



# **Congenital viral infections**

the smallest DNA virus

# Parvovirus B19

associated with childhood  
exanthem

- ~~Naked, icosahedral~~, SSDNA virus
- Three capsid proteins VP1-3
- cultured in BM cells, fetal liver cells.
- Globoside (P antigen) receptor found on erythroid progenitors, erythroblasts, megakaryocytes and endothelial cells.
- Primary site of replication is the nucleus of immature cell in the erythrocyte lineage where it is cytotoxic for erythroid progenitor cells; this results in temporary arrest of erythropoiesis - this effect is not typically seen in the normal child or adult
- Causes Erythema infectiosum or fifth disease  face rash and circumoral (sparing)
- Transmitted through respiratory route
- Fever, malaise, headache and myalgia and itching
- Indurated (lacey) rash on the face (slapped-cheek) which spreads in 1-2 days to arms and legs  ملمسه مثل الصوف
- LNs, enlarged spleen and liver.
- Illness lasts 1-2 wks, but rash may recur for 2-4 wks upon: exposure to heat or sun light, on exercise or emotional stress.
- Some times associated with arthritis and vasculitis

# Congenital Parvovirus Infection

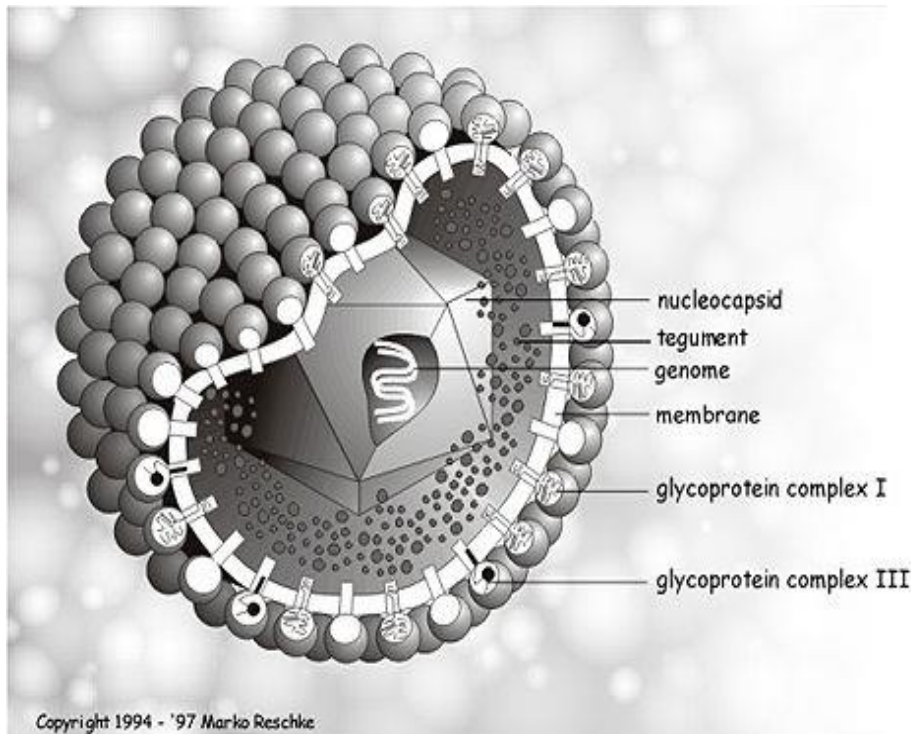
- **Some 50% of women of child-bearing age are immune**
- When acquired by a non-immune pregnant woman the transmission rate to the fetus is about 33%
- Known to cause fetal loss through hydrops fetalis; severe anaemia, congestive heart failure, generalized oedema and fetal death
- No evidence of teratogenicity.
- Risk of fetal death highest when infection occurs during the second trimester of pregnancy (12%).
- Minimal risk to the fetus if infection occurred during the first or third trimesters of pregnancy.
- Maternal infection during pregnancy does not warrant termination of pregnancy.

