

# AZERBAIJAN MEDICAL UNIVERSITY DEPARTMENT OF MEDICAL MICROBIOLOGY and IMMUNOLOGY

#### Lecture 9.

Hepatitis viruses. The causative agents of latent viral infections. Human immunodeficiency viruses (HIV). Oncogenic viruses. Prion infections

**FACULTY:** General Medicine

SUBJECT: Medical microbiology - 2

#### Lecture plan:

- 1. Hepatitis viruses, classification
- Hepatitis A virus. Characteristics of the virion. Resistance, ways of infection, pathogenesis. Microbiological diagnostics. Specific prevention.
- Hepatitis B virus. Virion structure, antigens, persistence, ways of infection. Pathogenesis of the disease. Immunity. Microbiological diagnostics. Specific prevention.
- Hepatitis D virus. Structure of the virion, pathogenetic features of the disease
- Hepatitis C virus, characteristics, genotypes, ways of infection, pathogenesis. Microbiological diagnostics. Specific prevention problem.
- Hepatitis E virus. Virion structural features, genome, antigens, cultivation, persistence, ways of infection. Pathogenesis, clinic, complications of the disease (during pregnancy). Microbiological diagnosis, specific prevention
- Hepatitis G virus. Virion structural features, epidemiology, role in human pathology. Microbiological diagnostics.
- 2. Retroviruses. Human immunodeficiency viruses, classification. Virion structure, structural and non-structural genes. Continuity, ways of infection. Pathogenesis. Opportunistic infections. Microbiological diagnosis of HIV infection. Prevention problem and treatment preparations.
- 3. Oncogenic viruses. Historical development of the concept of the role of viruses in the etiology of malignant tumors. Modern theories of carcinogenesis. Mechanism of viral oncogenesis. Classification of oncogenic viruses.
- 4. Oncogenic viruses that cause tumors in humans:
- □ DNA-containing oncogenic viruses:
- Herpesviridae family: cytomegalovirus, Epstein-Barr virus, human herpes virus type 8.
- Hepadnaviridae family hepatitis B virus
- Papillomaviridae family, general characteristics, types, pathogenetic characteristics of diseases caused by it, specific prevention.
- Poliomaviridae family. Merkel polyomavirus.
- ☐ RNA-containing oncogenic viruses:
- Retroviridae family: human T-lymphotropic viruses (Human T-lymphotropic virus, HTLV
- Family Flaviviridae Genus Hepacivirus hepatitis C virus.
- 5. Prion infections.

### **INTRODUCTION**

• VIRAL HEPATITIS- is a primary infection of the liver caused by heterogeneous group of 'hepatitis viruses'.

• hepatitis viruses cause inflammation of liver producing identical histopathologic lesions similar to illness such as fever, nausea, vomiting and jaundice.

### **CLASSIFICATION**

### 1. INFECTIVE OR INFECTIOUS HEPATITIS

- occurs sporadically or as epidemics.
- affects mainly children and young adults.
- transmitted through faecal-oral route.

# 2. HOMOLOGOUS SERUM JAUNDICE/SERUM HEPATITIS/TRANSFUSION HEPATITIS

- -transmitted mainly by inoculation or blood transmission.
- -associated with human or homologous antisera used for prophylaxis or therapy

### TYPES OF HEPATITIS VIRUSES

- Hepatitis A and B
- Non-A non-B hepatitis (NANB): C, D, E and G.
- All are RNA viruses except type B a DNA type.

- HAV: causes infectious hepatitis.
- HBV: causes serum hepatitis.
- HCV: causes post-transfusion hepatitis.
- HDV: is defective virus, need HBV for replication.
- HEV: agent of enterically transmitted Non-A, Non-B hepatitis.
- HGV.

### Hepatitis A

CLASSIFICATION:

Group: Group IV ((+) ssRNA)

Family: Picornaviridae

Genus: Hepatovirus

Specie: Hepatitis A virus

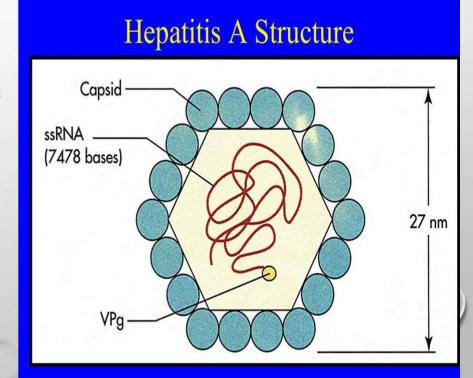
 Hepatitis A infection does not cause chronic liver disease and is rarely fatal, but it can cause debilitating symptoms.

### **HEPATITIS A VIRUS -HAV**

- belongs to the family **PICORNAVIRIDAE**.
  - GENUS: Hepatovirus.

#### **MORPHOLOGY**

- Size: 27-32nm
- Shape: spherical particles with icosahedral symmetry-with linear ssRNA.
- Has one serotype
- Does not cross-react with other hepatitis viruses.
- Genotypes: about seven are known.



# Epidemiology

- Most common Viral Hepatitis
- Source of Infection: patients.
- Route of spread : Faeco-oral
- Patient remains infectious 2 weeks prior to & for upto 1 week after onset of illness
- Overcrowding & Poor Sanitation
- No carrier state

### **CLINICAL MANIFESTATION**

- Incubation period: 15 to 45 days (mean 30)
- Onset is subacute.

#### **Characteristics of infection**

- -Pre-icteric phase: mainly GIT symptoms such as nausea and vomiting
- -Icteric phase or jaundice: dark urine, yellowish sclera and mucus membrane.
- Complete recovery: occurs in 98% cases.
- No chronic or carrier cases.

# LABORATORY DIAGNOSIS OF HAV

• Specimen: Stool and serum.

• **Direct demonstration**: virus can be visualized by immunoelectron microscopy (IEM) in fecal extracts during late incubation period and in the preicteric phase.

Serology: diagnosis is usually by antibody demonstration.

- Anti HAV antibody detection by ELISA.
- -Appearance of IgM during acute phase
- Liver enzymes elevated after 2 weeks- rise in IgM abs
- -IgM disappears within 3-6 months
- -IgG antibodies appear after a week after IgM appears, it persists for years.

#### Interpretation

- Anti-HAV IgM positive: indicates acute infection with HAV.
- Anti-HAV IgG antibody detection-in absence of IgM: indicates past infection or recovery.

### Detection of HAV particles

-HAV appears in stool from -2 to +2 weeks of jaundice.

-HAV is also detected in liver, bile and blood by immunoelectron microscopy.

### HAV antigen detection

-ELISA is used to detect HAV antigen from stool sample from -2 to +2 weeks of jaundice.

#### **Isolation**

- HAV is difficult to grow in cell line.
- Non-specific findings: elevated liver enzymes and serum bilirubin level.

### **TREATMENT**

• No specific antiviral drug available.

#### **Prevention**

- Improving hygiene
- -Hand hygiene before and after use of toilet.
- Sanitary disposal of infected faecal material b (disinfection with 0.5% hypochlorite).
- -Purification of drinking water by effective filtration and adequate chlorination with 1 mg/l chlorine.
- -Use of boiled water during outbreaks.

### **VACCINES**

- Formaldehyde inactivated vaccine:
- -Prepared from human fetal lung fibroblast cell lines such as MRC5 and WI 38.
- -Given to children after 12 months of age.
- -Single dose given intramuscularly
- -booster dose: given at 6-12 months gap.

