İmmünsüpresyon ve Latent Viral Enfeksiyonlar

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ÇÜTF KLİNİK MİKROBİYOLOJİ VE

ENFEKSİYON HST AD

İmmünsüpresyonu olan hastada viral enfeksiyon

- Diğer enfeksiyonlara göre daha çok bilinmezi olan enfeksiyonlar

- Bazı viral enfeksiyonlarda tanı kolay olmak ile beraber bazılarında nerede ise ölüm öncesi imkansız
  - yeterli laboratuvar yöntemlerin geliştirilmemesi,
  - laboratuvar olanaklarının yeterli olmaması,
  - bakteri ve mantar enfeksiyonları ile maskelenmeleri

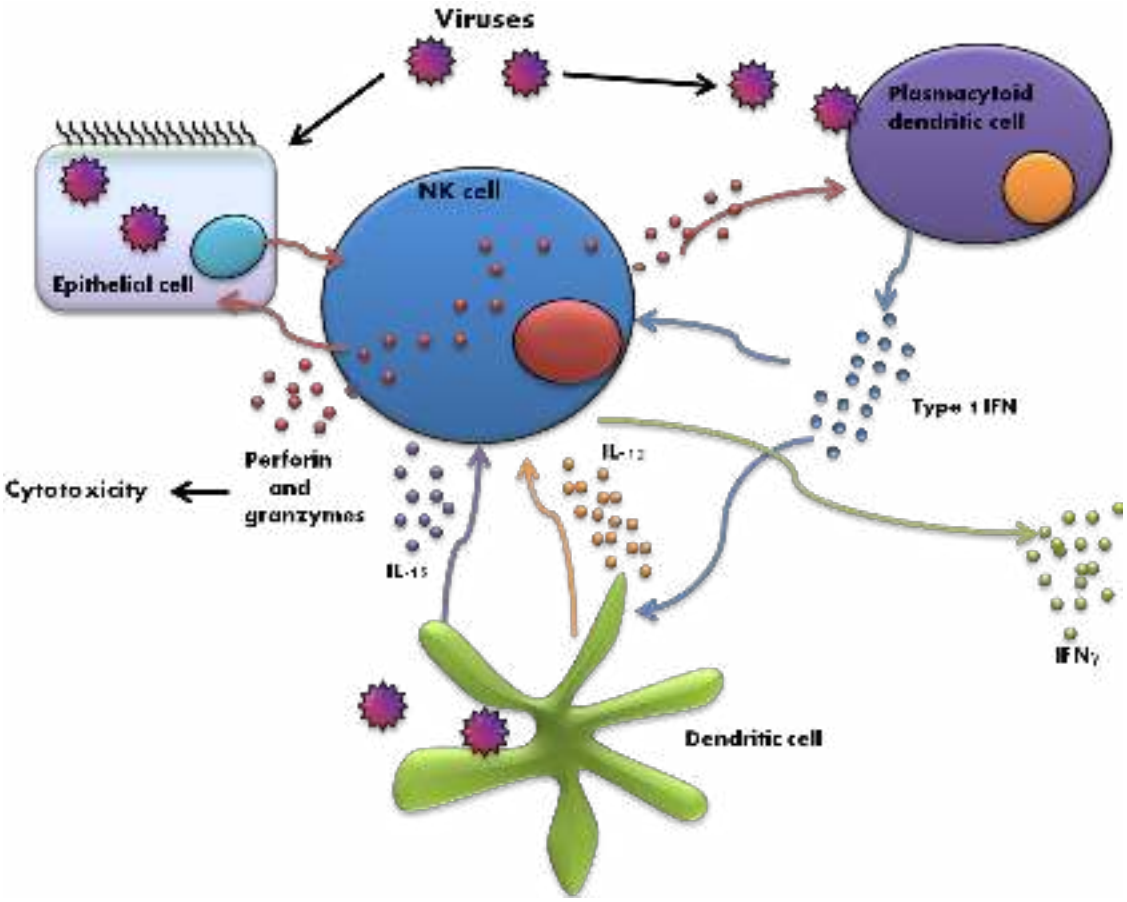
“ASIL TEHLİKE;

BİLİNMEYEN Mİ,

BİLİNİP GÖRÜLMEYEN Mİ,

GÖRÜLÜP TEDAVİ EDİLMEYEN Mİ?”

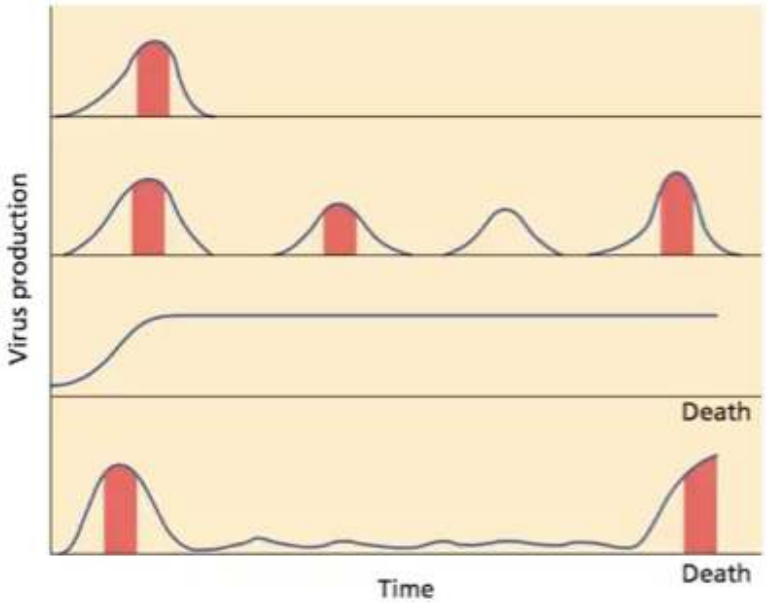
Virüs enfeksiyonlarında patogenez



Viral enfeksiyonların seyiri

- Konağın yaşı
- İmmün sistem
- Altta yatan hastalıklar
- Beslenme
- İlaç kullanımı..
- Virüse ait faktörler..

General patterns of infection



Acute
- Rhinovirus
- Rotavirus
- Influenza virus

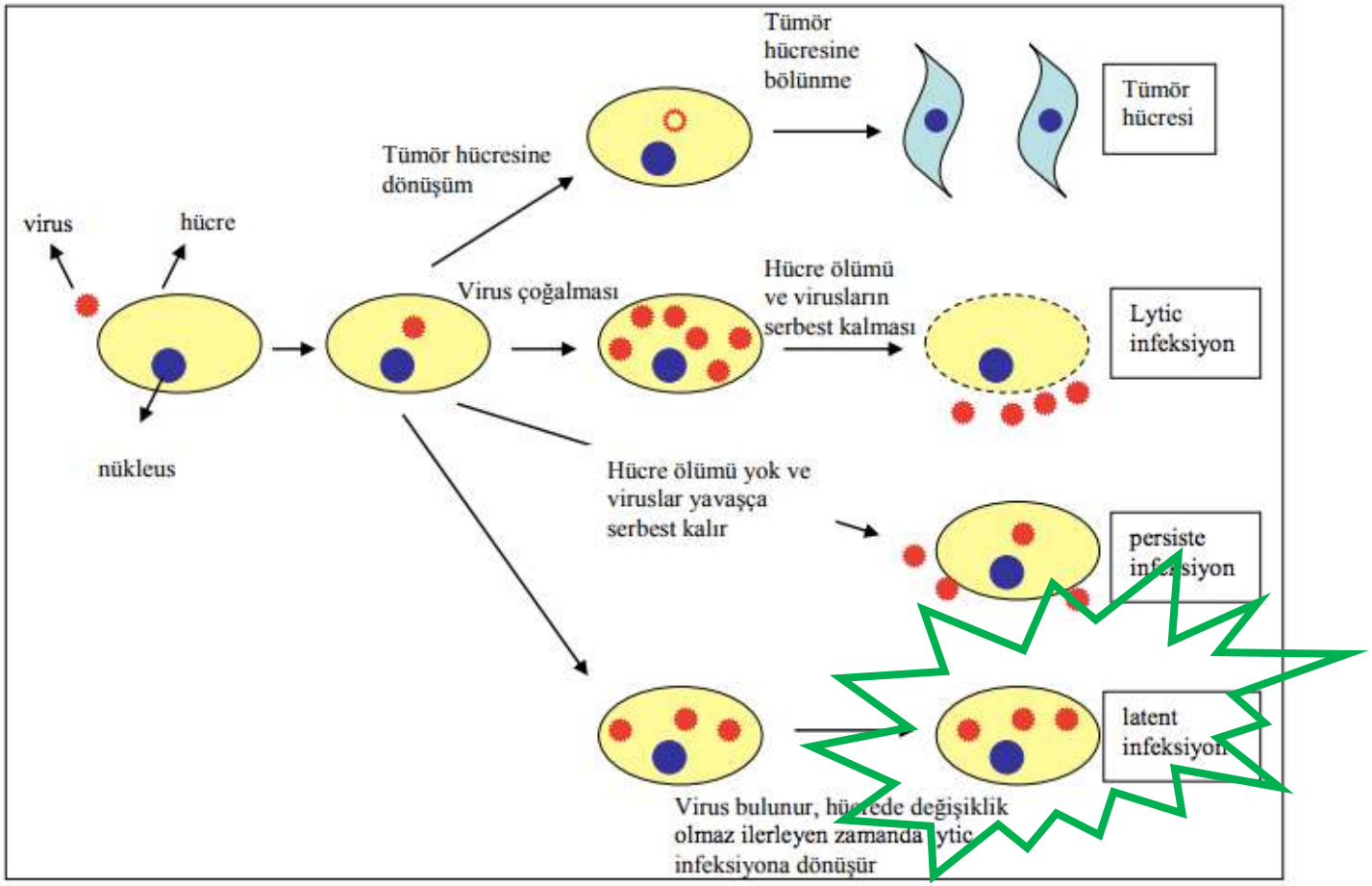
Latent
- Herpes simplex virus

Persistent: asymptomatic
- Lymphocytic choriomeningitis virus
- JC virus

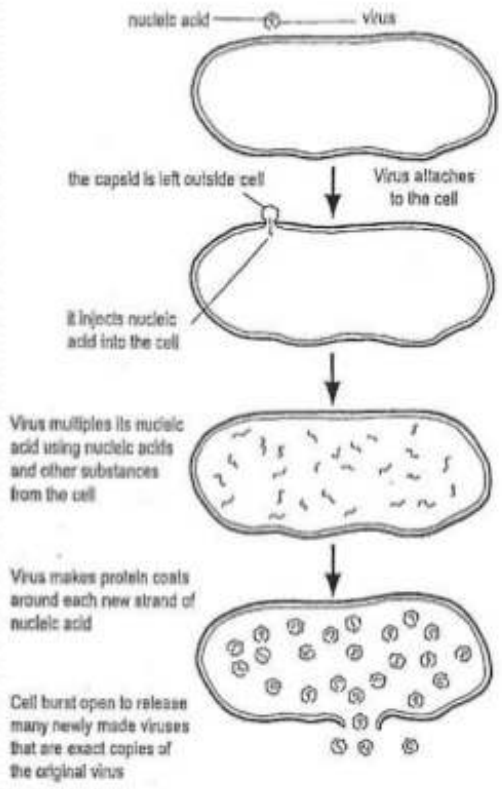
Persistent: pathogenic
- Human immunodeficiency virus
- Human T-lymphotropic virus
- Measles virus SSPE

Principles of Virology, ASM Press

Şekil 1: Virus hücreye girdikten sonra hücredeki değişimler.