# Parvovirus B19

- Anaemia: Clinical consequence is minimal unless pt compromised by chronic hemolytic process such as sickle cell and thalassemia
- cardiomyopathy, hepatic dysfunction
- **Diagnosis by IgM-specific Ab** seroconversion occurs during infection, with long life protection.
- Exchange transfusion *in utero* is appropriate therapy in severe cases
- Cases of diagnosed **hydrops fetalis** had been successfully treated in utero by intrauterine transfusions and administration of digoxin to the fetus.

# herpesviruses

- dsDNA , ~~linear, enveloped, 180-200 nm~~
- ~~Large genome, codes for 75 viral proteins~~
- 50-70% similarity
- **Cross reactivity between HSV and VZV**




HSV-2 virus particle. Note that all herpesviruses have identical morphology and cannot be distinguished from each other under electron microscopy.

- Three subfamilies:
  - Alphaherpesviruses - HSV-1, HSV-2, VZV
  - Betaherpesviruses - CMV, HHV-6, HHV-7
  - Gammaherpesviruses - EBV, HHV-8
- painfull skin ulcers, chickenpox, and encephalitis.
- Acute infection followed by latent infection *latency*
- **Latent:** virus genome present in the cell (episome), not integrated
- Reactivation gives recurrent disease
- **Replication:** receptor, heparan sulphate
- **IE** (proteins initiate and regulate transcription)
- **E:** non-structural proteins (DNA poly., TK)
- **L:** major structural proteins (capsid, spikes)
- role of TK, polymerase, in antiviral effect.
- Only 25% of DNA/protein produced incorporated into virions

# Neonatal Herpes Simplex

In reactivation we have lower viral load than in primary infection.

- Incidence of neonatal HSV infection varies inexplicably from country to country e.g. from 1 in 4000 live births in the U.S. to 1 in 10000 live births in the UK.
- The baby is usually infected perinatally during passage through the birth canal.
- Premature rupturing of the membranes is a well recognized risk factor.
- The risk of perinatal transmission is greatest when there is a florid **primary** infection in the mother.
- There is an appreciably smaller risk from recurrent lesions in the mother, probably because of the lower viral load and the presence of specific antibody. 
- The baby may also be infected from other sources such as transplacental, oral lesions from the mother or a herpetic whitlow in a nurse.

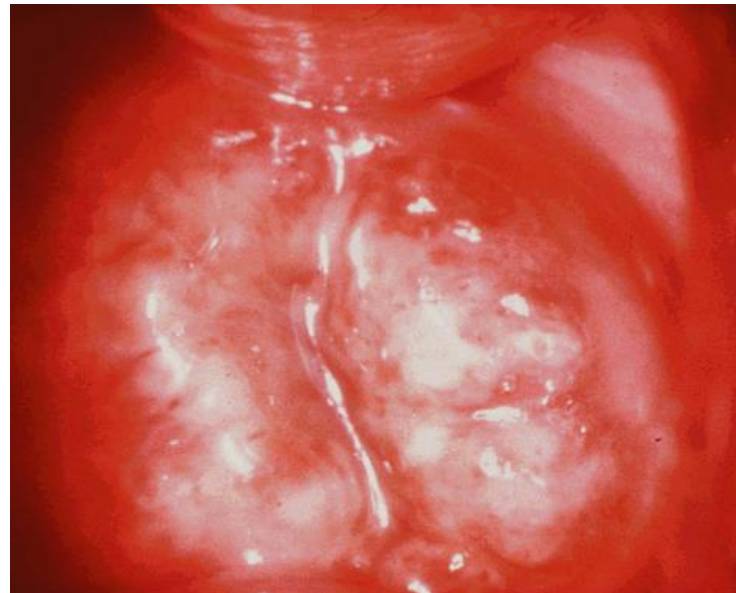
# Neonatal Herpes Simplex

- Recognition of primary herpes can require a high index of suspicion
- Type 1 infection typically produces less severe symptoms and relatively little local manifestation compared with type 2 infection
- The infection may be confined to the cervix

type 2 is more common as the baby is infected during delivery through the birth canal

Primary herpes of the cervix

primary infection is more dangerous as there is no seroconversion yet ( no Abs)





# Neonatal Herpes Simplex

- Manifestations generally occur between the 1st and 2nd wk of life but rarely may not appear until as late as the 4th wk
- The spectrum of neonatal HSV infection varies from a mild disease localized to the skin to a fatal disseminated infection (MR 60%)
- **Skin vesicles are common with either type, occurring in about 55% overall.** Neonates with no skin vesicles usually present with localized CNS disease.
- In neonates with isolated skin or mucosal disease, progressive or more serious forms of disease frequently follow within 7 to 10 days if left untreated.
- Infection is particularly dangerous in premature infants.

