



# HEMATOPOIETIC & LYMPHATIC SYSTEM

SUBJECT : \_\_\_\_\_

LEC NO. : 1

DONE BY : Tabark Aldaboubi



وَقُلْ رَبِّ زِدْنِي عِلْمًا

# 1- Epstein-Barr Virus and Parvoviruses B19

Hashemite University  
Faculty of Medicine, 2<sup>nd</sup> year  
Hematopoietic and Lymphoid system  
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\* بهذا السيستم الدر المنراحت رح تكون متنوعه بين الـ Virology و bacteriology و parasitology

# Objectives

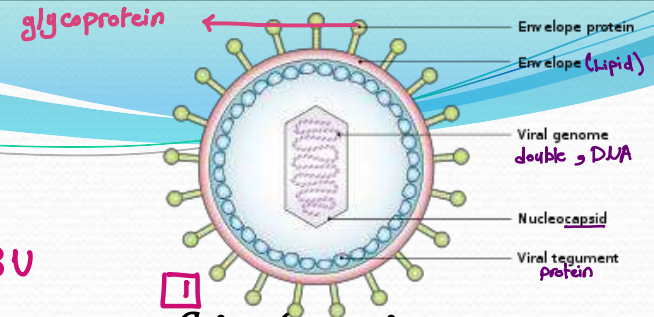
- Describe the virology, epidemiology, pathogenesis, clinical presentation and management of Epstein-Barr Virus
- Describe the virology, epidemiology, pathogenesis, clinical presentation and management of Parvovirus B19





# Epstein-Barr Virus (EBV)

# Virology



EBV بكل مجموعته من اليرقان العملي : [1]

● Epstein-Barr virus is the etiologic agent of infectious mononucleosis and African Burkitt's lymphoma [2]

لأنه يزيد الـ lymphocyte و monocyt

نسبة للعالم التي اكتشفها

● Its complete nucleotide sequence of 172 kbp is smaller than other herpes viruses [kelobase Pair]

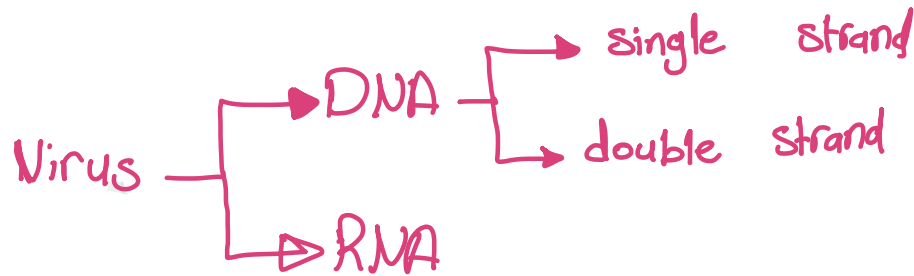
● The virus is approximately 120 nm to 180 nm in diameter and is composed of a double helix of DNA wrapped in a protein capsid. The capsid is surrounded by a tegument made of protein, which in turn is surrounded by an envelope made from lipids. The viral envelope contains glycoproteins, which are essential to infection of the host cell [Protein + Sugar] [دهمة لدرتيا العنروسا بخلايا جسم الانسان]

● In vivo, EBV is tropic for both human B lymphocytes and epithelial cells [II] [يرتبط بنوعين من الخلايا]

ذكر الدكتور  
هذوك

- (HHV-1) human herpes virus 1 = Herpes Simplex 1 → cold sores, fever blister (ulcer in mouth)
- (HHV-2) human herpes virus 2 = Herpes Simplex 2 → genital herpes.
- (HHV-3) human herpes virus 3 = Varicella zoster (responsible for chickenpox, shingles)
- (HHV-4) human herpes virus 4 = Epstein-Barr virus (causes infectious mononucleosis or kissing disease).
- (HHV-5) human herpes virus 5 = Cytomegalovirus (mostly seen in immunocompromised or those with chronic illnesses).

احد انواع ال herpes وهو اصغر من باقي ال انواع.





# History

اسماء الطغاء الي اكتشفوها.