Viruses: Life Cycle



1) Adsorption

Virus approaches a cell.

2) Penetration

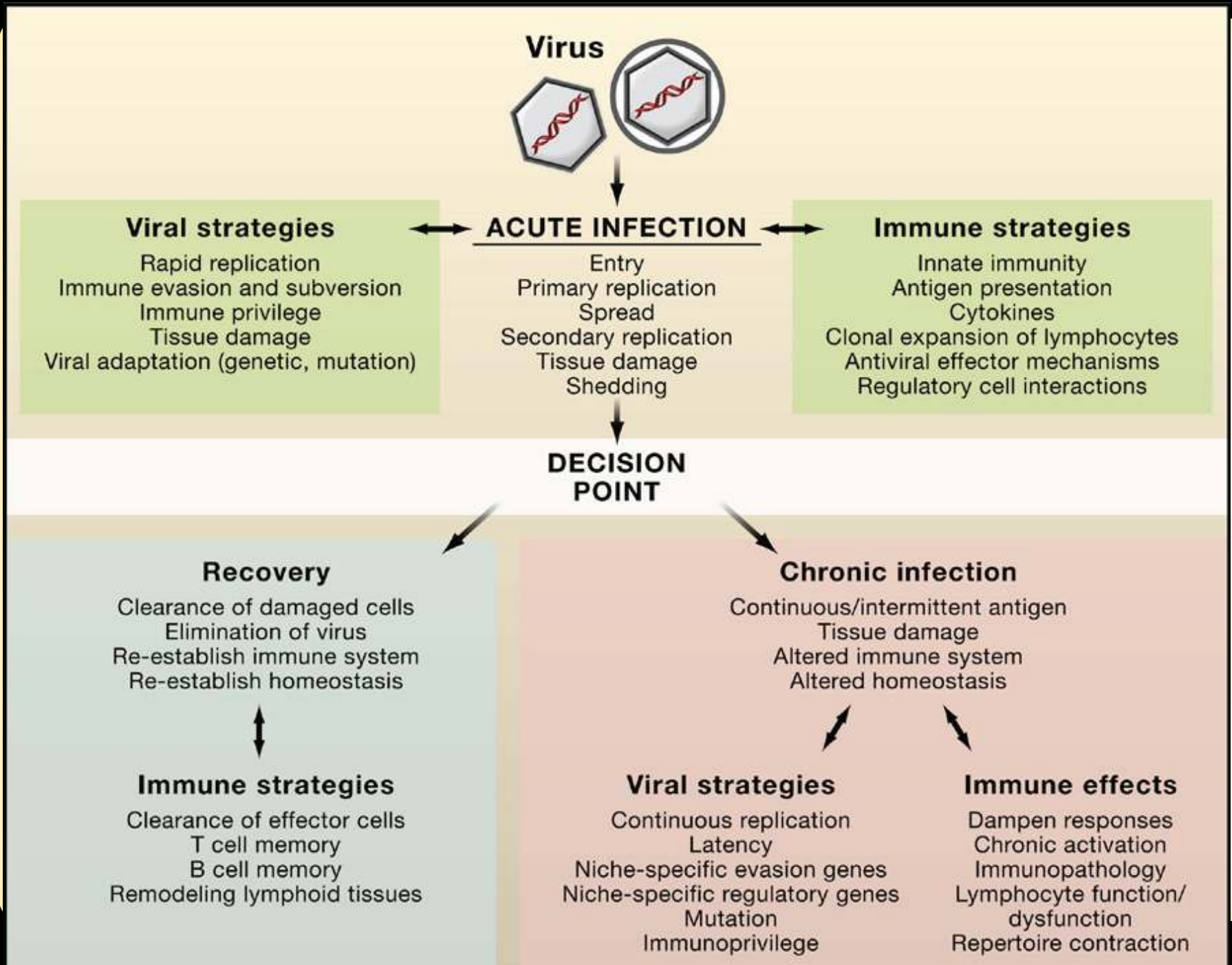
Virus attaches to the cell, injecting nucleic acid into the cell. Capsid left outside cell.

3) Latent phase

Virus multiplies its nucleic acid using materials from the host cell.

4) Lysis

Protein coats form around strands of nucleic acid. The cell releases viruses.


Virus
Viral strategies
Rapid replication
Immune evasion and subversion
Immune privilege
Tissue damage
Viral adaptation (genetic, mutation)
ACUTE INFECTION
Entry
Primary replication
Spread
Secondary replication
Tissue damage
Shedding
Immune strategies
Innate immunity
Antigen presentation
Cytokines
Clonal expansion of lymphocytes
Antiviral effector mechanisms
Regulatory cell interactions
DECISION POINT
Recovery
Clearance of damaged cells
Elimination of virus
Re-establish immune system
Re-establish homeostasis
Immune strategies
Clearance of effector cells
T cell memory
B cell memory
Remodeling lymphoid tissues
Chronic infection
Continuous/intermittent antigen
Tissue damage
Altered immune system
Altered homeostasis
Viral strategies
Continuous replication
Latency
Niche-specific evasion genes
Niche-specific regulatory genes
Mutation
Immunoprivilege
Immune effects
Dampen responses
Chronic activation
Immunopathology
Lymphocyte function/ dysfunction
Repertoire contraction

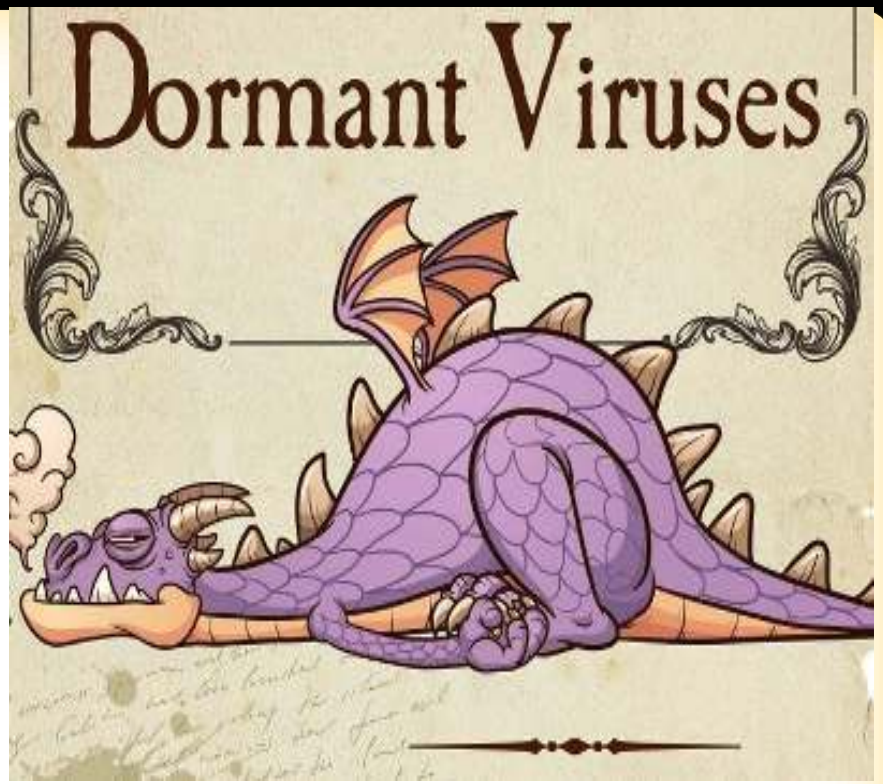
Viral Strateji Ve Konakçı Savunma Mekanizmaları

- Hücrelere zarar vermeden kaçış
- Hücreden hücreye saçılım
- Latent infeksiyonlar
- Viral gen ekspresyonunun sınırlandırılması ile infeksiyondan kaçış
- İmmun sistem hücrelerinin ve makrofajların yıkılması
- MHC antigen reseptörlerinin azalması ile kaçış