- · Live attenuated vaccine
- -Is a single dose given subcutaneously
- Uses H2 and L-A-1 strains of HAV
- Prepaid in human diploid cell line

### • Human immunoglobulin (HAV-Ig)

-Used for post-exposure prophylaxis of intimate contacts of persons with HAV or to travellers.

Dosage: 0.02ml/kg- gives protection for 1-2 months.

# HEPATITIS B

DNA virus

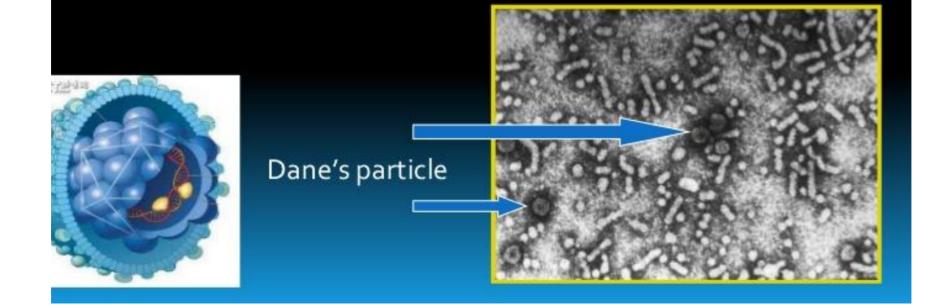
Family- Hepadnaviridae

Genus – Orthohepadnavirus

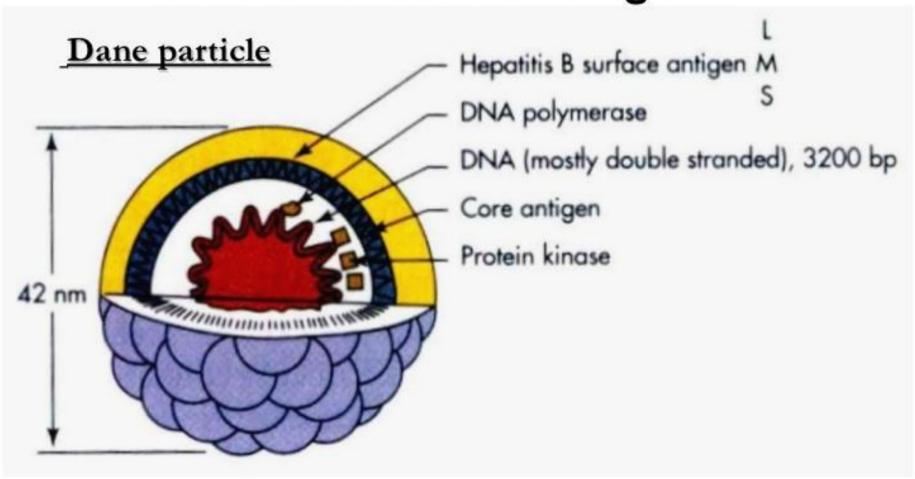
Hepatitis B virus is 30-42 nm in diameter.

# Hepatitis B virus (HBV)

- DNA virus (hepadnavirus).
- Complete virus particle is named Dane-particle,
- Genome is composed of incomplete doublestranded DNA.



### **HBV Structure & Antigens**



HBsAg = surface (coat) protein (4 phenotypes: adw, adr, ayw and ayr)

HBcAg = inner core protein (a single serotype)

**HBeAg** = secreted protein; function unknown

# Route of transmission

Body fluids contain viral particles

- Semen
- vaginal secretions
- Blood
- Saliva

### Route of transmission

- HORIZONTAL TRANSMISSION
  - Parenteral: Blood & blood products

Injections

Acupuncture needles

- Sexual
- VERTICAL TRANSMISSION
  - Hbs Ag positive mothers

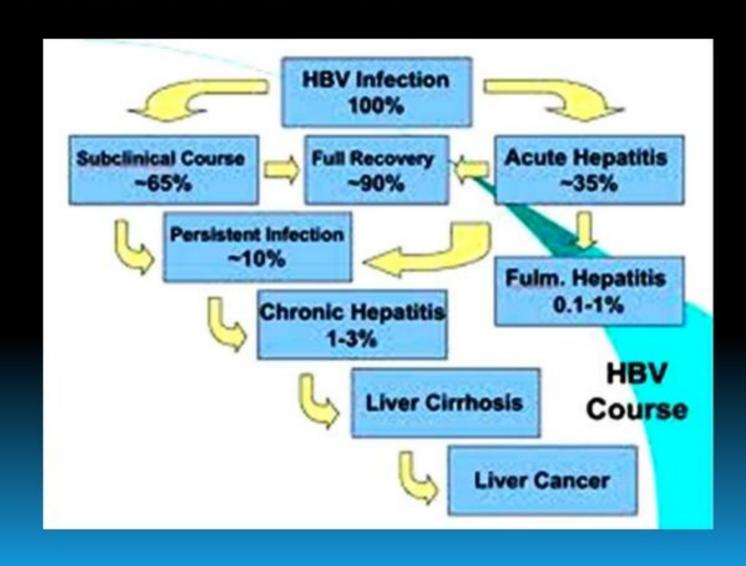
# Risk Groups

- Multiple sex partners
- IV drug abusers
- Hemodialysis patients
- Patients requiring repeated blood transfusions
  - Hemophilia
  - Thalassemia
- Health care workers

# Factors associated with the severity of hepatitis

- Infecting dose
  - Higher the dose of HBV, shorter is incubation period and more severe hepatitis.
- Age
  - Young age: mild initial hepatitis & more chance of chronicity.
- Immunological status
  - Immunological impaired hosts: Milder initial disease.

### CLINICAL COURSE



### ACUTE ICTERIC HEPATITIS

Incubation period - 70 days (30 - 180 days);

- Four clinical stages:
  - incubation period,
  - prodromal phase (pre-icteric phase),
  - icteric phase
  - convalescence.

# Pre-icteric phase

- Symptoms are nonspecific;
  - Moderate fever
  - \*Headache
  - Malaise and weakness
  - Anorexia, nausea, vomiting
  - A vague, dull, right upper quadrant pain.

# Icteric phase

- Clinical features of icteric phase:
  - Symptoms of pre-icteric phase being mild;
  - Jaundice (dark urine, skin and scleral icterus);
  - Stool light or clay colored;
  - Hepatomegaly
  - Liver function abnormalities
    - ALT and AST Î
    - Bilirubin (direct & indirect) 🕆



# Acute anicteric hepatitis

- ---No jaundice otherwise similar to acute icteric hepatitis,.
- ---The symptoms are less severe than that in acute icteric hepatitis.