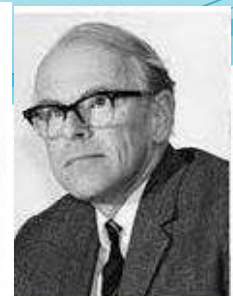
Tony Epstein



Bert Achong



Yvonne Barr



Denis Burkitt

- The Epstein–Barr virus is named after Epstein, a professor emeritus at the University of Bristol, and Barr a PhD graduate from the University of London
- Epstein attended a lecture on Children's Cancer in Tropical Africa by Burkitt, a surgeon practicing in Uganda
- Specimen was sent from Uganda to be cultured and virus particles were identified
- Later on, a technician in their laboratory developed mononucleosis and they were able to compare a stored serum sample, showing that antibodies to the virus developed and the virus was linked to mononucleosis

قصة هالاسم

كان في عالم جراح اسمه burkitt يعطي محاضرة لطلابه بأوغندا انه عندهم بافريقيا في سرطان منتشر بين الاطفال مو عارفين سببه فكان epstein من الطلاب الي بحضوروا المحاضرة بعدين فكروا يعملوا بحث يفهموا شو المسبب اجا epstein حكا عنا هيسنو باثولوجي لاب بنوخذ عينات وينشوف الكانسر وينحاول نشخص لنعرف المسبب اكتشفوا في virus بالانسحة

# Epidemiology

انتشار المرض

كيف ينتقل من شخص لأخر.



سرعة انتقالها بتكثف عاليت

!! most common

← respiratory system الي ينتقل بال

Virus الي ينتقل بال

- EBV is one of the **most common** viral infections to human
- EBV can be cultured from saliva of 10 to 20% of healthy adults and is intermittently recovered from most seropositive individuals
- It is of low contagiousness, and most cases are contracted after repeated contact between susceptible persons and those asymptomatically shedding the virus (by respiratory droplets)
- Secondary attack rates of infectious mononucleosis are low (<10%), because most family or household contacts already have antibody to the agent
- Worldwide 90-95% of adults are seropositive
- Infectious mononucleosis has also been transmitted by blood transfusions

الفيرس مستحيل يكون ك normal flora

rare

يرجع يصيب الشخص اشدي نادر لأنو اول مرة يكون Antibody

Antibody كونت

B-lymphocyte عشان لمسك بال



كونا فيروس [EBV] ← Common ليشها بنسمع فيها !!

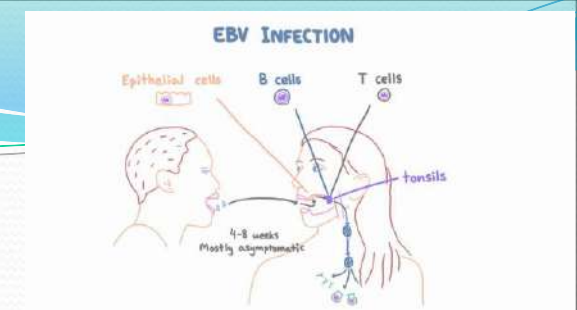
Asymptomatically □ الجسم يكون كونا Antibody

[ يكون الشخص اصاب فيه اعراضه حارة و pharyngitis  
والامعاء شتخموا المرض على انه pharyngitis بدون  
ما يعرفوا انه كان EBV ]



infectious mononucleosis

# Pathogenesis



- EBV initially infects epithelial cells
- The virus enters B lymphocytes by envelope glycoprotein binding to a surface receptor CD21, which is the receptor for the C3b component of complement
 

\* يرتبط الفيروس بال B-lymphocyte عن طريق ال glycoprotein وال receptor تعلق على ال B-lymphocyte هو CD21
- 18 to 24 hours later, EBV nuclear antigens are detectable within the nucleus of infected cells
 

خلال 18 ساعة يكون داخل على ال B-lymphocyte ولبش يخلوا يصنع مكونات.
- EBV has been associated with several lymphoproliferative diseases, including African Burkitt's lymphoma, nasopharyngeal carcinoma, and lymphomas in immunocompromised patients
 