Viral Strateji Ve Konakçı Savunma Mekanizmaları

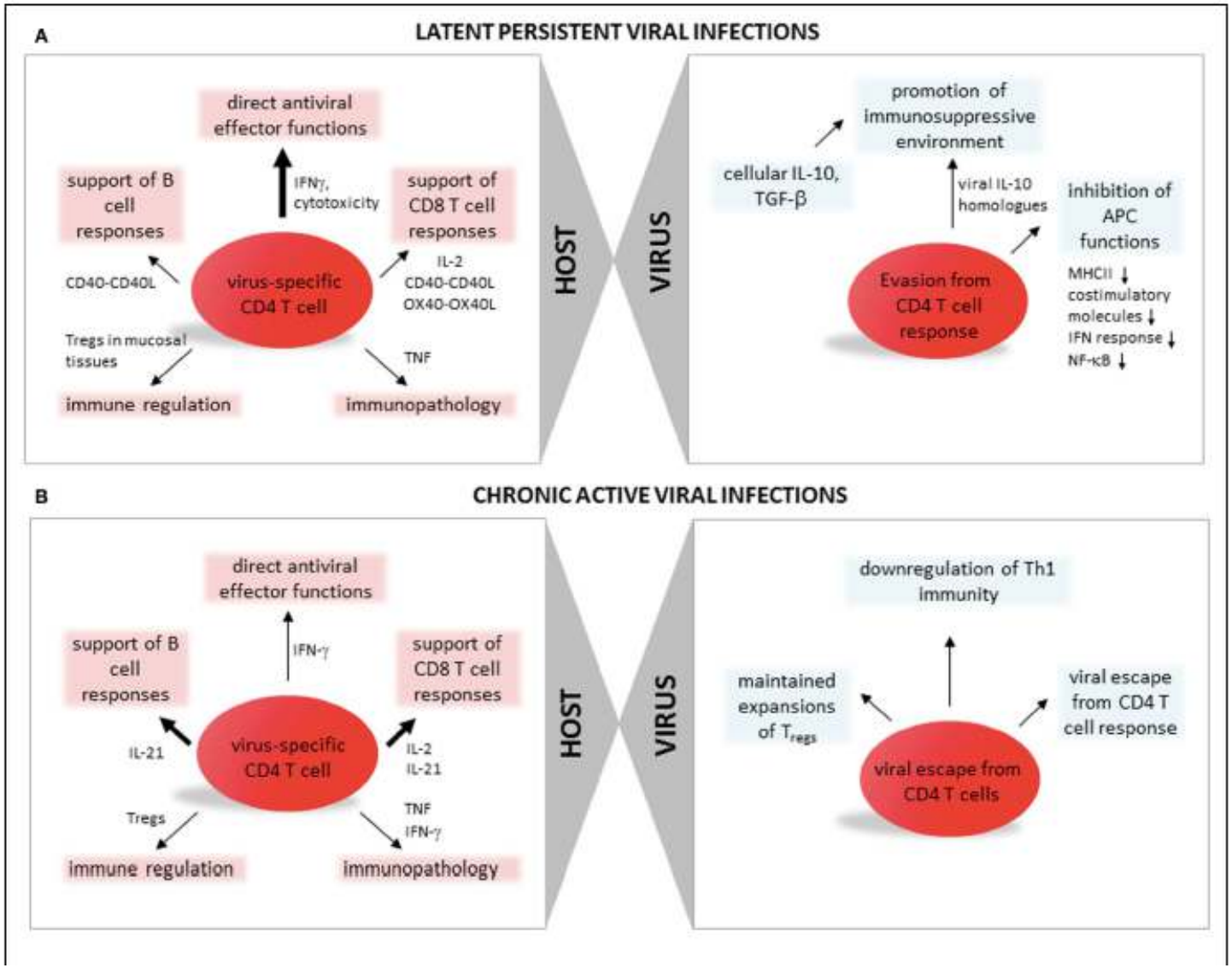
- Sitokinlerden kaçış
- Nötralize antikorlardan kaçış
- Nötralizan olmayan antikorlar ile kaçış
- İmmunolojik tolerans oluşumu ile kaçış
- İmmunolojik olarak ayrıcalıklı dokular ile kaçış
- Viral genomun konak genomuna entegre olması ile kaçış

Latentlik

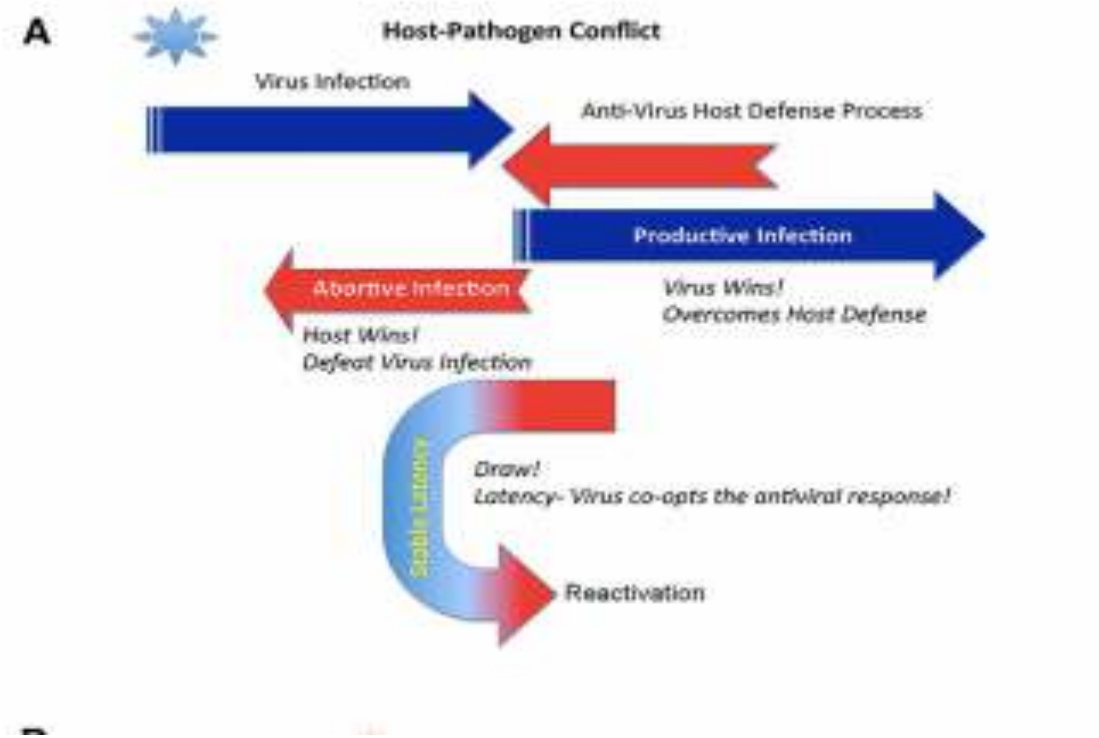


- "Long-term parking"
- "Dormant"
- Uzun süre inaktif
- Çeşitli uyaranlarla aktivasyon

www.jimmunol.org/cgi/doi/10.4049/jimmunol.1102719


A
LATENT PERSISTENT VIRAL INFECTIONS
direct antiviral effector functions
IFNγ, cytotoxicity
support of B cell responses
support of CD8 T cell responses
CD40-CD40L
virus-specific CD4 T cell
IL-2
CD40-CD40L
OX40-OX40L
Tregs in mucosal tissues
TNF
immune regulation
immunopathology
HOST
VIRUS
promotion of immunosuppressive environment
cellular IL-10, TGF-β
viral IL-10 homologues
inhibition of APC functions
Evasion from CD4 T cell response
MHCII ↓
costimulatory molecules ↓
IFN response ↓
NF-κB ↓
B
CHRONIC ACTIVE VIRAL INFECTIONS
direct antiviral effector functions
IFN-γ
support of B cell responses
support of CD8 T cell responses
IL-21
virus-specific CD4 T cell
IL-2
IL-21
Tregs
TNF
IFN-γ
immune regulation
immunopathology
HOST
VIRUS
downregulation of Th1 immunity
maintained expansions of T_{regs}
viral escape from CD4 T cell response
viral escape from CD4 T cells

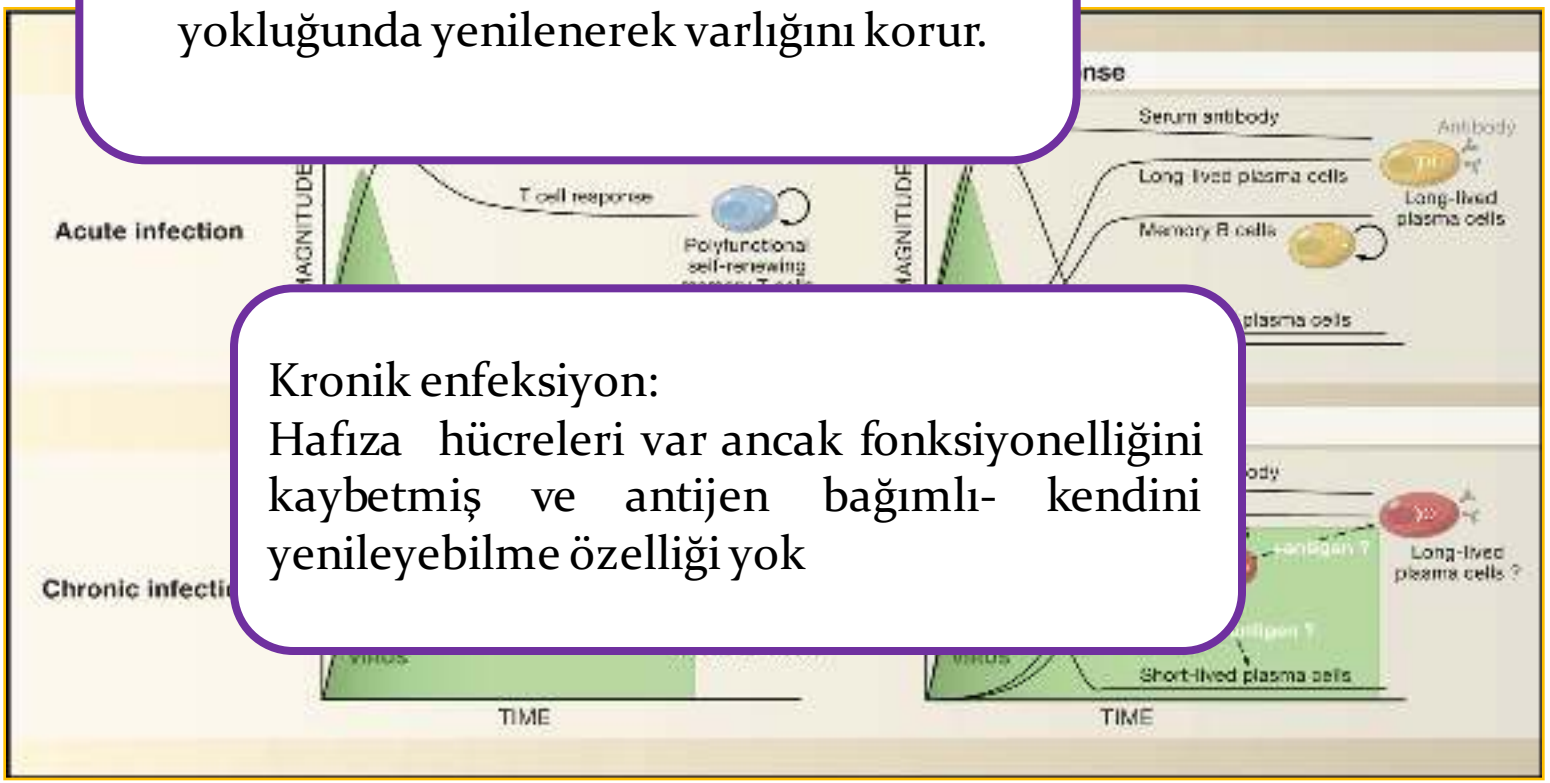
Virüs konak ilişkisi



Aku…la immün yanıt

Akut enfeksiyon:

- T hücreleri aktif rol oynar.
- Enfeksiyonun klirensinden sonra polifonksiyonel hafıza hücreleri antijen yokluğunda yenilenerek varlığını korur.



Kronik enfeksiyon:
Hafıza hücreleri var ancak fonksiyonelliğini kaybetmiş ve antijen bağımlı- kendini yenileyebilme özelliği yok

Kronik viral enfeksiyonlar nasıl sonuçlanır?