## Localized disease:

- Neonates with localized disease can be divided into 2 groups. One group has encephalitis manifested by neurologic findings, CSF pleocytosis, and elevated protein concentration, with or without concomitant involvement of the skin, eyes, and mouth. The other group has only skin, eye, and mouth involvement and no evidence of CNS or organ disease.

## Disseminated disease:

- Neonates with disseminated disease and visceral organ involvement have hepatitis, pneumonitis, disseminated intravascular coagulation, or a combination, with or without encephalitis or skin disease.

6C NS  
2 skin

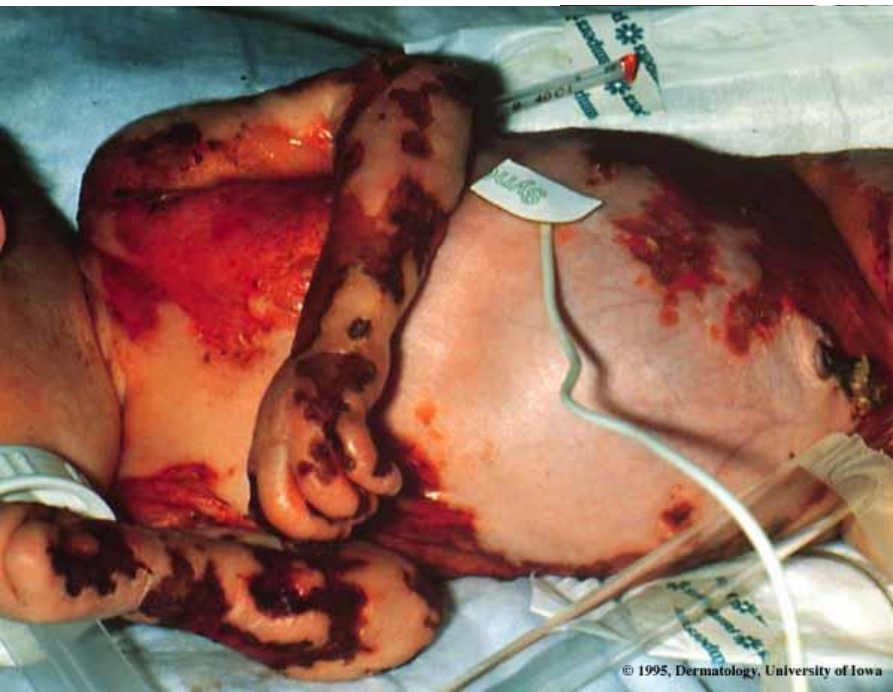


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## Presentations of congenital HSV



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# Diagnosis and treatment

for

- Samples are taken from skin vesicles (most common), nasopharynx, eyes and CSF.
- HSV culture or PCR
- Immunofluorescent testing of lesions
- Electron microscopy
- Tzanck test of the lesion base may show characteristic multinucleated giant cells and intranuclear inclusions
- Parenteral acyclovir (Zovirax)
- Supportive therapy: appropriate IV fluids, alimentation, respiratory support, correction of clotting abnormalities, and control of seizures
- Herpetic keratoconjunctivitis requires concomitant topical therapy with a drug such as trifluridine or vidarabine

# Prognosis and prevention

- The mortality rate of untreated disseminated disease is 85%; among neonates with untreated encephalitis, it is about 50%.
- Without treatment, at least 65% of survivors of disseminated disease or encephalitis have severe neurologic sequelae.
- Appropriate treatment, including parenteral acyclovir, decreases the mortality rate in CNS and disseminated disease by 50% and increases the percentage of children who develop normally from about 35% to 50-80%.
- Where the brain is involved, the prognosis is particularly severe. The encephalitis is global and of such severity that the brain may be liquefied. Mortality rate approaches 100%.
- A large proportion of survivors of neonatal HSV infection have residual disabilities.
- Universal screening has not been recommended or shown to be effective, and most maternal infections with risk of transmission are asymptomatic
- cesarean delivery for women known to have a high risk of transmission has been shown to decrease transmission and is recommended

C.S. here is very useful to prevent the infection.

