This sheet includes only extra notes that are mentioned by the doctor so you need to refer to the slides.

Slide# 8+9

EBV causes a wide variety of disorders and the most important aspect of EBV is its association with many important cancers especially Burkitt lymphoma.

Infection with EBV is associated with exposure to the virus in respiratory secretions. First, the virus infects the oral cavity and then gains access to lymphocytes in the tonsils through crypts, so as a consequence the virus spreads to the bloodstream.

**The Infected B lymphocytes are activated both monoclonally and polyclonally during the acute phase of infection** with the stimulation antiviral mechanism starting with natural killer cells and after a few days replaced by CD8 T-lymphocytes and with help of antibodies produced in activation of CD4 T-lymphocytes. B-cells proliferate and their number is under the control of T-cell (active T-cell response to EBV infected lymphocyte the infection associated with certain complications and the patient recovers from the infection but this recovery is not associated with the elimination of the virus, the virus is established in the infected individuals.

**A persistent infection develops in B lymphocytes with continuous activation of T lymphocytes.**

In the lytic type of infection, large number of the viral genes are activated.

From slide #10 to #16: the doctor read the slides as they are.

Slide #17

The incubation period of IM of primary EBV infection is relatively long, in the average of seven weeks and the virus can be recovered (isolated) few days after infection. So the EBV can be recovered long time before clinical manifestations appear. And the time until these manifestations show up is in weeks. This could be ascribed to the fact
that most clinical symptoms are due to the immune response (that civil war between T lymphocytes and the EBV-infected B lymphocytes).

T cell response is very vigorous that it leads to the reduction of infected B cells from 20% to one per million and that is associated with severe pathology involving multiple organs of the body like lymph nodes, spleen, etc, where the response is mounted and that’s why lymphadenopathy and elevation of antibodies both specific to the virus and non-specific which are polyclonally activated are seen in such cases.

Slide #18

The EBV-Infected cell undergo transformation

- **Years after primary EBV infection, EBV is closely associated with the emergence of other malignancies BL(Burkkit’s lymphoma), HD(Hodgkin Disease) and NPC(Nasopharyngeal Carcinoma).**

Slide #19

The virus has many antigens some structural and some are not which triggers production of antibodies against the virus They are used as markers for the diagnosis of the virus

- **EBV antigens that trigger an immune response include; EBNA, EA- D (diffused early antigen which present in both nucleus and cytoplasm), EA- R (restricted early antigen which is present in the cytoplasm), VCA(viral capsid antigen) , MA (membrane antigen) and LYDMA (lymphocyte defined membrane antigen which is another antigen defined by lymphocytes).**

Slide #20

The first antigen to appear is the EBNA antigen and the first antigen to appear is viral capsid antibody antibodies against EBNA are produced last in the course of infection which reveal recovery (immune marker)

- **Failure to produce antibodies to EBNA indicates a persistent infection in an immunodeficiency state and this may be associated with increased levels of antibodies to EBV lytic cycle**
antigens (EA, VCA) because the fail to resolve reflecting a high virus replication rate.

one marker is the production of **High IgA levels to EBV capsid antigen** are found in those at risk of developing nasopharyngeal carcinoma. So NPC is characterized by high IgA anti-VCA levels.

To summarize the pathogenesis of EBV: infection is acquired via respiratory droplets where a lytic type of a replicative cycle is established in the epithelial cells of the oropharynx to establish pharyngitis. The virus is shed there, and infects the B lymphocytes in the tonsilar crypts and cause tonsillitis. It gets access to the bloodstream, infecting more B lymphocytes and causing their proliferation that stimulates an immune response, in the form of mainly of cytotoxic T lymphocytes. T-cell activation is observed in all organs of the reticuloendothelial system as lymphadenopathy, hepatosplenomegaly. Heterophile antibodies are also observed. Those activated T cells are present in the peripheral blood as atypical lymphocytes (Downey cells). This coincides with the onset of clinical manifestations that starts on about the 30-50th day after infection (avg of 6 weeks). Antibodies generated are both specific and non-specific.

Antigens that act as targets for antibody production are

EBNA antigen: it is first to appear, but antibodies to which are produced late in the course of infection. Anti-EBNA antibodies mark recovery. If they are not produced this indicates continuous/persistent infection.

Early antigens of the restricted type which present in the cytoplasm and antibodies to them seen in lymphoma

Early antigens of the diffuse type and antibodies to them is seen in the infectious mononucleosis

Viral capsid antigen: blood-specific marker of EBV infection. The first marker to appear
LYDMA: an antigen that doesn’t cause production of antibodies. It is recognized by T-lymphocytes.
MA: the major membrane antigen of EBV. Gp350, gp220 are the antigens through which the virus interacts with CD21 (the viral receptor). The behavior of antibodies towards MA is similar to that towards VCA. Heterophile antibodies: produced as a consequence of polyclonal activation of B cells. Their detection marks the start of infection with EBV.

