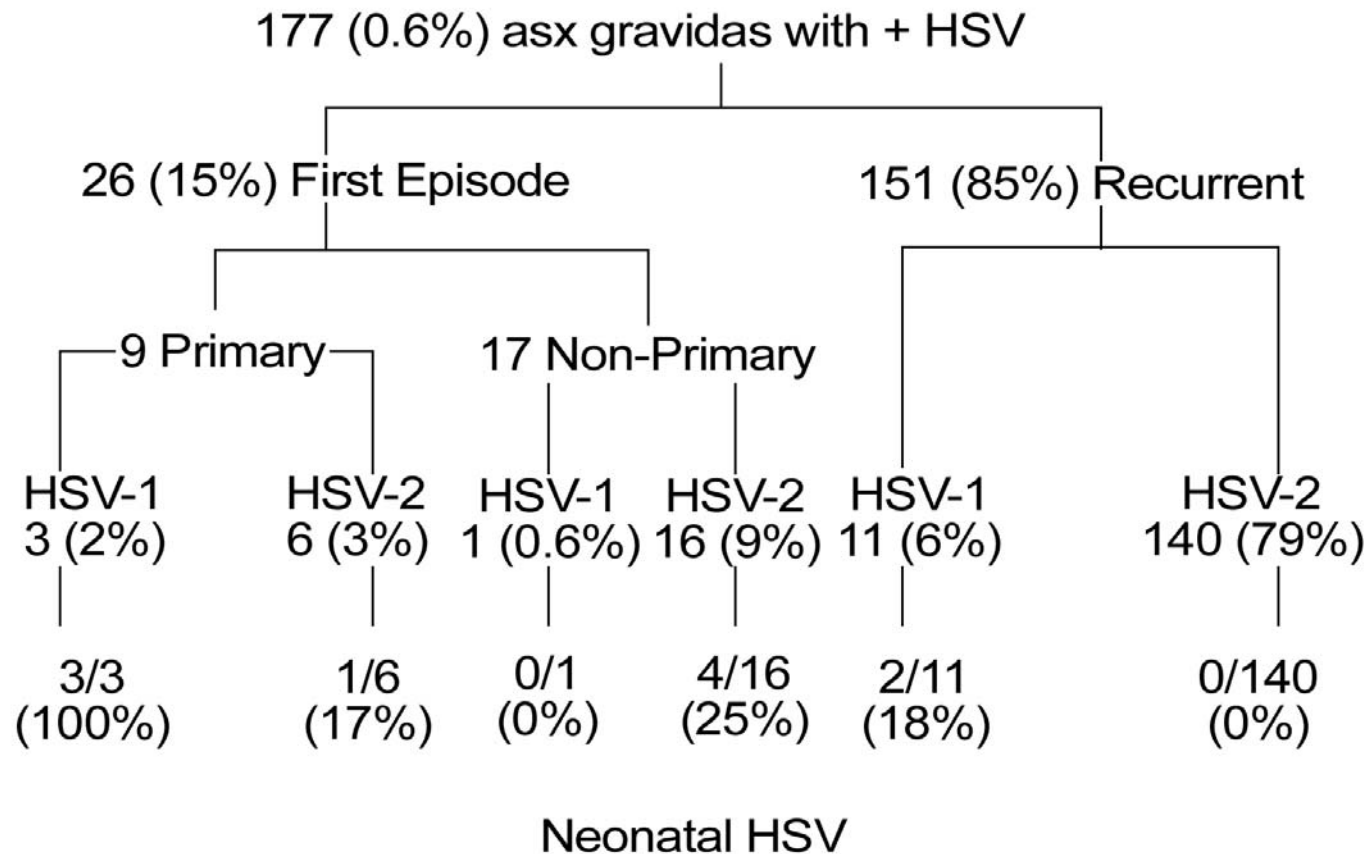
# Risk of neonatal Herpes

- Primary infection: transmission 50%
- Non-primary first episode: 33%
- Recurrent infection: 0-4%
- Asymptomatic shedding: very low risk (4 of 10,000)

# Brown et al.2003

## ***HSV Shedding in Labor***

*31,663 HSV culture/sero < 48th of delivery*



# Risk assessment HSV in pregnancy

- Cesarean section: OR 0.14
- Primary infection: OR 33,1
- HSV-1 subtype: OR 16.5
- Use of scalp electrode during labor: 6.8

# Recommendations

## A. HSV lesions in pregnancy

### ■ Primary or non-primary first episode?

#### Yes

- Treatment
- If third trimester: cesarean section
- Baby: Swabs after birth

#### No

- Treatment not necessary
- If lesions from 36th week on: treatment. If lesions/prodromi around time of delivery: cesarean section and baby: swabs