# Varicella-Zoster Virus

chicken box in children / shingles in adults

- Belong to the alpha herpesvirus subfamily of herpesviruses
- Double stranded DNA enveloped virus
- One antigenic serotype only, although there is some cross reaction with HSV.
- Major mode of transmission respiratory. Contact with lesion
- Communicability 2 days before, 3-4 days into the rash
- The virus is thought to gain entry via the respiratory tract and spreads shortly after to the lymphoid system.
- URTI, LNs, viremia, RES, viremia, skin.
- Following the primary infection, the virus remains latent in the cerebral or posterior root ganglia. In 10 - 20% of individuals, a single recurrent infection occurs after several decades.
- The virus reactivates in the ganglion and tracks down the sensory nerve to the area of the skin innervated by the nerve, producing a varicella form rash in the distribution of a dermatome.

# Varicella-Zoster Virus

بس عليه حكي كثير there is vaccine for VZV

- 90% of pregnant women already immune, therefore primary infection is rare during pregnancy

10%  
• Primary infection during pregnancy carries a greater risk of severe disease, in particular pneumonia

- bf  
the 1st
- In general, exposure to zoster, or the appearance of maternal zoster does not lead to fetal infection



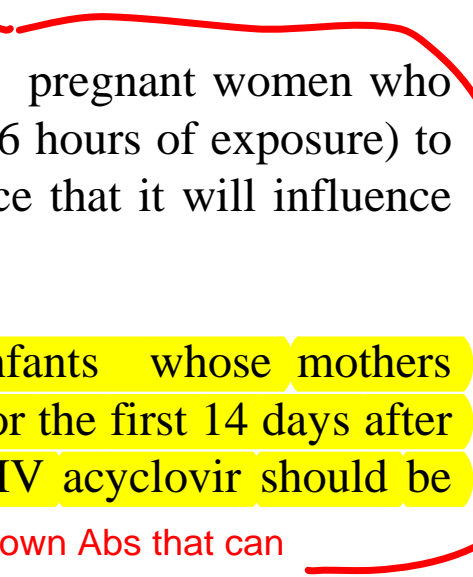
First 20 weeks of Pregnancy

→ up to 3% chance of transmission to the fetus, recognised congenital varicella syndrome;

- Scarring of skin
- Hypoplasia of limbs may be short limbs
- CNS and eye defects
- Death in infancy normal



# Neonatal Varicella

- VZV can cross the placenta in the late stages of pregnancy to infect the fetus congenitally.
- Neonatal varicella may vary from a mild disease to a fatal disseminated infection. Acute varicella in the time period from 2 days before to 5 days after delivery is associated with a high risk of severe disseminated varicella in the newborn
- If rash in mother occurs **more than 1 week** before delivery, then sufficient immunity would have been transferred to the fetus. 
- Zoster immunoglobulin should be given to susceptible pregnant women who had contact with suspected cases of varicella (within 96 hours of exposure) to modify the illness in the mother; there is little evidence that it will influence the development of the congenital varicella syndrome
-  **Zoster immunoglobulin should also be given to infants whose mothers develop varicella during the last 7 days of pregnancy or the first 14 days after delivery. careful observation; if any lesions develop, IV acyclovir should be given**  **#more than 7 days before delivery, the body formed its own Abs that can cross the placenta.**