- Sürekli çoğalma
  - HBV, HCV, HIV
- Latent kalma- Reaktivasyon
- Genoma invazyon

- Genelde tek, nadiren birden çok mekanizma
  - HIV: sürekli çoğalma+latentlik

Latent kalabilen virüsler

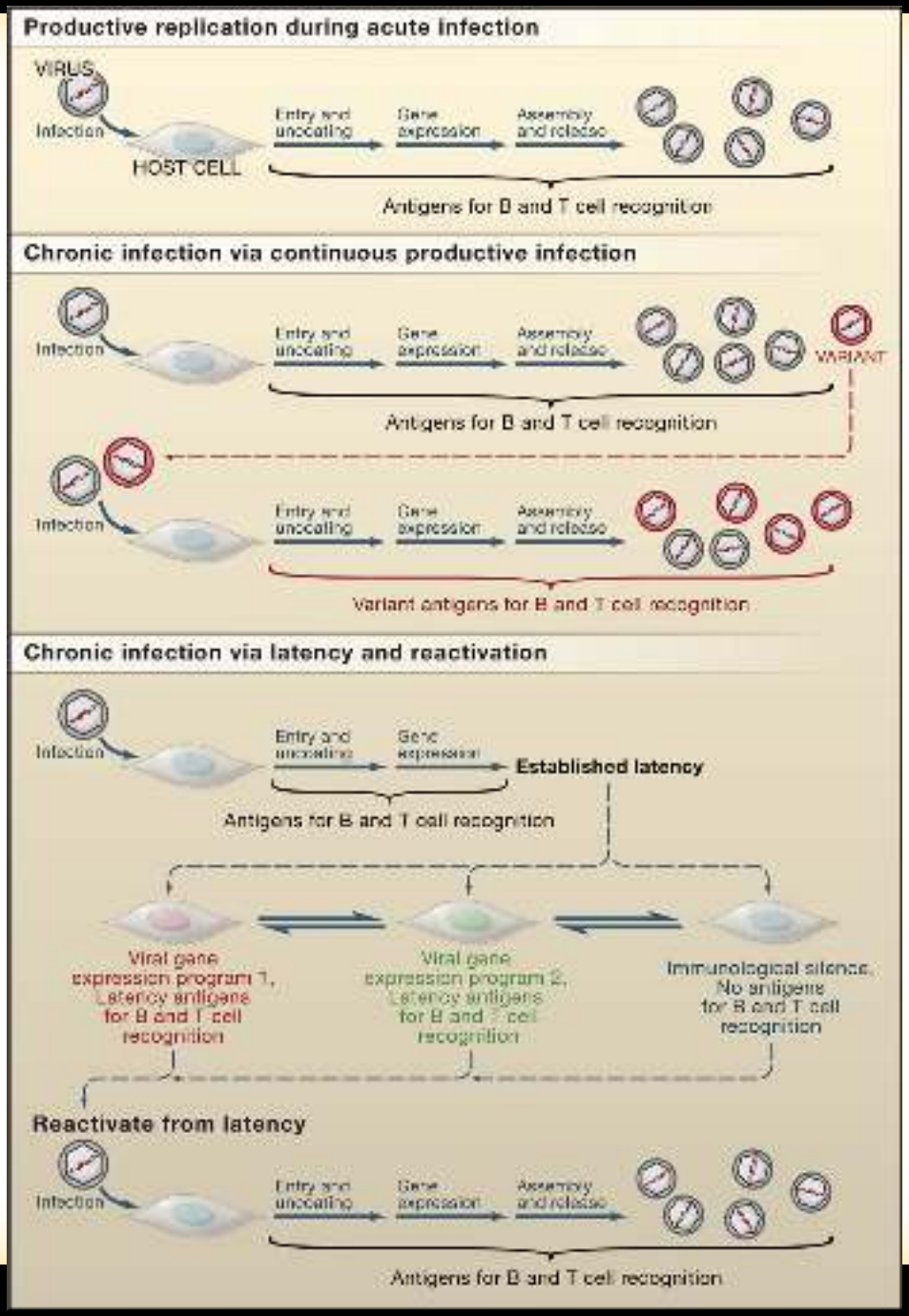
- *Herpesviridae*
- *Polyomaviridae*,
- *Parvoviridae*
- *Adenoviridae*

Table 1. Continued

Virus, Primary Nucleic Acid, Estimated Percent of Humans Infected	Major Site of Persistence (Organ or Cell)	Acute Infection Examples	Disease during Chronic Infection: Within Normal Hosts	Disease during Chronic Infection: Within Immunocompromised Hosts	References
Hepatitis C virus (HCV), RNA, 170 million, ~2.5%	Hepatocytes	Hepatitis	Cirrhosis, hepatocellular carcinoma	Same diseases	Rehermann and Nascimbeni, 2005; Lemon et al., 2007
Human immu… ciency virus (… HIV-2), RNA, … ~0.5%				AIDS	UNAIDS, 2008; Kuritzkes and Walter, 2007
Hepatitis D vi… RNA, 15 milli…			…on of …V infection	Unknown	Taylor et al., 2007
Human T cell … virus type 1 (… RNA, 10–20 … ~0.2%			…leukemia …carriers), …astic para- …elopathy, …matitis	Unknown	Matsuoka and Jeang, 2007; Lairmore and Franchini, 2007
Xenotropic m… kemia virus-re… (XMLV), RNA,			…ancer?	Unknown	Urisman et al., 2006; Dong et al., 2007
HTLV II, III, IV, unknown				Unknown	Matsuoka and Jeang, 2007; Lairmore and Franchini, 2007
Polyomavirus unknown			…carci-	Unknown	Zur, 2008
Polyomavirus unknown				Unknown	Zur, 2008
Polyomavirus unknown				Unknown	Zur, 2008
Rubella virus, measles, RNA			…rubella …alitis	Unknown	Hobman and Chantler, 2007
Parvovirus B1… rare			…sis in …nemia, …alis, …ne marrow	Red cell aplasia	Berns and Parrish, 2008; Norja et al., 2008
Measles virus… rare			…cleros- …ephalitis, …clusion …phalitis	Unknown	Griffin, 2007
Coxsackie, R…			…	Unknown	Chapman and Kim, 2008; Whitton and Feuer, 2004

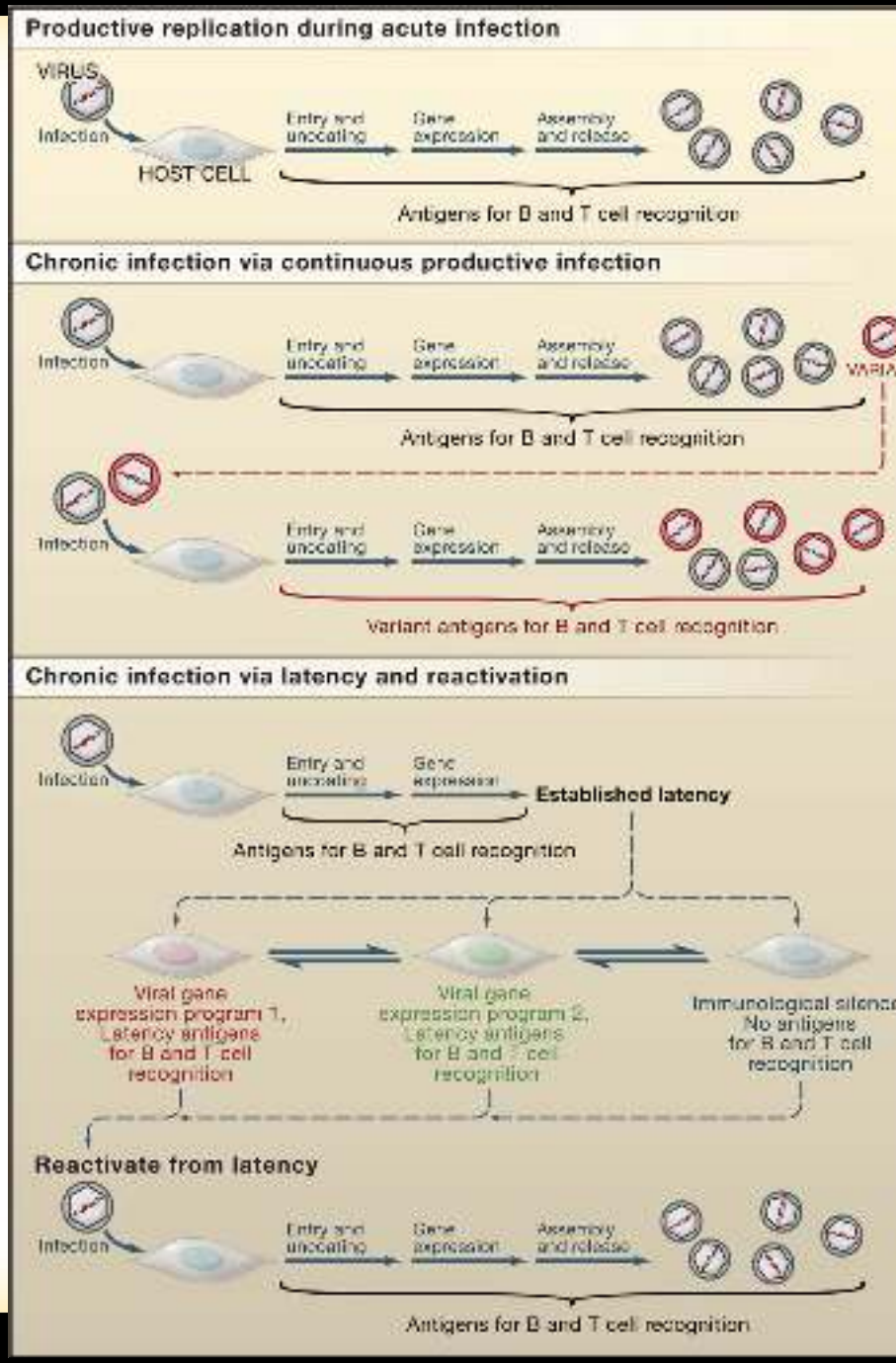
Shown in the … infection in hu… are not clearly … pletely define… …ans, their primary nucleic acid type, and an estimate of the prevalence of …ction and the diseases associated with infection. When incidence numbers …substituted. For many viruses, the specific sites of persistence are incom- …xhaustive list. CNS, central nervous system.