### COMPLICATIONS

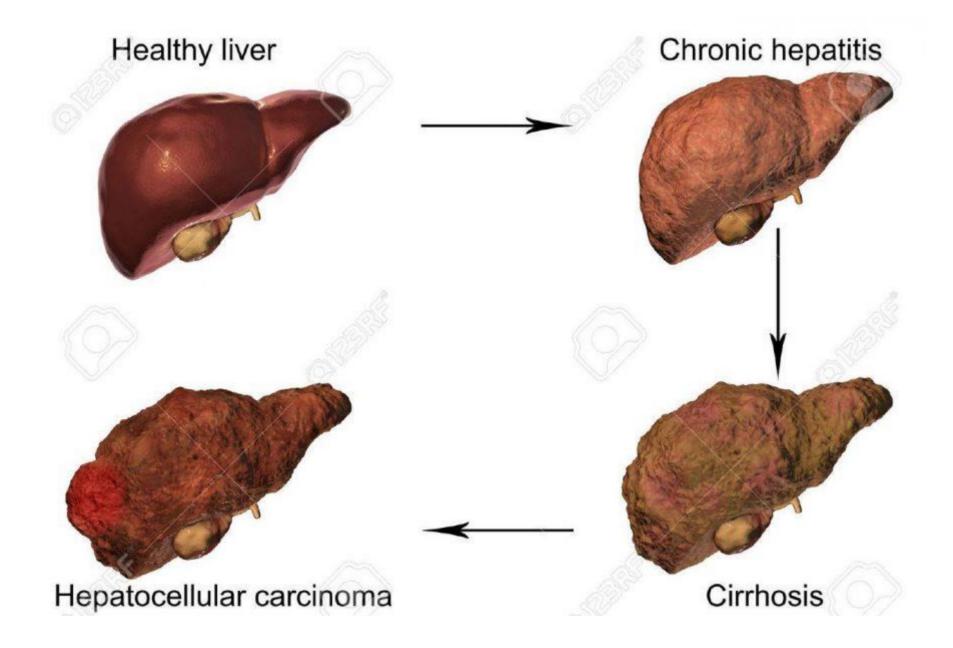
- Fulminant Hepatitis
- Chronic Hepatitis
- Rare complications:
  - Pancreatitis,
  - Myocarditis
  - Atypical pneumonia
  - Aplastic anemia
  - Transverse Myelitis

# CHRONIC HEPATITIS

- Chronic viral hepatitis: Inflammatory disease of the liver
- > 6 months.

### CLINICAL FEATURES

- Fatigue, anorexia, abdominal distension, diarrhea are common, but they are fluctuant.
- Hepatomegaly, splenomegaly, hepatic facies, liver palms, spider angioma can be seen.



### **DIAGNOSIS**

**SEROLOGY** 

- HBsAg
- ❖Anti HBcAg IgM
- ❖HBV DNA by PCR is most sensitive

test

### **DIAGNOSIS**

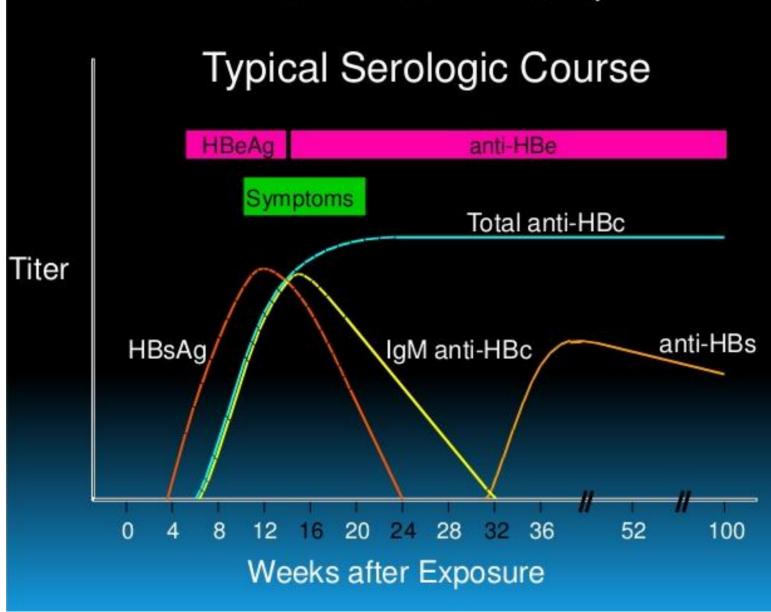
### **SEROLOGY**

- HBsAg positive > 6 months
- Anti-HBc IgG in blood
- Serum HBV DNA > 10<sup>5</sup> copies/ml (20,000IU/ml)
- HBeAg or Anti HBeAg may be present

### Serological Markers of HBV

- HBsAg: Marker of infectivity
- Anti-HBs: Marker of immunity
- HBcAg: No commercial test available.
- Anti-HBc: Marker of past or current infection.
  - ❖ IgM anti-HBc: Recent infection.
  - ❖ IgG anti-HBc: Older infection.
- HBeAg: Marker of high degree of infectivity.
- Anti-HBe: May be present in infected or immune person.

Acute HBV Infection with Recovery



# **HBV Markers in different Stages:**

Stage of infection	HBV DNA	HBsAg	HBeAg	Anti- HBc Ig M	Anti- HBc Total	Anti- HBe	Anti- HBs
Susceptible	-	-	_	_	-	_	
Early incubation	+	-	-	-	-	-	
Late incubation	+	+	+/_	-	-	-	<del>-</del> ×
Acute infection	+	+	+	+	-	-	-
Recent infection	_J+	-	Dr.Ru	<b>+</b> qaiyah	+	+	<b>+++</b> 60

Stage of infection	HBV DNA	HBsAg	HBeAg	Anti-HBc Ig M	Anti- HBc Total	Anti- HBe	Anti- HBs
Remote infection	or very	-	-	-	+	+/_	+
HBsAg-ve Acute infect	_	_	_	+	+		-
HBsAg variant infect.	_/+	-	_J+	+/_	+		-
Immune active carrier	++	+	_J+	_/+	+++	-	-
Healthy HBsAg carrier	_	+	-	_	+	+	-
Vaccination response	-	-	- Dr.Rugaiy	 vah	-	->	<b>+</b>

# **HBV – SEROLOGY INTERPRETATION**

### Acute infection

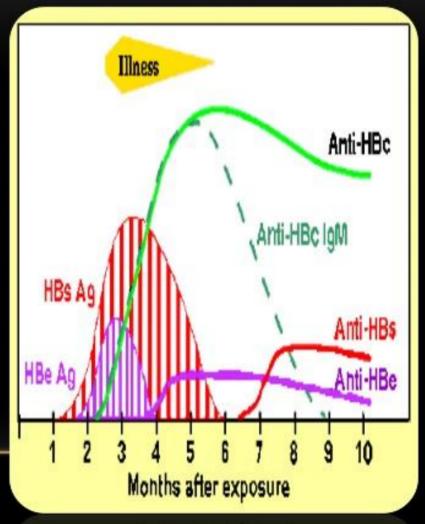
- HBsAg positive and anti-HBcAg IGM
- · Rarely, IgM anti-HBc only marker
  - Usually seen in acute fulminate Hep B

#### Chronic infection

HBsAg positive and anti-HBcAg

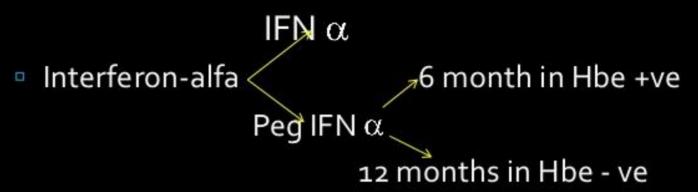
#### · Previous Infection

- HBsAg negative
- anti-HBs positive
- IgG anti-HBc positive



# Treatment of Chronic Hepatitis B

DRUGS: No specific therapy available



- Lamivudine :100mg OD 48 weeks
- Adefovir : 10 mg OD 48 weeks
- Entecavir
- Telbivudine
- Liver Transplantation