# Recommendations

## B. History of HSV genitalis

- No routine sampling recommended
- Virus culture only if lesions are present
- History of recurrences: Acyclovir or Valacyclovir should be offered from 36th week of gestation on

# Therapy of herpes genitalis

- First episode: Acyclovir 400mg tid; Valacyclovir 1000mg bid; 7-14 days
- Recurrence: Acyclovir 400mg tid 5 days or Valacyclovir 500mg bid 5 days
- Suppression: like recurrence

# Herpes neonatorum

- Most cases without history or symptoms of genital HSV in the pregnant
- Asymptomatic primary infection or
- Seronegative mother and infection of the baby after birth through sibling or other person

# Case report

- Baby develops fever, thrombopenia, hepatitis and then sepsis-like syndrome from 6th day p.p.
- History: delivery by cesarean section in 38th week of pregnancy
- „Torch“ serology „normal“

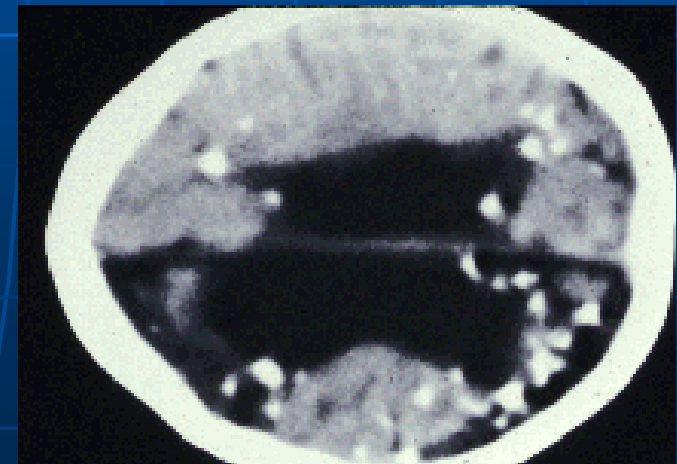
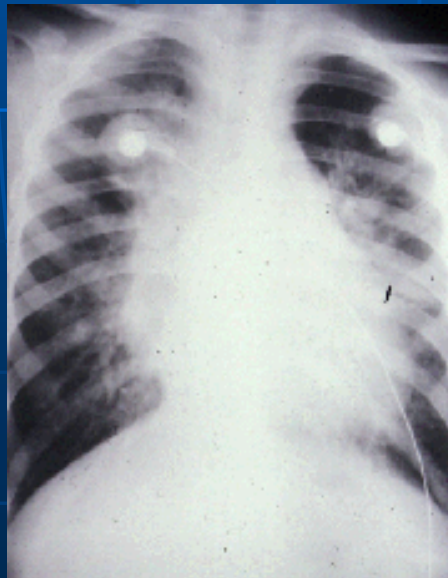
# Case report

- After 2 days without specific findings situation deteriorates, baby dies
- Histology shows inclusion bodies in hepatocytes
- Immune histochemistry positive for HSV-1
- PCR from liver and blood: HSV1-DNA
- No IgG for HSV
- Mother had oesophagitis in late pregnancy, reason for cesarean section

# Herpes neonatorum

- Symptoms begin between 2 und 28 days p.p.
- 10-50% without skin lesions
- Begin with uncharacteristic symptoms
- 30 -45% localized disease of skin, eye, mouth
- CNS symptoms 35%, 15% mortality, 65% sequelae
- Hepatitis, pneumonitis, encephalitis, thrombocytopenia, DIC, sepsis: mortality 60-80%, 40% sequelae