- HHV-6
- HHV-7
- VZV
- EBV
- BKV
- JCV
- HSV 1-2
- Adenovirüs
- HHV-8
- HPV
- HBV
- HCV
- HIV
- HDV
- HTLV
- Parvovirüs B19

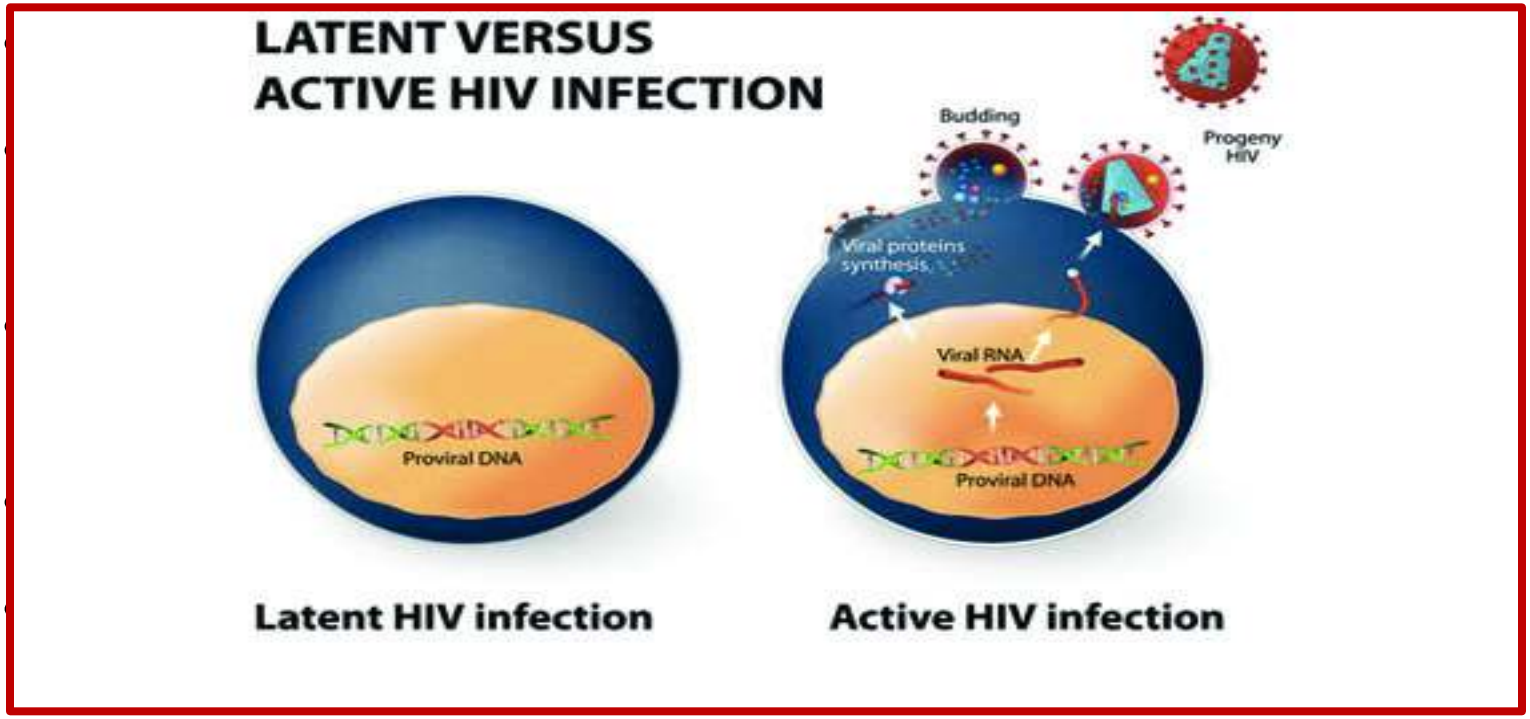

Productive replication during acute infection
VIRUS
Infection
HOST CELL
Entry and uncoating
Gene expression
Assembly and release
Antigens for B and T cell recognition
Chronic infection via continuous productive infection
Infection
Entry and uncoating
Gene expression
Assembly and release
VARIANT
Antigens for B and T cell recognition
Infection
Entry and uncoating
Gene expression
Assembly and release
Variant antigens for B and T cell recognition
Chronic infection via latency and reactivation
Infection
Entry and uncoating
Gene expression
Established latency
Antigens for B and T cell recognition
Viral gene expression program 1, Latency antigens for B and T cell recognition
Viral gene expression program 2, Latency antigens for B and T cell recognition
Immunological silence, No antigens for B and T cell recognition
Reactivate from latency
Infection
Entry and uncoating
Gene expression
Assembly and release
Antigens for B and T cell recognition

Kronik produktif enfeksiyon:

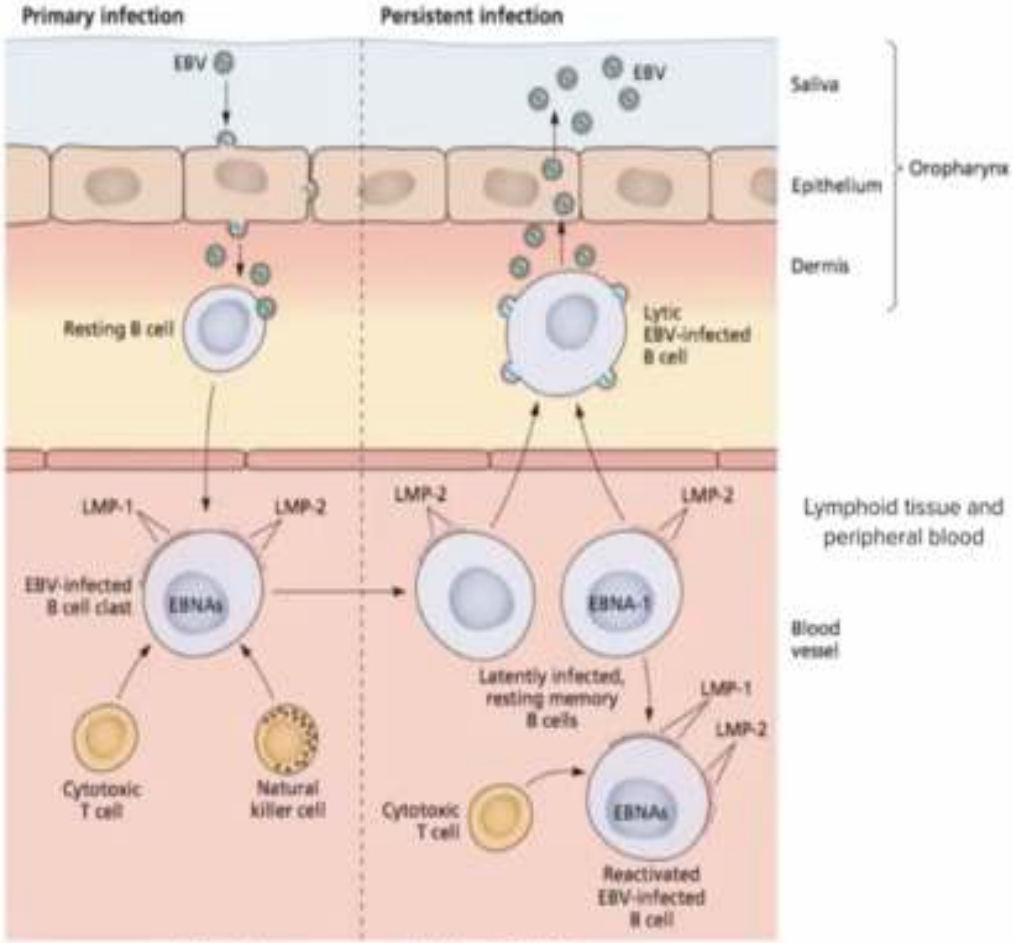
- Replikasyon
- İmmün sistem üzerinde süreğen etki
- Düşük düzey doku hasarı
- İnflamatuvar sitokin salınımı
- Sessiz inflamasyon sinyalleri
- Replikasyon=genom değişimi için yatkınlık!