# PREVENTION



- HBV Vaccine
  - DNA Recombinant vaccine
  - IM (deltoid but not gluteal)
  - 3 doses o, 1, 6



Duration of protection – 5 to 10 yrs

### **❖**POST-EXPOSURE PROPHYLAXIS

Combination of HBIG & HB vaccine (24 hrs)

# ❖ PERINATAL PROPHYLAXIS OF

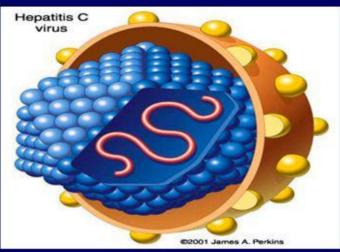
### INFANTS

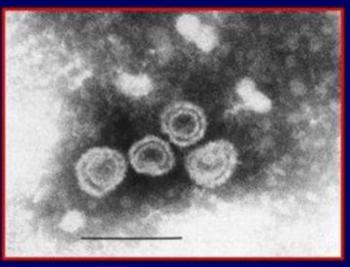
- HBIG o.5ml IM in thigh immediately after birth
- Full course of HB vaccine started within 12 hrs
   of birth

# Hepatitis C

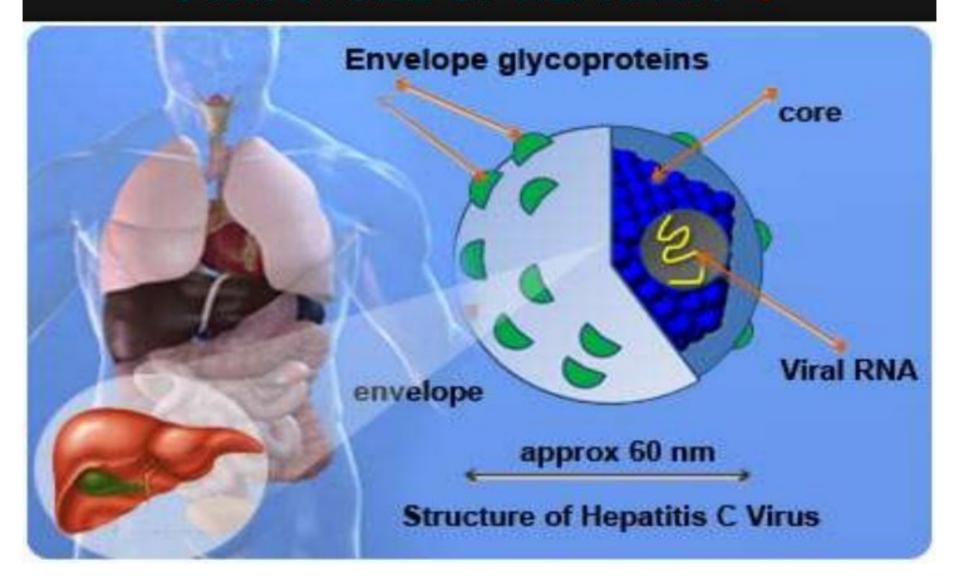
# Hepatitis C virus: Classification & structure

- Family: Flaviviridae.
- > Genus: hepacivirus.
- ➤ The virus is small, 60 80 nm in diameter.
- ➤ Consists of an outer envelope, icosahedral core and linear positive polarity ss-RNA gemone.
- ➤ There are 6 major genotypes (1 6), genotype 4 is the dominant in Saudi patients.

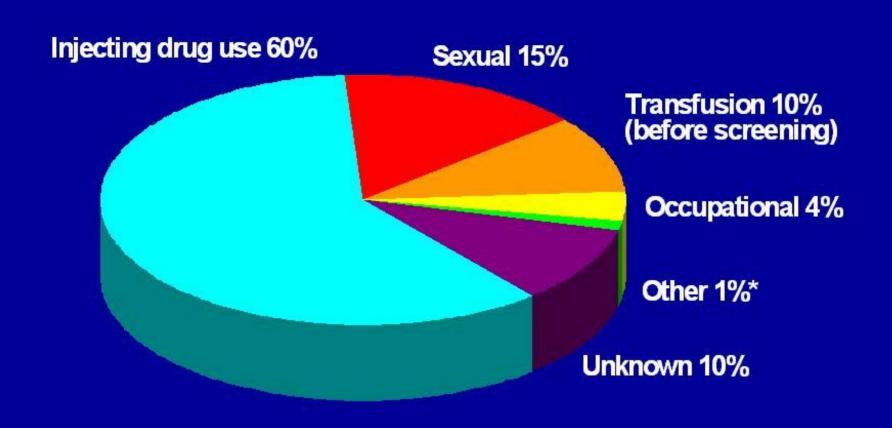




# STRUCTURE OF HEPATITIS C



# Routes of Transmission



\* Nosocomial; iatrogenic; perinatal

# CLINICAL FEATURES

- Incubation period: 50 days (15 150 days)
- 90% : Asymptomatic
- 10%: Mild flu like illness with jaundice & raised serum amino transferrases
- Extrahepatic Manifestation: Arthritis

Glomerulonephritis

# Clinical Course

■ 85% : Chronic liver disease

■ 15 – 20% : Cirrhosis in 10 – 30 yrs

■ 7 – 15% of cirrhosis patient: Hepatocellular carcinoma

# DIAGNOSIS

- HCV RNA detected in 1 2 weeks after infection
- Anti HCV is + ve 6 weeks after infection

# Treatment for Chronic HC

For CHC: IFN-α + Ribavirin 6 - 12 months

Side Effects

- Ribavirin: Hemolytic anemia
- Interferon: Flu like symptoms
- Liver Tranplantation in Cirrhosis

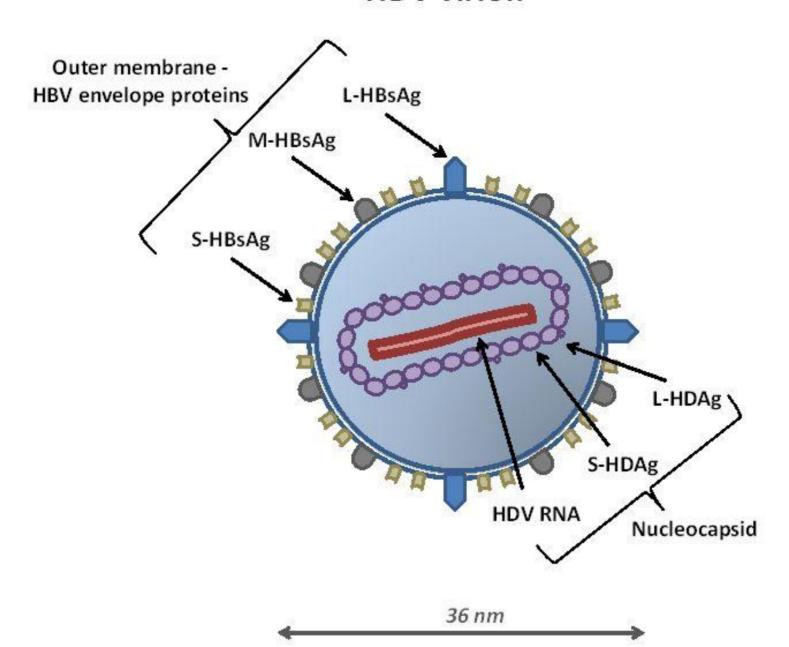
### **HEPATITIS D VIRUS**

- Is a defective virus
- Cannot replicate by itself- depends on HBV for survival.