# Hepatitis B

15%

chronic  
adults

85%

acute  
children

التهاب الكبد B



# Hepatitis B DNA virus

all hepatitis viruses are RNA viruses except HBV

partial dsDNA

- Of the recognized forms of primary viral hepatitis, only hepatitis B virus (HBV) is a major cause of neonatal hepatitis.
- Infection with other viruses (eg, cytomegalovirus, herpes simplex virus) may cause liver inflammation along with other manifestations
- HBV infection occurs during delivery from an infected mother.
- The risk of transmission is 70 to 90% from women seropositive for hepatitis B surface antigen (HBsAg) and hepatitis B e antigen (HBeAg) at the time of delivery.
- Women without the e antigen or with anti-HBe transmit the infection only 5 to 20% of the time when the virus is not actively replicating
- Mother–infant HBV transmission results primarily from maternofetal microtransfusions during labor or contact with infectious secretions in the birth canal. will not advise C. section
- Transplacental transmission is identified in < 2% of infections.
- Postpartum transmission occurs rarely through exposure to infectious maternal blood, saliva, stool, urine, or breast milk.
- Up to 90% of infants infected perinatally will develop chronic infection

# Symptoms and signs

- Most neonates with HBV infection are asymptomatic but develop chronic, subclinical infection characterized by persistent HBsAg antigenemia and variably elevated transaminase activity.
- Many neonates born to women with acute hepatitis B during pregnancy are of low birth weight, regardless of whether they are infected
- Possible outcomes of hepatitis B infection:
  - acute hepatitis B, which is usually mild and self-limited. They develop jaundice, lethargy, failure to thrive, abdominal distention, and clay-colored stools.
  - Occasionally, severe infection with hepatomegaly, ascites, and hyperbilirubinemia (primarily conjugated bilirubin) occurs.
  - Rarely, the disease is fulminant and even fatal. Fulminant disease occurs more often in neonates whose mothers are chronic carriers of hepatitis B
- **Chronic HBV** infection with persistence of HBsAg occurs in
  - up to 90% on infants infected vertically,
  - 30% of children 1 to 5 years old infected after birth
  - in 5 to 10% of older children, adolescents and adults with HBV infection

# Diagnosis

- Serologic testing:
  - Measure HBsAg, HBeAg, antibody to hepatitis B e antigen (anti-HBe), and quantitation of HBV DNA in blood.
- Other initial tests include CBC with platelets, ALT and  $\alpha$ -fetoprotein levels, and liver ultrasonography

## Hepatitis B Serology\*

Marker	Acute HBV Infection	Chronic HBV Infection	Prior HBV Infection <sup>†</sup>
HBsAg	<b>+</b> released in active replication	<b>+</b> if persists more than 6 months	—
Anti-HBs	—	—	+ <sup>‡</sup>
<b>IgM anti-HBc</b>	<b>+</b> +only serological marker at window period	—	—
IgG anti-HBc	—	+	±
<b>HBeAg</b>	<b>±</b> released during active replication	<b>±</b>	—
Anti-HBe	—	±	±
HBV-DNA ( <b>viral load</b> )	+	+	—

\*Antibody to hepatitis D virus (anti-HDV) levels should be measured if serologic tests confirm HBV and infection is severe.

<sup>†</sup>Patients have had HBV infection and recovered.

<sup>‡</sup>Anti-HBs is also seen as the sole serologic marker after HBV vaccination.

Anti-HBc = antibody to hepatitis B core; anti-HBe = antibody to HBeAg; anti-HBs = antibody to HBsAg; HBeAg = hepatitis B e antigen; HBsAg = hepatitis B surface antigen; HBV = hepatitis B virus

# Treatment

- Symptomatic care and adequate nutrition are needed.
- Neither corticosteroids nor hepatitis B immune globulin (HBIG) is helpful for acute infection.
- No therapy prevents the development of chronic, subclinical hepatitis once infection is acquired *acute to chronic development can't be prevented*
- All children with chronic HBV infection should be immunized with hepatitis A vaccine.
- Children with chronic HBV infection may benefit from antiviral drugs (eg, interferon alfa)

in jordan ,hepatitis B vaccine is available and given at the beginning of the 3th, 4th and 5th months of age . While in western countries they give the baby at his first day two injection, one is vit. k while the other is hepatitis b vaccine . Also they give two injections of hepatitis b vaccine after 2 and 4 months of age. For medical field workers who are not immune as were not vaccinated they take 3 doses as follows ; at day 0 , 1 and 6 months after. Medical field workers who have low titers of anti- HBs antigen , they take a booster.