Hücresel latentlik



EBV primary and latent infection

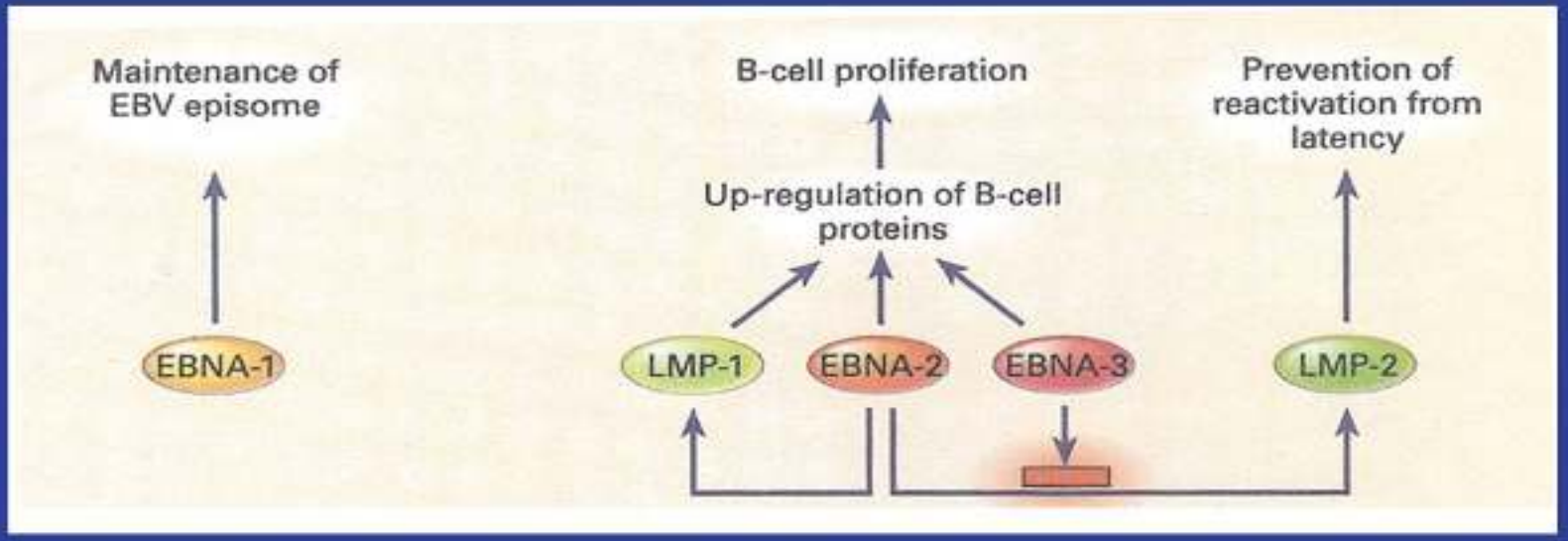


Infectious mononucleosis

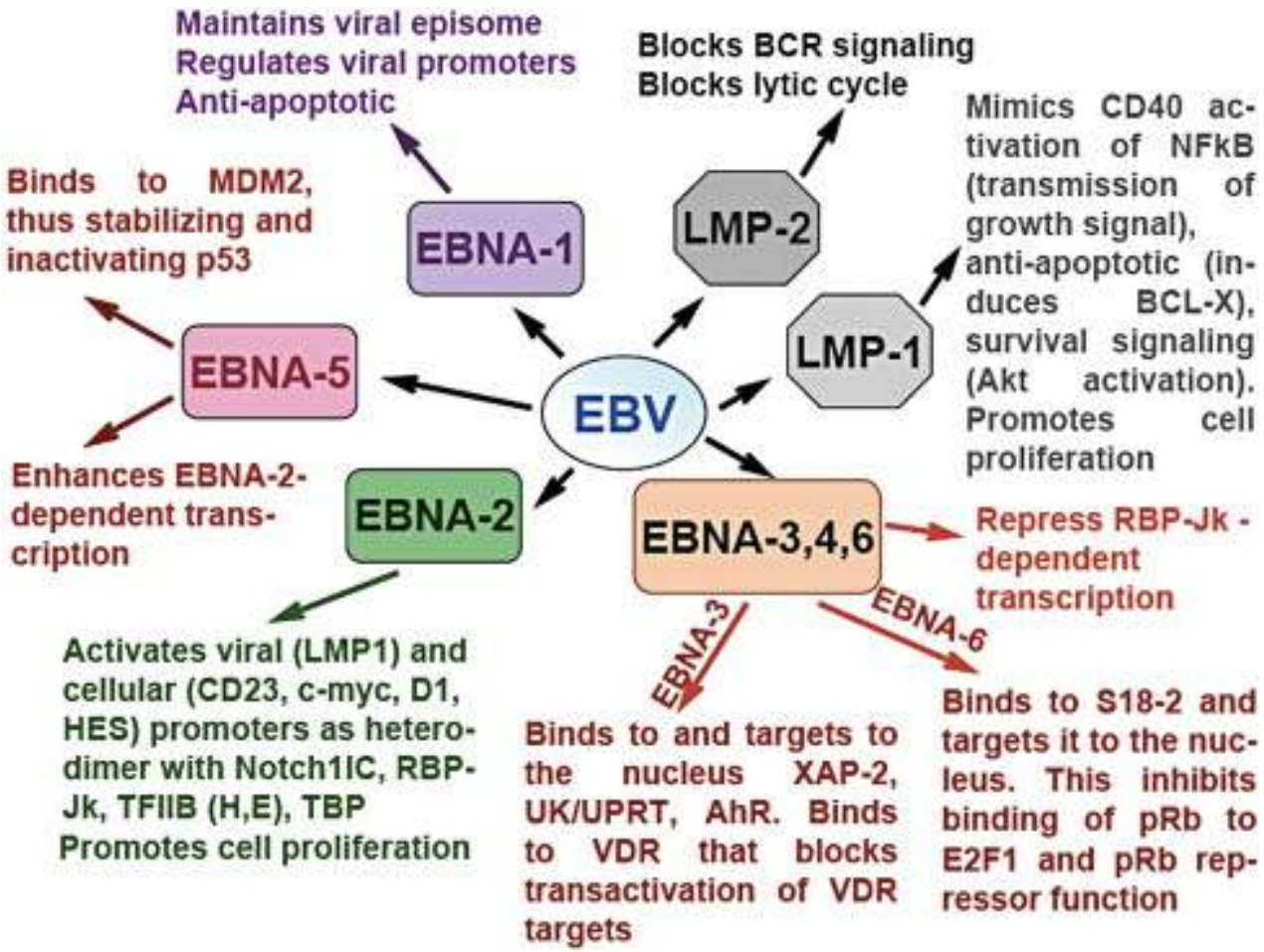
B cells are essential for EBV latency

Principles of Virology, ASM Press

EBV Latency Proteins

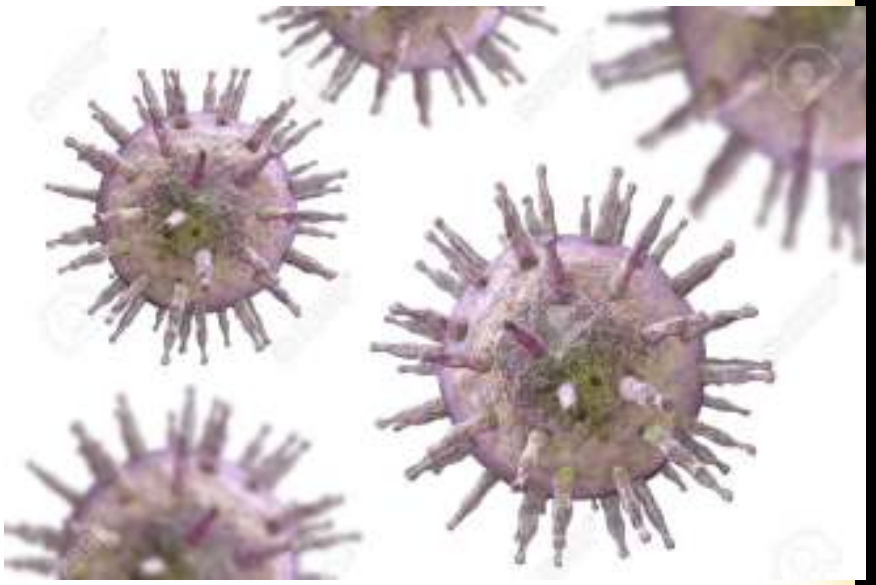


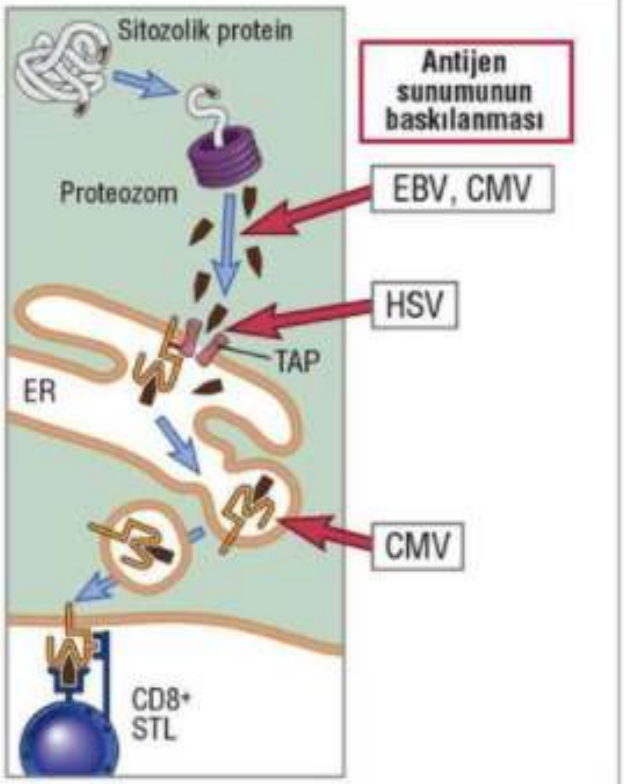
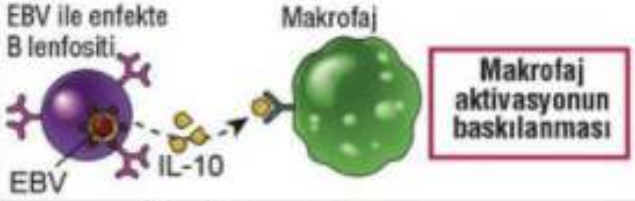
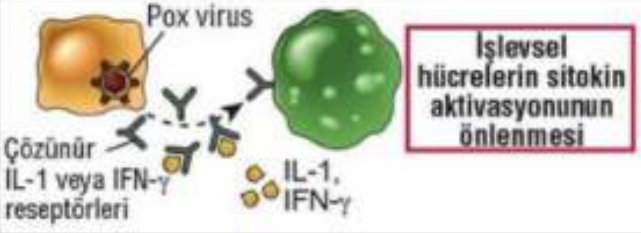
Cohen NEJM 2000