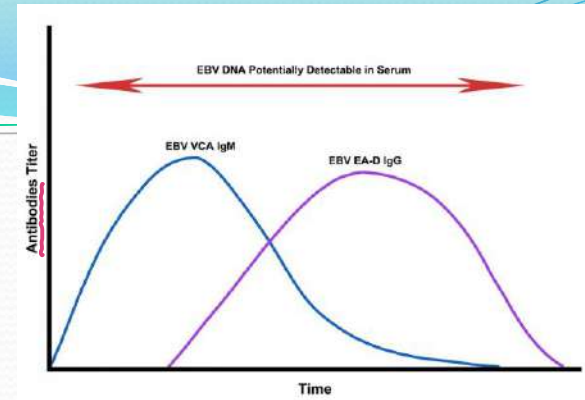
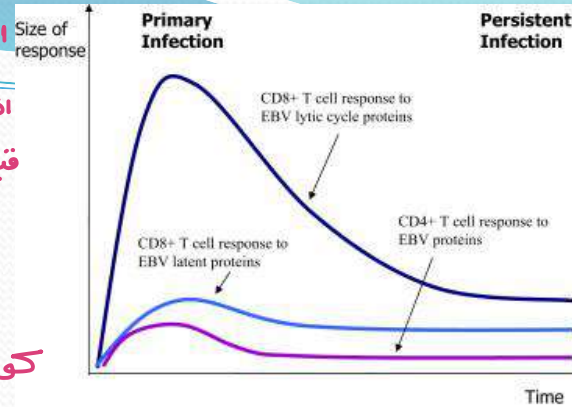
[1]  
[2]  
[3]
- The distribution of EBV infections in Africa has suggested an infectious cofactor, such as malaria, which may cause immunosuppression

الAntibody الي يزيد هو الIgG → Acute infection

اذا بدنا نشوف قديش واحد عنده immunity واحد صالفيروس قبل ١٠ اسنين شو الAntibody الي يشوفوا !! IgG

# Immunity

كونه تكون Antibody فعلا فيه immunity



- Virus-induced infectious mononucleosis is associated with circulating antibodies against specific viral antigens

- The “atypical” lymphocytosis associated with infectious mononucleosis is caused by an increase in the number of circulating T cells, which appear to be activated cells developed in response to the virus-infected B lymphocytes

- With recovery from illness, the atypical lymphocytosis gradually resolves, and cell-mediated immune functions return to preinfection levels, although memory T cells maintain the capacity to limit proliferation of EBV-infected

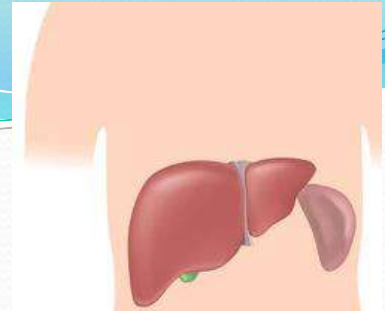
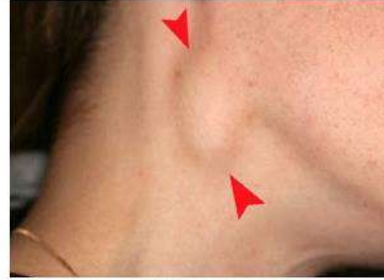
بتساعد انه الجسم يحمي عنده حمايت

B cells الviral infection وفي عندها الphagocyte B-lymphocyte وبتطهرها وبتستخدمها لانتاج المركبات اليه

ما بتقدر تشتغل عليه فلاتزم تروح تحترق ال B عند تعارب الفيروس فيصير Atypical lymphocytosis

المصنع بهمير ينتج اكثر من طاقته ولأنه الinfection جوا B-lymphocyte بيش الشكل يتخير.