#### Morphology

- Resembles viroids
- Small size: 35nm
- Consists of circular, negative-sense ssRNA.
- Protein coat made of single protein-hepatitis d antigen (HDAg).
- Surrounded by envelope protein derived from HBsAg from HBV-hence called defective virus.

### **HDV** virion



#### **TRANSMISSION**

Parenteral route, sexual and vertical routes.

→Co-infection: occurs when person is exposed to serum containing both HDV and HBV.

→Super-infection: occurs when a chronic carrier of HBV is exposed to serum with HDV.

-Results in disease 30-50 days later with two phases

→Acute phase- HDV replicates actively with high transaminase levels with suppression of HBV.

→ Chronic phase- HDV replication decreases, HBV replication increases, transaminase levels fluctuate, disease progresses to cirrhosis and hepatocellular carcinoma (HCC).

- Mortality rate higher (> 20%).

### LABORATORY DIAGNOSIS

A. In co-infection: IgM against both HDAg and HBcAg are elevated -IgM anti-HDV appears late and is short-lived.

- B. In super-infection: HBV appears already as carrier, IgG anti-HBc is detected
- -Anti-HDV would be IgM type initially
- -In chronic state: mixture of IgM and igg persists for months or longer.

- C. Anti HBc antibody differentiates between co-infection and super-infection.
- -IgM anti HBc + IgM anti-HDV: indicates co-infection.
- -IgG anti HBc + mixture of IgM and IgG anti-HDV: indicates super-infection.

 HDV RNA is detected in blood and liver before and early days of acute phase of both infections.

#### **Epidemiology**

- Globally- 15 million people are infected with HDV- where 5% of 350 million are infected with HBV.
- Infection occurs world wide.

#### **Treatment**

-IFN-a

#### **Prevention**

HBV vaccination and prophylaxis measures.

# **HEPATITIS E VIRUS (HEV)**

• Causes an enterically transmitted hepatitis- in young adults.

#### Morphology

- Resembles caliciviruses.
- Size: small (30-32 nm), non-enveloped with icosahedral symmetry.
- Contains positive-sense, ssRNA and a specific antigen (HEV-Ag).

#### **Genotypes**

- HEV has a single serotype, five genotypes.
- Genotypes: -four are detected in humans.
  - Type 1 and 2 appear to be more virulent.
  - Type 3 and 4 are more attenuated and account for subclinical infections.

### **CLINICAL MANIFESTATION**

- Incubation period: 14-60 days.
- Mostly present as self-limiting acute hepatitis lasting for several weeks.
- Fulminant hepatitis- occurs in 1-2% of cases; except for pregnant women at higher risk (20%).
- No chronic infection or carrier state.

### **EPIDEMIOLOGY**

- HEV is a zoonotic disease- affects monkeys, cats, pigs and dogs.
- Transmission: faecal-oral route via sewage contamination of drinking water or food.
- Epidemics: most common in India, Asia, Africa and Central America.
- Age: young adults (20-40 years).

### LABORATORY DIAGNOSIS

- Specimens: stool, serum.
- HEV RNA is detected by reverse transcriptase PCR.
- HEV virions- detected by electron microscopy.

- Serum antibody detection- by ELISA.
- →IgM anti-HEV: appears in serum same time with appearance of liver enzymes-indicates acute infection.
- → Igg anti-HEV: replace IgM in 2-4 weeks- indicates recovery or past infection.

# **TREATMENT**

• No specific antiviral drugs available.

#### **Prevention**

• Same prevention measures like for HAV.

# **HEPATITIS G VIRUS (HGV)**

- · Also referred as GB virus C.
- Related to hepatitis c.
- Family: flaviviridae, genus: Pegivirus.
- Transmission: contaminated blood or blood products via sexual contact.
- Does not cause hepatitis- replicates in bone marrow and spleen.
- Classified into 6 genotypes.
- Commonly co-infects people with HIV.

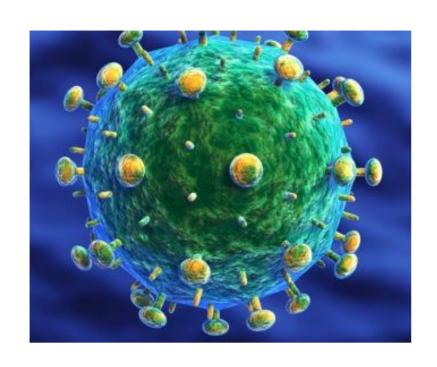
# Retroviridae family (retroviruses)

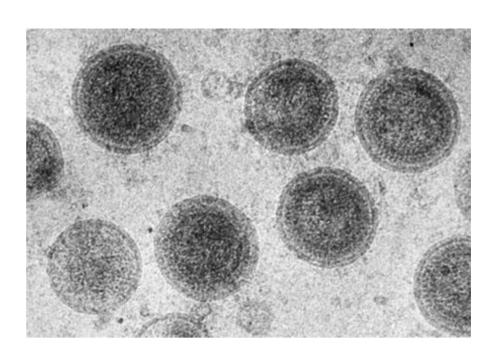
- The retroviridae family consists of single-stranded RNA viruses. The family is named after an enzyme that enables the synthesis of DNA from RNA in virions (RNA-dependent DNA polymerase, or reverse transcriptase).
- Retroviruses are spherical in shape and measure 80-110 nm. The core of the virion consists of a helical nucleoprotein surrounded by an icosahedral capsid, surrounded on the outside by a lipid-like membrane. There are glycoprotein spikes on the surface of the outer membrane.
- At the center of the central part is the presence of the viral genome and the complex reverse transcriptase associated with it.
- The genome consists of two identical positive-stranded, linear RNAs

### Classification of retroviruses

- The Retroviridae family consists of 7 genera with many representatives. Most of them cause malignant tumors (cancer, sarcoma, leukemia, etc.) in various animals.
- Human immunodeficiency virus (IIV-1, IIV-2) and human T-lymphotropic viruses (HTLV-1 and HTLV-2) are more important in human pathology.

# Human immunodeficiency virus



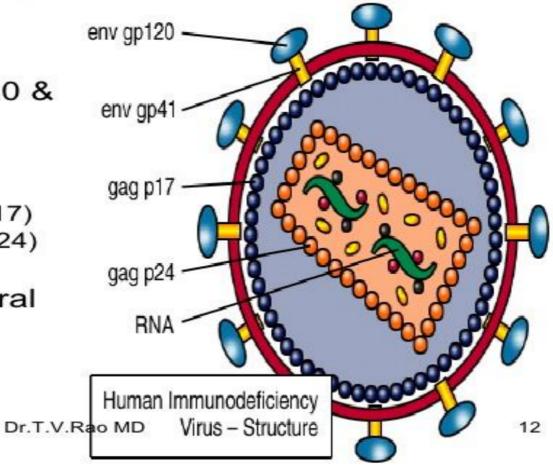


# Introduction

- HIV was first Identified in 1981 in USA among homosexuals
- In 1983, French investigator named Lymphadenopathy associated virus (LAV).
- In 1984 virus was isolated by Gallo and coworkers from national institute of health in United States.
- They named Human T-cell Lymphotropic virus III (HTLV-III).