# Herpes neonatorum

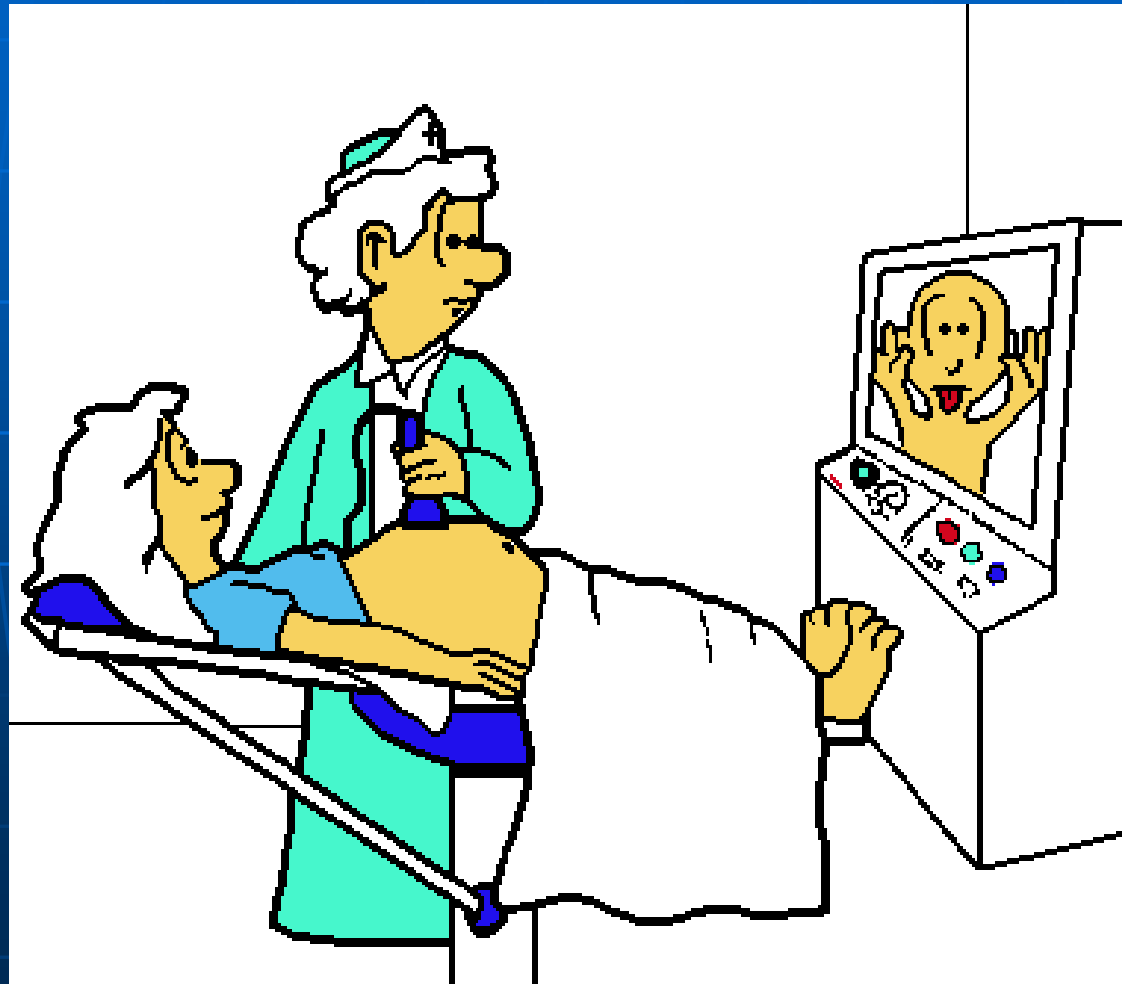


# Herpes neonatorum - diagnosis

- History of HSV in mother: swab from mouth, eye, anus 24h post partum: PCR
- With lesions: swab from lesion
- without lesion: EDTA blood and/or Liquor: PCR
- Serology not usefull!!!!!!

# Herpes neonatorum – Therapy

- Suspect of infection (don't wait for result): 45mg/kg/day i.v. (8h) for localized symptoms, 60mg/kg/day for CNS or disseminated disease
  - 14 days/21 days
- If PCR post partum positive: 14 days treatment
- CNS: >80% sequelae
- Mortality of disseminated disease with therapy 56%



# Varicella

- substantial number of women seronegative !! (growing?)
- Around 3-5 cases/1000 pregnancies/year
  - Ca. 2000-4000 cases/year

# Varicella primary infection in pregnancy

- higher incidence of complications and mortality (pneumonia 20%)
- fetal varicella syndrome (FVS) if infection in the first 22(28) weeks of gestation (0.5-2%)
- neonatal varicella with high mortality if infection in the last 3 weeks of pregnancy

# VZV in pregnancy

## A. Contact in early pregnancy

- History of Chickenpox: test for IgG (history of chickenpox usually reliable), if negative apply VZIG in between 96h of contact
  - may be effective up to 10 days after contact
- When symptoms appear, Acyclovir i.v., especially if signs of pneumoniae or persisting fever

# Varicella in early pregnancy

- Ultrasonographic controls from 22 weeks on +
- PCR from amnion fluid from 16th-20 th week
  - If no DNA and US normal until 23 weeks: minimal risk
  - If US abnormal + DNA positive: high risk
- Varicella syndrome
  - skin ulcerations, limb hypoplasia, CNS symptoms



# Varicella in late pregnancy

- Maternal infection at term: significant risk of varicella of the newborn
- Elective delivery should be avoided until 5–7 days after the onset of maternal rash to allow for the passive transfer of antibodies from mother to child
- If rash begins 5-21 days before delivery, neonatal varicella infection without complication

# Management VZV peripartal