زيادة بال lymphocyte

enlargement in lymph node

cervical lymph node

الفيروس يستقر بال- Upper respiratory tract

inflammation بعد

infection بالدم يتفشخ

فقيرة خلايا الدم ، كبيرة lymph node خاصة للدم فاذا فيه

# Clinical Manifestations

## 1. Infectious Mononucleosis (Glandular fever)

- Most primary EBV infections are asymptomatic
- Clinically apparent infectious mononucleosis is characterized by fever, malaise, pharyngitis, tender lymphadenitis, and splenomegaly
- These symptoms persist for days to weeks; they slowly resolve
- **Complications** such as laryngeal obstruction, meningitis, encephalitis, hemolytic anemia, thrombocytopenia, or splenic rupture may occur in 1 to 5% of patients

خامبة cervical lymph node

الفيروس يستقر بال- Upper respiratory tract

inflammation بعد

infection بالدم يتفشخ

فقيرة خلايا الدم ، كبيرة lymph node خاصة للدم فاذا فيه

يضعف الفيروس موجود ويضعف Attached وبعده infection

## 2. Lymphoproliferative Syndrome

- Patients with primary or secondary immunodeficiency are susceptible to EBV-induced lymphoproliferative disease  
يزداد عدد ال B-lymphocyte و بتصير lymph node enlargement
- The risk is greatest in patients experiencing primary EBV infection rather than reactivation  
يزداد عدد ال Atypical
- Most characteristic is persistent fever, lymphadenopathy, and hepatosplenopathy





كيف اميز بين (1 و 3) !! ال Antibody ، ال Symptom قد يمش وقتا بتضل اذا طولت لشهور  
بنصير نفكر بال Burkitt lymphoma

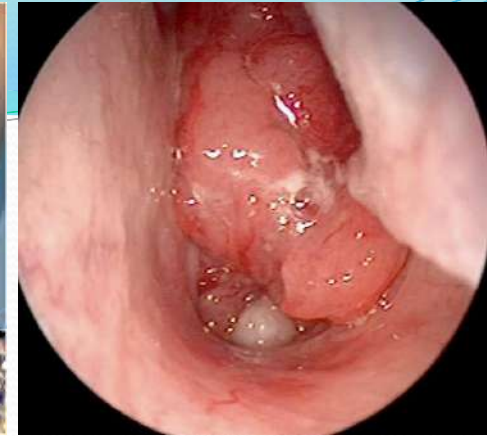
### 3. Burkitt's lymphoma

في مجموعة من الكانسر مختمين بالاطفال

- In sub-Saharan Africa, Burkitt's lymphoma is the most common malignancy in young children malignant tumor of lymph node
- The risk is greatest in equatorial Africa, where there is a high incidence of malaria
- Burkitt's lymphoma is thought to result from an early EBV infection that produces a large pool of infected B lymphocytes
- Malarial infection may further increase the size of this pool and provide a constant antigenic challenge
- Serologic screening for increased IgA antibody levels can be used for early diagnostic purposes سباعد بتشخيص المرض



ليش بختلف التشخيص من كل دولة للثانيات !!  
السبب مش معروف للآن بس ممكن يكون genetic و life style  
بالاردن حكا الاغلب يكون Infectious Mononucleosis



#### 4. Nasopharyngeal Carcinoma

- Nasopharyngeal carcinoma (NPC) is endemic in southern China, where it is responsible for approximately 25% of the mortality from cancer
- The high incidence of NPC among the southern Chinese people suggests that genetic or environmental factors in addition to EBV may also be important in the pathogenesis of the disease

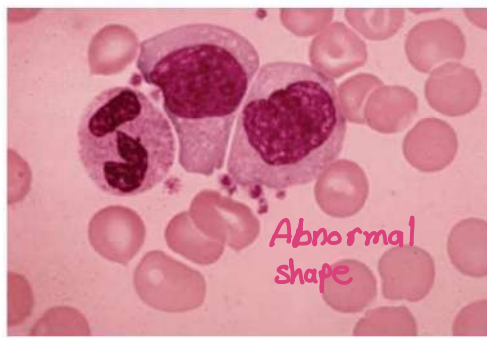
تشو الفحوصات الحي بنطلبها !!