Slide#23
IM Develops in susceptiple adults or adolescents, those who are not infected early in life, infection with EBV takes place very early in life in first 5 or 6 years of life, almost 100% of children in developing countries develop this infection early in life ,less than 1 % or 2 % has remain susceptible, but in the developed countries the rate is less, 60% or 70% more remain susceptible until adolescence or adulthood, if infection develop at this age (adulthood) it almost always symptomatic ,and almost always asymptomatic in childhood ,that's why those individual develop infectious mononucleosis after incubation period of 7 weeks,

Slide #24
This is sore throat due to the virus & enlargement of tonsil cause obstruction of airway, it can be exudative streptococcal sor throat similar in clinical manifestation to that's caused by streptococci, if the diagnosis indicate streptococcal infection antibiotic is usual given , but in those individual receive antibiotics skin rash will develop, that's mean development skin rash as a result of immune response to ampicillin or amoxillin is characteristic feature of infectious mononucleosis, antibiotic should not be given because this not a bacterial infection but it's given bacterial infection skin rash will develop & the way to distinguish between both is throat culture for bacteria

Slide#25
pharyngitis is very prominent & consistent feature

slide# 26
the doctor read the slide as it is

slide# 27
most common manifestation is enlargement of post. Cervical lymph node enlarged epitrochlear node is characteristic feature lymphadenopathy is very consistent similar to pharyngitis
slide#28
Tenderness can be detected by palpation or percussion
Spleen can rupture without trauma
Those can develop with acute abdominal surgical intervention

Slide#29&30
Circulating IgG & IgM Abs against ampicillin is immune complex
disease, it's immune mediated type of skin rash that's developed in
response to infection

This is (in picture) the characteristic rash that develops after treatment
with ampicillin it can be scattered or intense involving the trunk of such
individual

Slide #31
Those symptoms for minority of childrens who develop clinical
manifestation but most childrens are totally asymptomatic

Slide#32
In most cases it's abnormal liver function not frankly hepatitis
Acute upper airway obstruction because of tonsillar enlargement
Hemolytic anemia(immuno-mediated)
Splenic rupture because of trauma
the Most common is neurological complications like: meningitis,
meningoencephalitis, encephalitis & guillain-barre syndrome which is
self-limited ascending paralysis that result in 95% of cases or more

Slide#33
the most infectious mononucleosis cases resolve within period of weeks
leaving the patient exhausted, weak because of the long duration of
illness, however some patients don't fully recover and they enter a
chronic active EBV infection
chronic fatigue syndrome is(*** sorry I couldn’t hear this
word,you can refer to it at the record 26:50) clinical entity
most commonly affect females characterized by chronic fatigue it's
believed to caused by enterovirus ,recently one of the viruses that's
suspected to cause chronic fatigue syndrome is EBV but we know this
association due to chronic active EBV infection that develop in such
individual so it's not the cause but it can represent in clinical picture similar to chronic fatigue syndrome

**slide#34**

EBV-induced lymphoproliferative disease occurs in immunocompromised patients who lack T cell immunity (fails to resolve EBV infection) which can be fatal in such individuals

any T cell deficiency can lead to the lymphoproliferative disease but X-linked lymphoproliferative (Duncan syndrome) is more distinct & specific.

SAP: group of proteins involved in innate immunity

Duncan syndrome cause liver disease result in death of 75% in acute phase & 80% of survivals will develop immunodeficiency

PTLD with fatal outcome

**Slide# 35**

Oral hairy leukoplakia is one of the AIDS identifying illness

**Slide# 36**

This is the characteristic that's seen in AIDS patients

**slide#37**

epidemiologically IM isn't common but EBV infection is common (every individual is affected with EBV)

**Slide#39**

Viral shedding isn't correlated with antibody titer of those individuals

**Slide#40**

the Source of infection is the oral secretion

Other mode transmission :blood products,transplanted organs, CMV (more common),

Intrauterine infections

**Slide#41**

diagnosis can be made by lymphadenopathy because individuals develop Characteristic fever with tonsillitis or pharyngitis
lymphocytosis:>50% of white blood cells is lymphocytes Abs distinguish between CMV mononucleosis & EBV mononucleosis, in EBV is positive & in CMV there are not present otherwise they are prodused similar clinical & laboratory findings 
sens:sensitivity.spec:specificity,FP:false positive test can be seen in lymphoma ,CTD ,viral hepatits & malaria such conditions are associated with heterophile Abs production
Monospot is the test that detect the heterophile Abs & the diagnosis confirmed by antiviral Abs

LFT ;liver function test

Slide#42
Those are the atypical lymphocytes seen in different blood in a patient with EBV or CMV mononucleosis but the difference is the lack of heterophile Abs

Slide#43
Infections can be classified as acute or chronic or past by the markers that we have mentioned
Susceptible invidual lack all markers but acute primary characterized by heterophile Abs which appear only in acute primary, in chronic primary there is no EBNA Abs because of failure to eliminate the virus & so on……

( the doctor read almost all the table)

Slide# 44
The rest because of mononucleosis is exhausting type of illness

Sorry for any mistakes

اليوم هو الغد الذي كنت قلقا عليه بالأمس

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