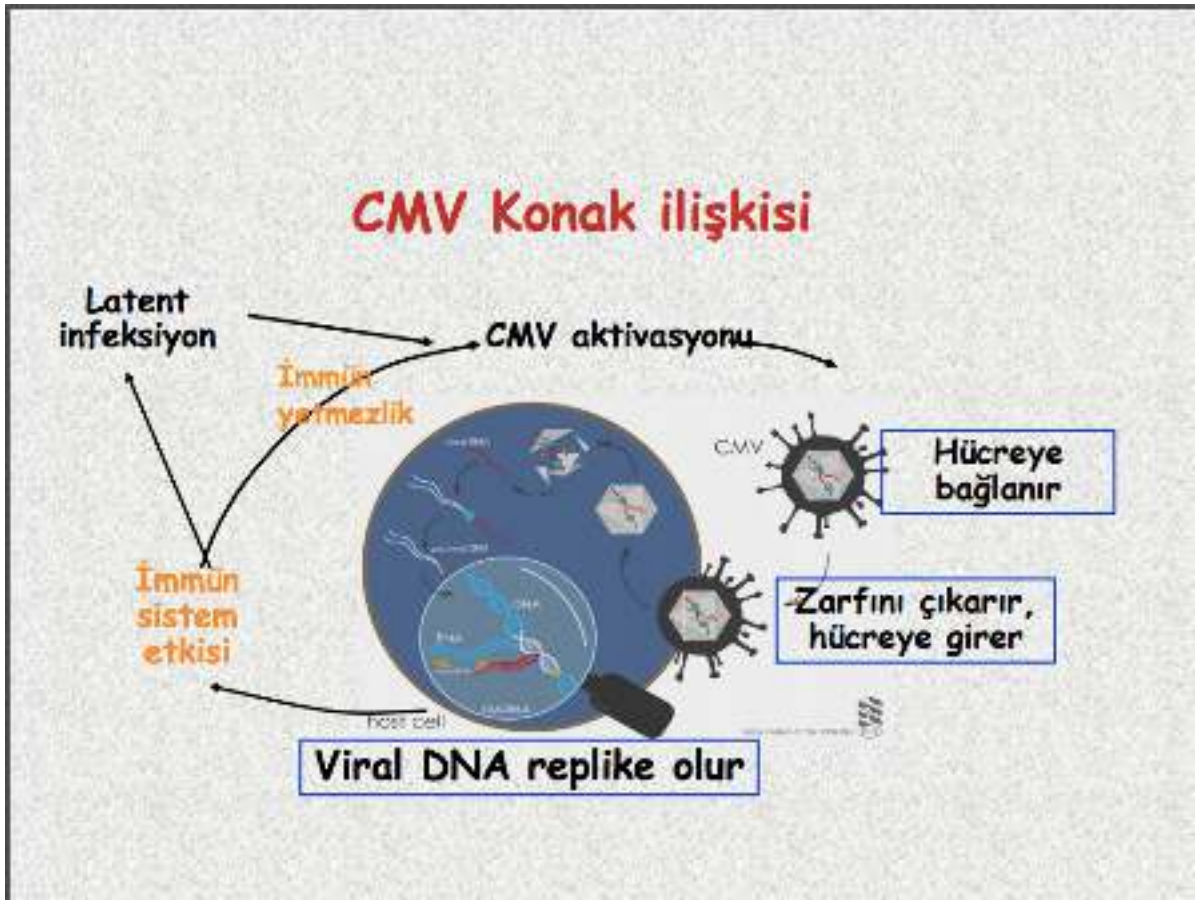

Maintains viral episome
Regulates viral promoters
Anti-apoptotic
Blocks BCR signaling
Blocks lytic cycle
Mimics CD40 activation of NFkB (transmission of growth signal), anti-apoptotic (induces BCL-X), survival signaling (Akt activation). Promotes cell proliferation
Binds to MDM2, thus stabilizing and inactivating p53
EBNA-1
LMP-2
LMP-1
EBNA-5
EBV
Enhances EBNA-2-dependent transcription
EBNA-2
EBNA-3,4,6
Repress RBP-Jk - dependent transcription
EBNA-3
EBNA-6
Activates viral (LMP1) and cellular (CD23, c-myc, D1, HES) promoters as heterodimer with Notch1IC, RBP-Jk, TFIIB (H,E), TBP
Promotes cell proliferation
Binds to and targets to the nucleus XAP-2, UK/UPRT, AhR. Binds to VDR that blocks transactivation of VDR targets
Binds to S18-2 and targets it to the nucleus. This inhibits binding of pRb to E2F1 and pRb repressor function

EBV ilişkili hastalıklar

- İnfeksiyöz mononükleoz
- Burkitt lenfoma
- Nazofarenks ca
- İmmün yetmezliklerde maligniteler
  - HL
  - HIV-Pr SSS lenfoması
  - Lenfoproliferatif hastalık
  - Leiomiyosarkom
  - Diğer B hücre lenfomaları
  - Saçlı oral lökoplaki

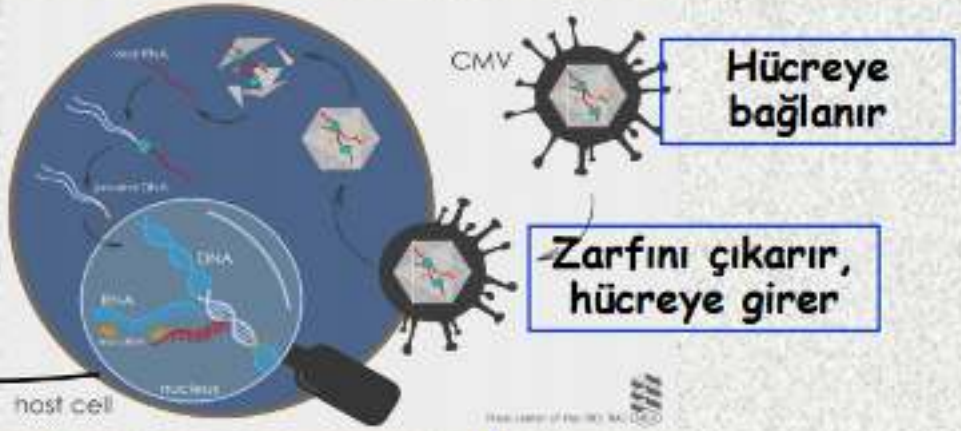


Herpes Simplex Virus (HSV)	Antijen sunumunun baskılanması: HSV peptidi TAP taşıyıcısını engeller	
Sitomegalovirus (CMV)	Antijen sunumunun baskılanması: proteozomal aktivitenin baskılanması; endoplazmik retikulumdan (ER) sınıf I MHC moleküllerinin uzaklaştırılması	
Epstein-Barr virüsü (EBV)	Antijen sunumunun baskılanması: proteozomal aktivitenin baskılanması	
Epstein-Barr virüsü (EBV)	IL-10 üretimi, makrofaj ve dentritik hücre etkinleşmesi baskılanması	
Çiçek virüsü	İşlevsel hücre etkinleşmesi baskılanması; çözünür sitokin reseptörlerinin üretimi	


CMV Konak ilişkisi
Latent infeksiyon
CMV aktivasyonu
İmmün yetmezlik
İmmün sistem etkisi
CMV
Hücreye bağlanır
Zarfını çıkarır, hücreye girer
Viral DNA replike olur

CMV Konak ilişkisi

Latent infeksiyon



İmmün sistem etkisi

Viral DNA replike olur

CMV Konak ilişkisi

LATENT ENFEKSİYON

Konak hücre

-Mononükleer hücreler
-PMNL
-Vasküler endotel
-Fibroblast
-nöronal hücreler
-Renal epitel hücreler, vb.

CMV Konak ilişkisi

LATENT ENFEKSİYON → İMMÜN ETKİ

Konak hücre

-Mononükleer hücreler
-PMNL
-Vasküler endotel
-Fibroblast
-nöronal hücreler
-Renal epitel hücreler, vb.

T hücre ilişkili

- T hücre cevabı uzun süreli ve
- kuvvetli (CD4/CD8)

- Latent enfeksiyon patogenezi?
  - CMV
    - peptid salınımını azaltır
    - hücre yüzeyine MHC-1 sunumunu engeller
    - HCMV casusu CD4+ ler ?

CMV Konak ilişkisi

LATENT ENFEKSİYON → İMMÜN YETMEZLİK

Konak hücre

-Mononükleer hücreler
-PMNL
-Vasküler endotel
-Fibroblast
-nöronal hücreler
-Renal epitel hücreler, vb.

T hücrelerin baskılanması

AKTİVASYON

-Kemik iliği
-Karaciğer
-GİS
-Akciğer
-Beyin vb.

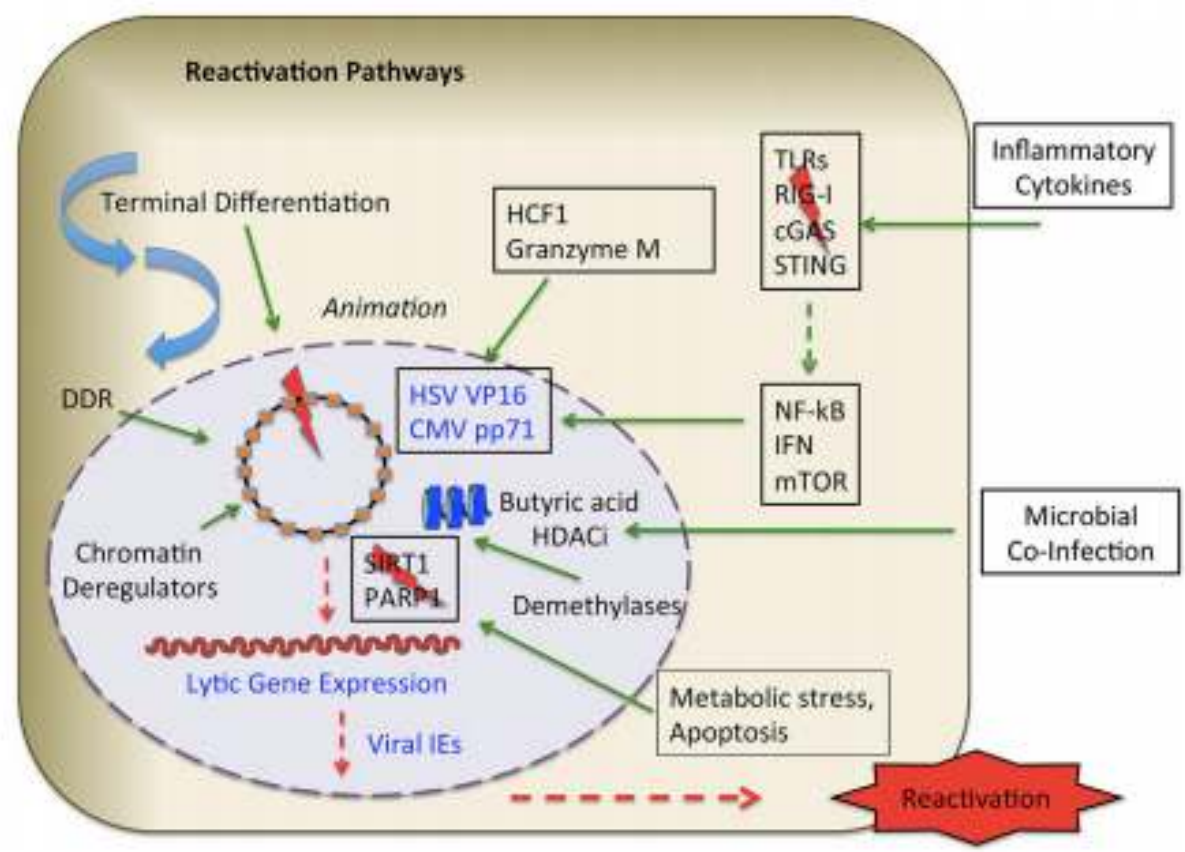
Reaktivasyon ne zaman?