\* نطلب Antibody (IgM و IgA) \*

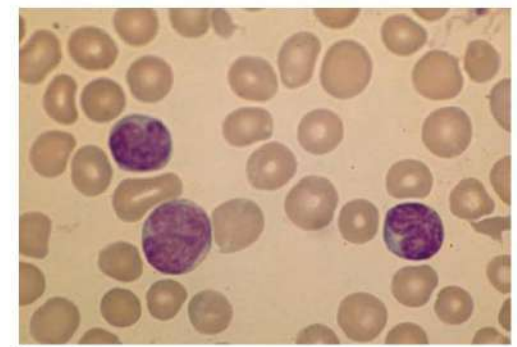
\* CBC ← white blood count (Lymphocytosis) \*

\* blood serum \* PCR \* ultrasound (Spleen) \*

# Diagnosis



A



B

**FIGURE 14-9.** A. Atypical lymphocytes (Downey cells) in blood smear from a patient with infectious mononucleosis. Note indented cell membranes. Polymorphonuclear leukocyte is adjacent to the two affected cells. B. Normal lymphocytes contrast sharply with those in A.

- Positive EBV- specific serologic findings
- PCR studies is confirmatory
- Hematologic examination reveals a markedly raised lymphocyte and monocyte count with more than 10% atypical lymphocytes
- Atypical lymphocytes, although not specific for EBV, are present with the onset of symptoms and disappear with resolution of disease
- Alterations in liver function tests may also occur, and hepatosplenomegally is a frequent finding



# Treatment and Prevention

Paradol

بنقدر نخطي السريجن

Vaccine not approved

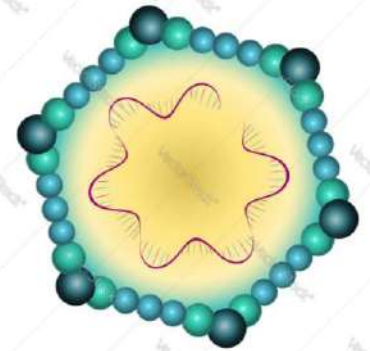
- Treatment of infectious mononucleosis is largely supportive. More than 95% of patients recover uneventfully
- In a small percentage of patients, splenic rupture may occur; restriction of contact sports or heavy lifting during the acute illness is recommended
- Systemic acyclovir makes little or no impact on the clinical illness  
repair ما يسيروا spleen refture ر
- Laryngeal obstruction should be treated with corticosteroids
- Immunization with virus specific antigen have shown to be effective against Burkitt's lymphoma and nasopharyngeal carcinoma in animal model and the vaccine is under development





# Parvovirus B19 Infections

# Virology



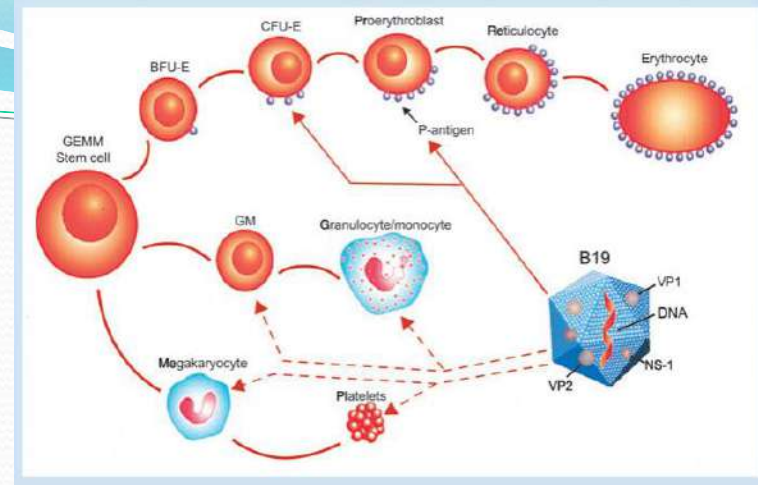
ParvoVirus B19

- Parvoviruses are very small (18 to 26 nm), naked virions that contain a linear single-stranded DNA molecule
- The major cellular receptor for the virus is globoside (also known as blood group P antigen, which is commonly found on erythroid progenitors, erythroblasts, megakaryocytes, and endothelial cells)
- A primary site of replication appears to be the nucleus of an immature cell in the erythrocyte lineage. Such infected cells then cease to proliferate, resulting in an impairment of normal erythrocyte development