# Prevention and prognosis

- Pregnant women should be tested for HBsAg during an early prenatal visit. Failing that, they should be tested when admitted for delivery
- Treatment of some HBsAg-positive women with lamivudine or telbivudine during the 3rd trimester may prevent perinatal transmission of HBV
- Neonates whose mothers are HBsAg-positive should be given 1 dose of HBIG IM within 12 h of birth. Recombinant HBV vaccine should be given IM in a series of 3 doses 0, 1, 6 months.
- The first dose is given concurrently with HBIG but at a different site to avoid neutralization
- Infants born to mothers with unknown HBsAg status at the time of delivery should receive their first dose of vaccine at birth and receive HBIG IM as soon as possible (up to 7 days) after delivery if maternal testing is positive for HBsAg.
- Testing for HBsAg and anti-HBs at 9 to 15 mo is recommended for all infants born to HBsAg-positive mothers
- Separating a neonate from its HBsAg-positive mother is not recommended, and breastfeeding does not seem to increase the risk of postpartum HBV transmission, particularly if HBIG and HBV vaccine have been given
- The development of the carrier state following vertical transmission has been estimated to ↑↑ the risk of chronic liver disease x20 times & hepatoma x86 times

# Hepatitis C

- Most transmission is around the time of birth
- Vertical transmission rate = 6.7% and there is a high rate of spontaneous clearance (25-50%) in the children (acute)
- Factors associated with an increased rate of infection include membrane rupture of longer than 6 hours before delivery and procedures exposing the infant to maternal blood.
- \* • Cesarean sections are not recommended. Breastfeeding is considered safe if the nipples are not damaged not cracked
- The presentation in childhood may be asymptomatic or with elevated liver function tests.
- While infection is commonly asymptomatic both cirrhosis with liver failure and hepatocellular carcinoma may occur in childhood
- Treatment: with interferon, ribavirin and Sofosbuvir.
- Prevention: Identify mothers at risk

# **Human Immunodeficiency Virus**

## Risk factors

The following factors increase the risk of MTCT:

Higher levels of maternal viraemia.

Lower maternal CD4 count.

Primary HIV Infection occurring during pregnancy.

Co-existing other [sexually transmitted disease](#).

Invasive intrapartum procedures, eg fetal scalp electrodes, forceps, ventouse.

Rupture of membranes (especially if delivery is more than 4 hours after the membranes ruptured).

Vaginal delivery.

Advanced maternal age.

Preterm birth.



# HIV - Vertical Transmission

- perinatal in most cases
- transmission rate 15 - 25%
- Role of Caesarean section in reduction of transmission in some cases

# HIV - Vertical Transmission

- transmission can be decreased by approximately 2/3 by administration of anti-retrovirals
  - to the mother in pregnancy (po), in labour (iv and po) &
  - to the infant for the first 4 weeks (po) - this is post-exposure prophylaxis

# **HIV - Antenatal testing**

Unlinked testing indicated that only 25-50% of HIV+ women were identified

Routine anti-HIV testing introduced  
Rotunda January 1998

National programme commenced April  
1999, based on the Rotunda model

# HIV

- **>90% of cases of paediatric HIV are due to vertical transmission**
- **prevention is dependent on identification of infected mothers and**
  - **antiretroviral therapy, antepartum and intrapartum with post-exposure prophylaxis to the infant**
  - **caesarean section in selected cases**

# Control & Prevention of Congenital, Perinatal & Neonatal infection

# Control & Prevention

## General Medical

- precautions with clinical examination
- use of standard / universal precautions when coming into contact with blood or secretions that may contain blood

# Prevention of congenital and perinatal infection

- Serological screening in pregnancy
  - Rubella, syphilis, Hepatitis B, HIV: “routine”
- Handwashing + GBS
  - CMV, toxoplasmosis
- Modification of “at risk” behaviour
  - Blood borne viruses
  - Sexually transmitted infection

# Prevention of congenital and perinatal infection

- Avoidance of certain foods avoid listeriosis
  - Soft cheeses, undercooked meats
- Active herpes at term - avoid vaginal delivery do C.S.