# Family: Retroviridae Subfamily: Lentivirus

- RNA virus, 120nm in diameter
- Envelope gp160; gp120 & gp41
- Icosahedral symmetry
- Nucelocapsid
  - Outer matrix protein (p17)
  - Major capsid protein (p24)
  - Nuclear protein (p7)
- Diploid RNA with several copies of reverse transcriptase



# **HIV Modes of Transmission**

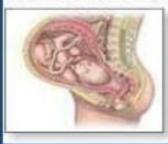


Unprotected sex with an infected partner



Sharing needles with infected person

Almost eliminated as risk factors for HIV transmission are:



Transmission from infected mother to fetus

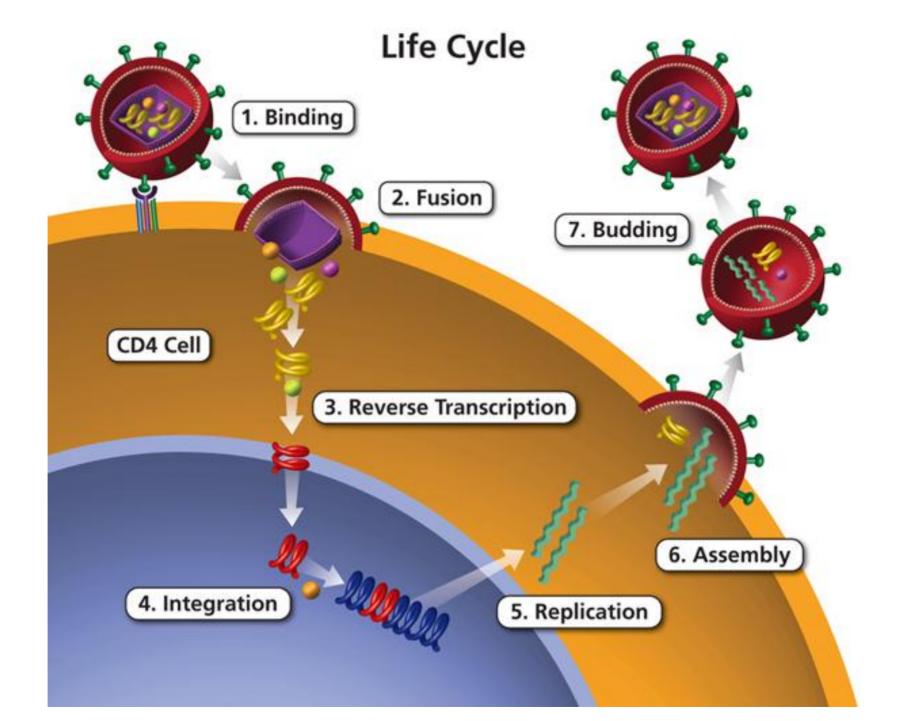


Infection from blood products

- vertical transmission of HIV from mother to child is the main route by which childhood HIV infection is acquired
- the risk of perinatal acquisition is 25-40% without intervention

- The body fluids have been proven to spread HIV:
- · blood
- semen
- · vaginal fluid
- · breast milk
- other body fluids containing blood
- cerebrospinal fluid surrounding the brain and the spinal cord
- · synovial fluid surrounding bone joints





#### PATHOGENESIS:

- Attachment of virus at the CD4 receptor and chemokine co-receptors.
- o viral fusion and uncoating
- Reverse transcriptase.
- Migration to nucleus
- Integration of the viral DNA into cellular DNA by the enzyme integrase
- Transcription and RNA processing
- Protein synthesis.
- protease cleaves polypeptides into functional HIV proteins and the virion assembles
- virion budding
- Virion maturation

# FOUR STAGES OF HIV



### STAGE 1 - PRIMARY:

- flu like illness occurs two to six weeks after infection or there may be
- o no symptoms at all
- Infected person can infect other people





# Stage 2 - Asymptomatic



- This stage is free from symptoms
- There may be swollen glands.
- HIV antibodies are detectable in the blood
- o This stage is last for about ten years

#### STAGE 3 - SYMPTOMATIC:

The person starts showing symptoms like fever, skin disease.

The immune system deteriorates emergence of opportunistic infections and cancers



#### STAGE 4 - HIV ⇒ AIDS :

- The immune system weakens
- The illnesses become more severe leading to AIDS
- The illnesses become more severe leading to emergence of opportunistic infections and cancers

#### SYMPTOMS:

#### The symptoms of this:

- o diarrhea
- o fatigue or weakness
- fever
- headache
- o joint pain
- o night sweats
- rash
- swollen glands
- weight loss
- yeast infections (of the mouth or vagina) that last a long time or occur frequently



## Diagnostic Tests for HIV Infection

- Serological methods for detection of antibody
  - Rapid tests
  - ELISA
  - Western blot
- Antigen detection methods
  - P24 antigen capture test
  - Polymerase Chain Reaction (also known as PCR or viral load)

#### HIGHLY ACTIVE ANTIRETROVIRAL DRUGS

♦ NUCLEOSIDE REVERSE TRANSCRIPTASE

Zidovudine Stavudine

\* NON-NUCLEOSIDE REVERSE TRANSCRIPTASE INHIBITOR

Efavirenz Nevirapine

\* PROTEASE INHIBITOR

Atazanavir

Darunavir



#### **PREVENTION**

There's no vaccine to prevent HIV infection and no cure for AIDS. But it's possible to protect yourself and others from infection. That means educating yourself about HIV and avoiding any behavior that allows HIV-infected fluids — blood, semen, vaginal secretions and breast milk — into your body.



# ONCOGENIC VIRUS

## Introduction

- Oncogenesis An abnormal growth of tissue resulting from uncontrolled, progressive multiplication of cells and serving no physiological function. Result of genetic changes that alter the expression or function of proteins that play critical roles in the control of cell growth and division.
- □ Proto-oncogenes normal gene, present in normal cells, conserved in their genomes, code for proteins which regulate cell growth and differentiation.
- Oncogenes mutated versions of proto-oncogenes that contribute to cancer development by disrupting a cell's ability to control its own growth.

ONCOGENIC VIRUSES

Viruses that produce tumours in their natural host/experimental animals or which induce malignant transformation of cells on culture.

#### TYPES:

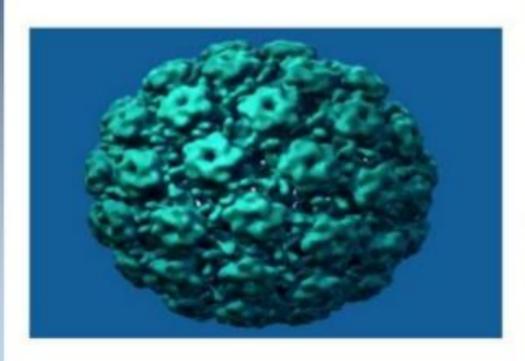
Oncogenic RNA Viruses

Retroviruses are divided into oncoviruses, lentiviruses, and spumaviruses.

Oncogenic DNA Viruses

Oncogenic human DNA viruses include hepatitis B viruses, herpesviruses, and papillomaviruses.