# Pathogenesis

المرضى الذين يعانون من أمراض متفشية كثيراً تتسبب في تكسير خلايا RBC  
إذا عانوا من تلاسيميا ويصابوا بهذا الفيروس بصير  
severe symptom



- The clinical consequences of the viral effect on erythrocytes are generally trivial, unless patients are already compromised by a chronic hemolytic process, such as sickle cell disease or thalassemia
- Primary infection in such individuals often produces an acute, severe, sometimes fatal anemia manifested as a rapid fall in RBC counts and hemoglobin
- Patients may present initially with no clinical symptoms other than fever, and is commonly referred to as aplastic crisis



# Epidemiology

- The viral infection is common among children 5-15 years old
- Epidemiologic evidence suggests that spread of the virus is primarily by the respiratory route, and high transmission rates occur in households
- Once skin rash appears the virus is no more contagious لما يصير فيه rash يبطل يتقل من طريق التنفس
- Outbreaks tend to be small and localized, particularly during the spring months, with the highest rates among children and young adults ينتشر بالاماكن المغلقة
- Seroepidemiologic studies have demonstrated evidence of past infection in 30 to 60% of adults EBV common بين اقل من ال

# Clinical Manifestations

خامس مرض بسبب rash ↑

مسببات اخرى

- Erythema infectiosum (also referred to as fifth disease, slapped cheek, apple face, or academy rash) is attributable to parvovirus B19  
كانه وفيروس كفا ←
- After an incubation period of 4 to 12 days, a mild illness appears, characterized by fever, malaise, headache, myalgia, and itching in varying degrees  
منتشش بالمرساة ↓
- A confluent, indurated rash appears on the face, giving a “slapped-cheek” appearance. The rash spreads in a day or two to other areas, particularly exposed surfaces such as the arms and legs, where it is usually macular and reticular
- During the acute phase, generalized lymphadenopathy or splenomegaly may be seen, along with a mild leukopenia and anemia



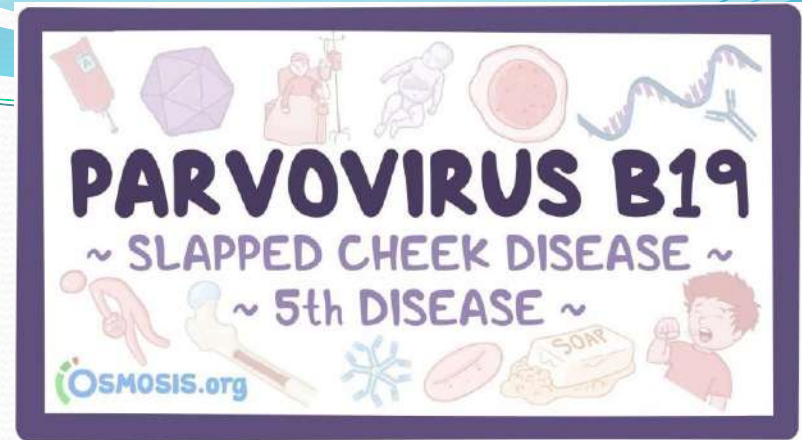
- The illness lasts 1 to 2 weeks, but rash may recur for periods of 2 to 4 weeks thereafter, exacerbated by heat, sunlight, exercise, or emotional stress
- Arthralgia sometimes persists or recurs for weeks to months, particularly in adolescent or adult females
- Serious complications, such as hepatitis, thrombocytopenia, nephritis or encephalitis are rare
- like rubella, active transplacental transmission of parvovirus B19 can occur during primary infections in the first 20 weeks of pregnancy, sometimes resulting in stillbirth of fetuses that are profoundly anemic





اذا كان عندك تلاسيميا لآنو بيحي الفيرس بجلعك باوتے RBC

# Diagnosis



- Viremia usually lasts 7 to 12 days but can persist for months in some individuals
- CBC (low Hb)
- It can be detected by specific DNA probe or polymerase chain reaction (PCR) methods
- Alternatively, the presence of IgM-specific antibody late in the acute phase or during convalescence strongly supports the diagnosis



وإن كان الأمر

معقد

فلطف الله

ممتد

TO ALLAH 1394