#### Human Papillomavirus (HPV)



Double-stranded DNA virus
Infects human epithelial cells

- >200 different strains of the virus
  - 30-40 anogenital
  - 15-20 oncogenic

Genital warts, cervical dysplasia not-reportable, so prevalence data incomplete

Considered the most common sexually transmitted infection in the United States

# HPV

- Small
- Non-enveloped
- Virion –Icosahedral
- Genome double stranded ,circular DNA (8000bp )
- 16 genera (5 human infections)

#### **Epidemiology:**

- HPV induced cervical cancer is 2nd most common cancer worldwide
- 16% of all female cancers are linked to HPV
- Papilloma virus is found in 90% of women with cervical cancers

## HPV DISEASES

- □ Genital HPV is a very common sexually transmitted infection which usually causes no symptoms and goes away by itself, but can sometimes cause serious illness. HPV is responsible for:
- almost all cases of genital warts and cervical cancer
- 90% of anal cancers
- ☐ 65% of vaginal cancers
- ☐ 50% of vulva cancers
- □ 35% of penile cancers
- ☐ 60% of oropharyngeal cancers (cancers of the back of the throat, including the base of the tongue and tonsils).
- ☐ Four out of five people have at least one type of HPV at some time in their lives. It is sometimes called the 'common cold' of sexual activity. HPV infects both men and women.

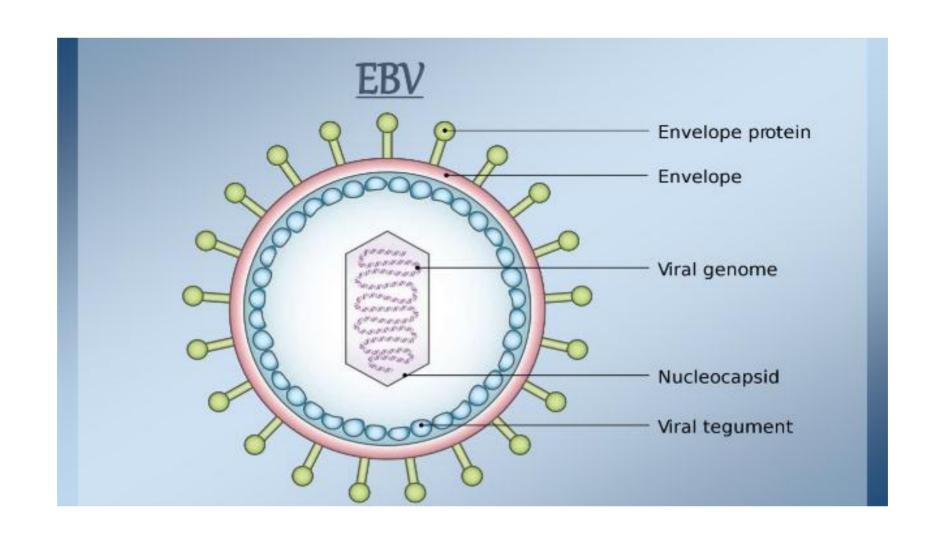
# Diagnosis

- ☐ The Pap test can find abnormal cells on the cervix so that they can be removed before cancer develops. Abnormal cells often become normal over time, but can sometimes turn into cancer. These cells can usually be treated, depending on their severity and on the woman's age, past medical history, and other test results.
- An HPV DNA test, which can find certain HPV types on a woman's cervix, may also be used with a Pap test in certain cases (called cotesting). Even women who were vaccinated when they were younger need regular cervical cancer screening because the vaccines do not protect against all cervical cancers.

# Treating HPV

HPV vaccination could prevent most cancers and other diseases caused by HPV. There is **no treatment** for the virus itself, but there are treatments for the problems that HPV can cause.

- ✓ In most cases the immune system clears HPV from the body naturally over time and has no long-lasting effects. Most people with HPV have no symptoms and will never know they have it.
- ✓ For women, having regular Pap tests once they become sexually active is the only way to detect abnormal cells on the cervix caused by HPV.
- ✓ Genital warts can be treated by doctors or at sexual health clinics.
- ✓ Recurrent Respiratory Papillomatosis (RRP), a rare condition in which warts grow in the throat, can be treated with surgery or medicines.



# EBV

- ☐ Infectious mononucleosis
- ☐ Burkitt's lymphoma
- □ Epstein-Barr virus (EBV), also known as human herpesvirus 4, is a member of the herpes virus family. It is one of the most common human viruses. EBV is found all over the world.
- □ Epidemiology
  - Ubiquitous
  - Burkitt's lymphoma children in Central Africa
  - Nasopharyngeal carcinoma Cantonese China, Alaskan eskimos.
- Malaria cofactor

# Symptoms

- □Once you're infected with EBV, symptoms can take 4 to 6 weeks to show up. When they do, they're often mild, especially in young children. Kids' symptoms may be more like those of a cold or flu. Teens often have more obvious symptoms of mononucleosis. If you do get symptoms, most likely you'll have:
- Fatigue
- Fever
- Lack of appetite
- Rash
- Sore throat
- Swollen glands in the neck
- · Weakness and sore muscles

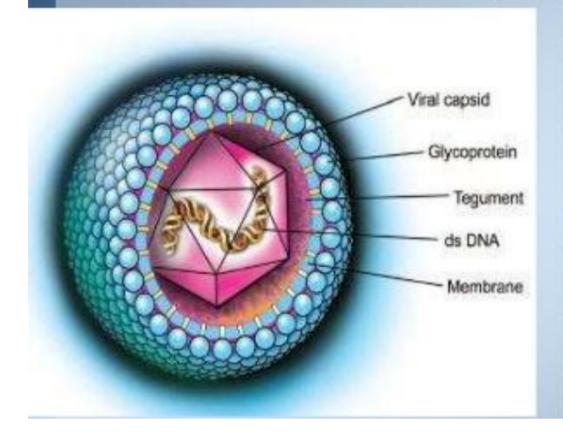
# Symptoms of Burkitt's Lumphoma

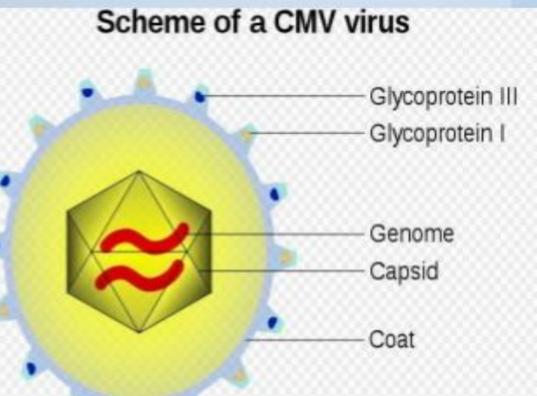
- ☐ The symptoms depend on the type.
- ☐ The endemic (African) variant usually starts as tumors of the jaw or other facial bones. It also can affect the gastrointestinal tract, ovaries, and breasts and can spread to the central nervous system, causing nerve damage, weakness, and paralysis.
- ☐ The sporadic and immunodeficiency-associated types usually start in the bowel and form a bulky tumor mass in the abdomen, often with massive involvement of the liver, spleen, and bone marrow. These variants also can start in the ovaries, testes, or other organs, and spread to the brain and spinal fluid.

# TREATMENT

☐ Treatments for Burkitt lymphoma may include intensive chemotherapy in combination with: Rituximab (Rituxan), a monoclonal antibody that sticks to proteins on cancer cells and stimulates the immune system to attack cancer cells ☐ Autologous stem cell transplantation, in which the patient's stem cells are removed, stored, and returned to the body ☐ Radiation therapy ☐ Steroid therapy ☐ In some cases, surgery may be needed to remove parts of the intestine that are blocked, bleeding, or have ruptured





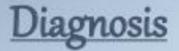


# **CMV**

- □Cytomegalovirus or CMV, is a common virus that infects people of all ages. In the United States, nearly one in three children are already infected with CMV by age 5 years. Over half of adults by age 40 have been infected with CMV. Once CMV is in a person's body, it stays there for life and can reactivate. A person can also be reinfected with a different strain of the virus.
- ☐ Most people infected with CMV show no signs or symptoms. That's because a healthy person's immune system usually keeps the virus from causing illness. However, CMV infection can cause serious health problems for people with weakened immune systems, as well as babies infected with the virus before they are born (Congenital CMV).

# Signs & Symptoms

- Most people with CMV infection have no symptoms and aren't aware that they have been infected. In some cases, infection in healthy people can cause mild illness that may include
- ·Fever,
- Sore throat,
- ·Fatigue, and
- Swollen glands.
- Occasionally, CMV can cause mononucleosis or hepatitis
- □ People with weakened immune systems who get CMV can have more serious symptoms affecting the eyes, lungs, liver, esophagus, stomach, and intestines. Babies born with CMV can have brain, liver, spleen, lung, and growth problems. Hearing loss is the most common health problem in babies born with congenital CMV infection.



- Blood tests can be used to diagnose CMV infections in people who have symptoms.
- A person who has been infected with cytomegalovirus (CMV) will develop **antibodies** to the virus that will stay in the body for the rest of that person's life. A blood test for these antibodies can tell whether a person has ever been infected with CMV.
- ☐ Tests that can indicate when a person was infected are **not** widely available commercially.
- ☐ If the virus is detected in the blood, saliva, urine or other body tissues, it means that the person has an active infection.

#### **Treatment**

- ☐ Healthy people who are infected with CMV usually **do not** require medical treatment.
- Medications are available to treat CMV infection in people who have weakened immune systems and babies who show symptoms of congenital CMV infection.
- ☐ If treatment is needed, it's most often in the form of **antiviral drugs**.

  Antiviral drugs slow the virus reproduction, but can't cure it.
- ☐ The antiviral medications against CMV include the following:
  - Ganciclovir (Cytovene)
  - Valganciclovir (Valcyte)
  - Foscarnet (Foscavir)
  - Cidofovir (Vistide)

## The causative agents of slow viral infections

- In humans, slow viral infections include measles, mumps, poliomaviridae, JC-virus, and others.
- Typical slow viral infections in animals include Visna and Maedi viruses of the genus Lentivirus of the family Retroviridae.
- Visna virus infects in the form of DNA-virus integration with the genome of cells. The disease affects all internal organs of sheep, pathological changes occur, especially in the brain, lungs and reticuloendothelial system.
- Diseases similar to slow viral infections are also caused by prions.

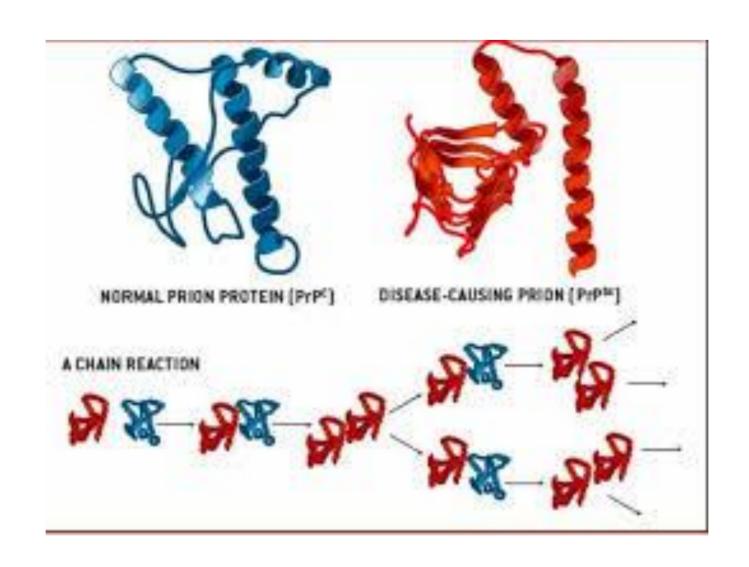
#### **Prions**

- The term prion, proposed by the American scientist S.Pruziner, is derived from the English word "proteinaceous infectious particle", which means "infectious protein particle". Prion protein (PrP prion protein) can be in two forms cellular, normal (PrPC) and altered, pathological (PrPSC).
- Normal prion protein (Prc) is present in both animal and human organisms. Found on the surface of cells anchored to the membrane by the glycoprotein of the molecule, this protein performs a number of regulatory functions it is involved in the transmission of nerve impulses, the regulation of diurnal biorhythms.

# Infectious prion protein

- In prion diseases, the normal prion protein becomes an infectious form. It is referred to as PrPSc (Sc from the English word "scrape", which is a prion disease of sheep and goats).
- Infectious prion protein differs from normal prion protein in its tertiary and quaternary structure. PrPSC has a molecular weight of 27-30 kDa and is a pathological, posttranslated altered form of the prion protein.
- These prions are resistant to proteases, boiling, high temperature, ionizing radiation, 50% ethyl alcohol, 3.7% formaldehyde, glutaric aldehyde, betapropionate.
- They can be inactivated by 90% ethyl alcohol, ether, strong detergents, as well as autoclaving at 121C for 1 hour. Quanidine thiocyanate is very effective in neutralizing medical instruments and accessories.

## PrPc və PrPSc

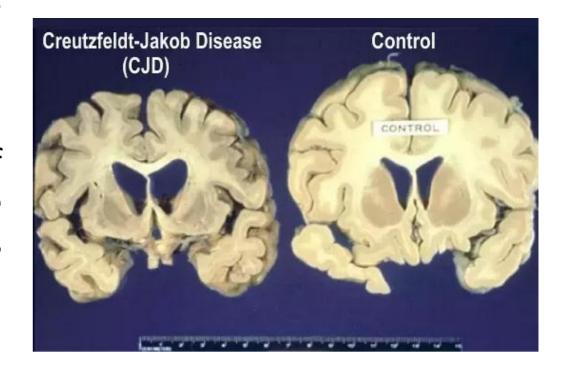


#### Prion diseases

- Prions are unusual pathogens that cause transmissible spontaneous encephalopathy.
- In humans (kuru, Kreitsfeldt-Jacob disease);
- in animals (scrap in sheep and goats, sponge-like encephalopathy in cattle, etc.)

## Clinical forms of prion diseases

• Kreitsfeldt-Jacob's disease is infected by the use of undercooked animal products, such as beef from the brain of cattle with spongiform encephalopathy, and by the use of other substances in the transplantation of tissues, such as the cornea and meninges.



## Clinical forms of prion diseases

• **Scraping** - severe itching of the skin in various animals, especially sheep and goats, hair loss ("sheep disease"), damage to the central nervous system, progressive impairment of coordination of movements with the inevitable death of the animal.



## Clinical forms of prion diseases

- Spongeal encephalopathy of cattle ("mad cow disease", "cattle rabies") is a scrapie-like disease associated with the addition of bone meal made from the bones of sick sheep to the feed of animals as a feed additive.
- The disease is accompanied by damage to the central nervous system, impaired coordination of movements, ataxia and eventually death.



### Diagnosis of prion diseases

- Diagnosis of prion diseases is based on histological examination of sections of the brain.
- Spongeal changes in the brain, astrocytosis (gliosis), amyloidosis are detected in prion pathology.
- Amyloid areas are detected by staining with Congo red.
- Inflammatory changes are not characteristic.