- İmmünitede bozulma
- Kimyasal değişiklikler
- Stres
- UV
- İlaçlar
- …

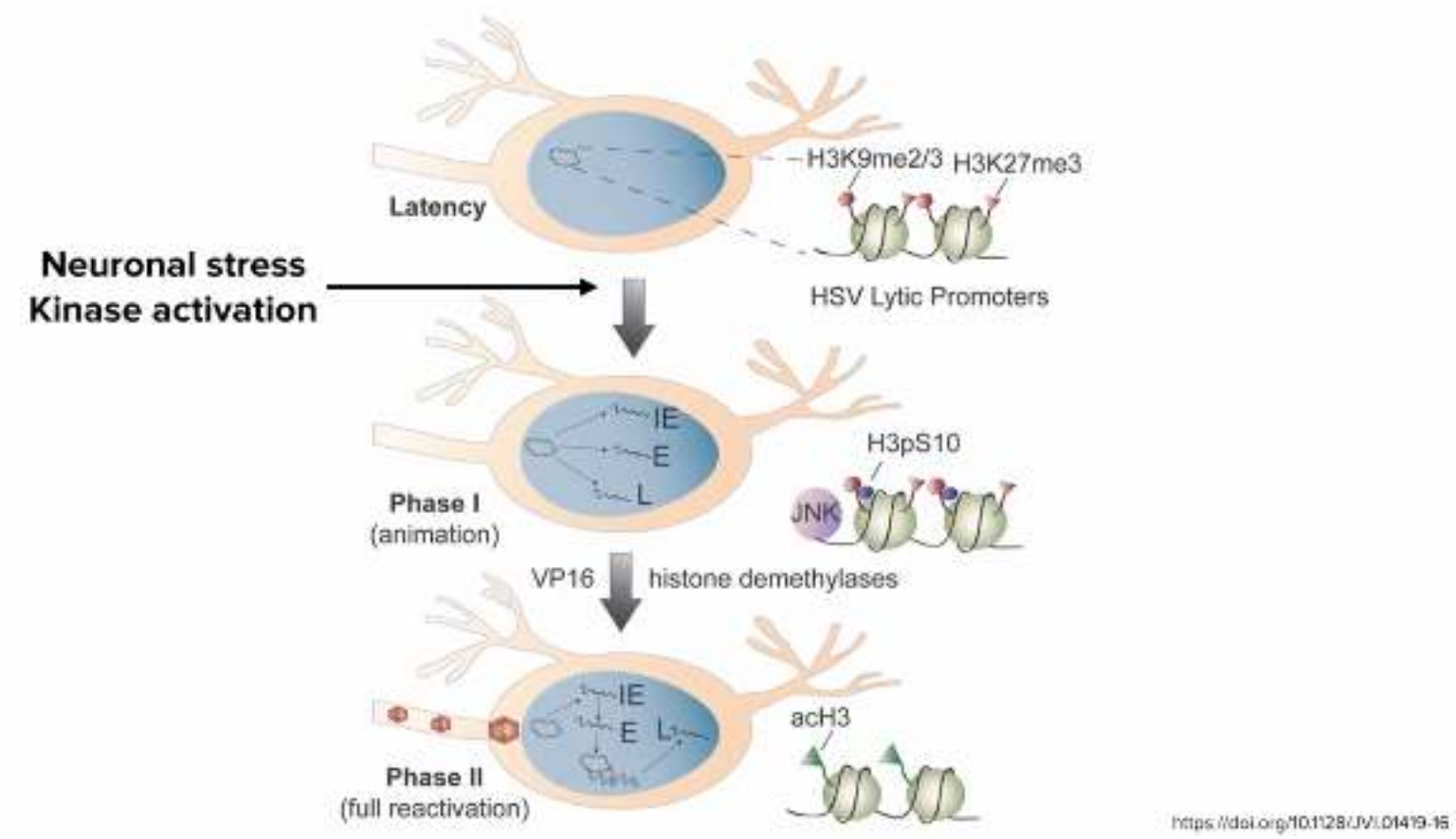
Epigenetics and Genetics of Viral Latency. Cell Host & Microbe, 2016

Reaktivasyon

- Konak intrinsik faktörleri
- Çevresel stres (hipoksi, inflamasyon)

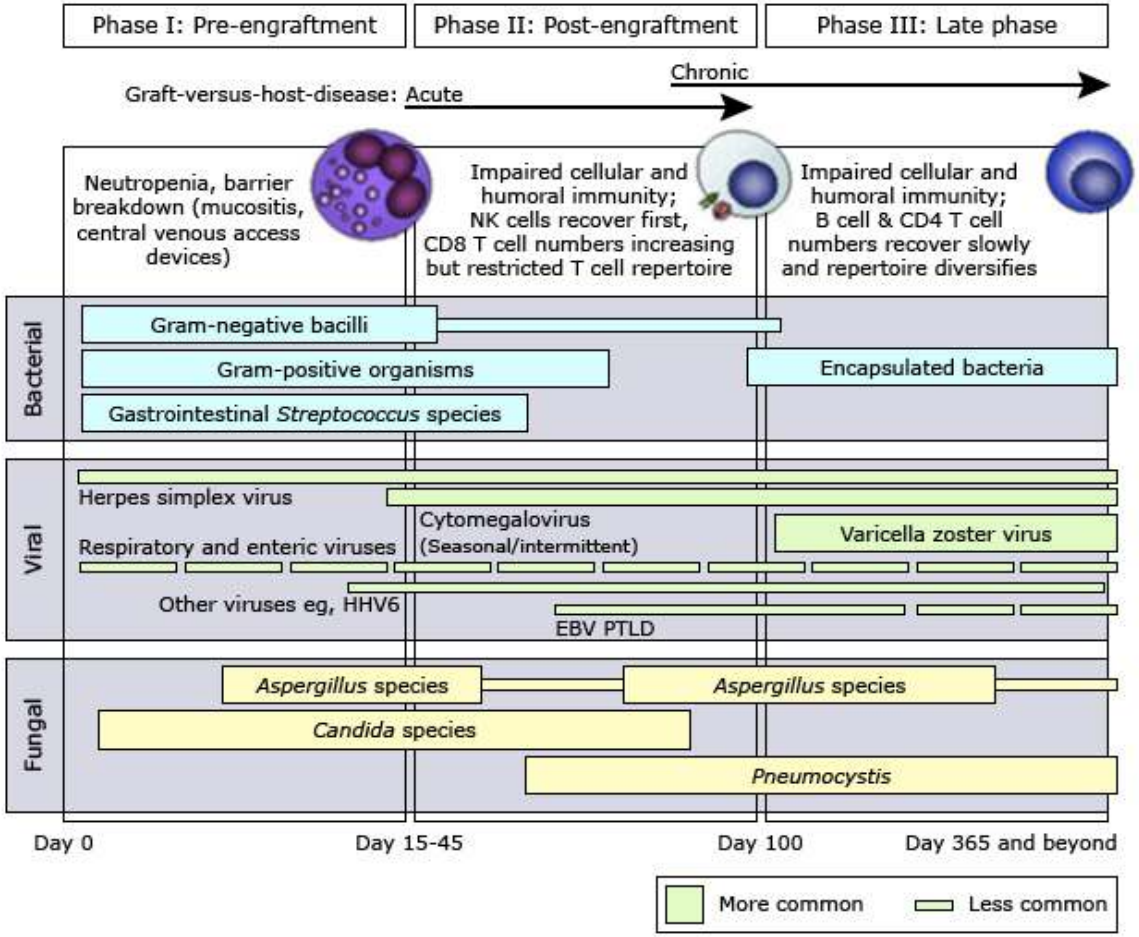


Epigenetics and Genetics of Viral Latency. Cell Host & Microbe, 2016

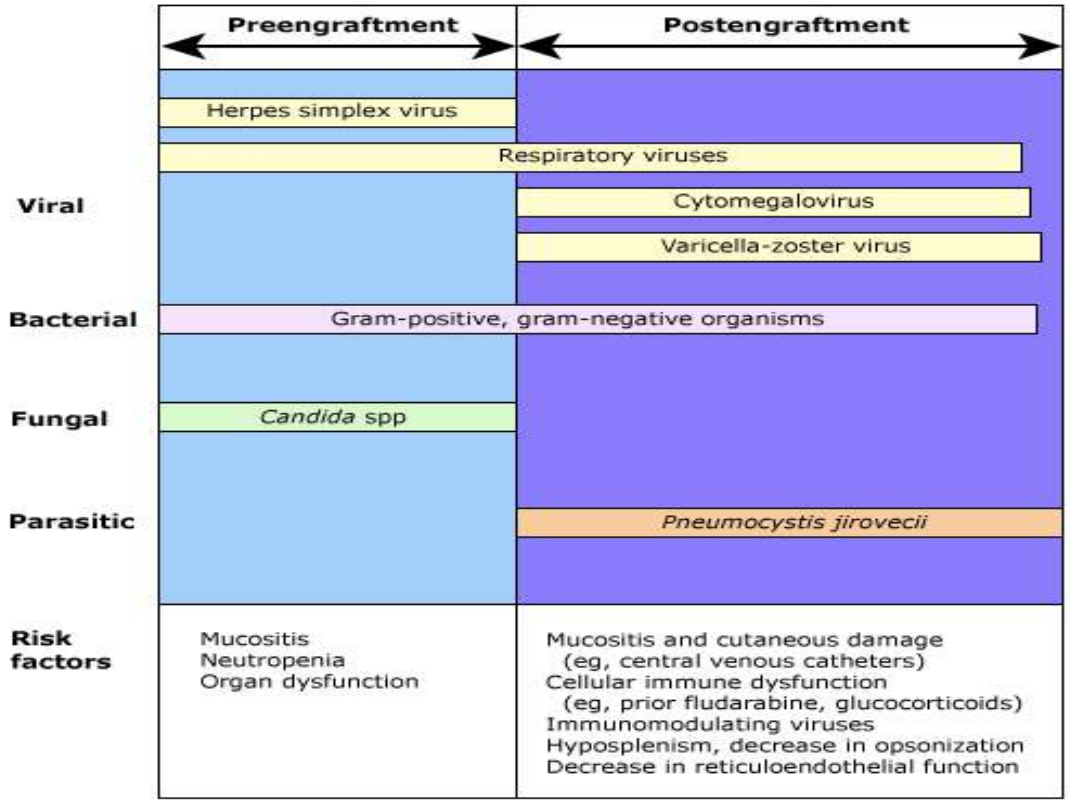


https://doi.org/10.1128/JVI.01419-16

Allojenik KHN



Otolog KHN


Preengraftment
Postengraftment
Herpes simplex virus
Respiratory viruses
Viral
Cytomegalovirus
Varicella-zoster virus
Bacterial
Gram-positive, gram-negative organisms
Fungal
Candida spp
Parasitic
Pneumocystis jirovecii
Risk factors
Mucositis
Neutropenia
Organ dysfunction
Mucositis and cutaneous damage
(eg, central venous catheters)
Cellular immune dysfunction
(eg, prior fludarabine, glucocorticoids)
Immunomodulating viruses
Hyposplenism, decrease in opsonization
Decrease in reticuloendothelial function

CMV reaktivasyonu

- Otolog HKHT alıcılarında CMV hastalığı ender (Tomblyn M 2009)
- Risk grupları
  - Tüm vücut irradyasyonu
  - T-hücre deplesyonlu (CD34 seleksiyonu yapılmış) greft
  - HKHT öncesi 6 ay içinde alemtuzumab, fludarabin veya 2- chlorodeoxyadenosine almış olmak

CASE REPORTS

CMV Pneumonitis following Bendamustine containing Chemotherapy

Sumeet Vimal Kishor Singhania[1], Pujan Parikh[2], Sandeep Goyle[3]

Abstract

Bendamustine has been increasingly used for treatment of indolent lymphoma for the past few years. The data on safety profile of this drug is still emerging with the increasing use of this drug. The higher occurrence of CMV reactivation with this drug has been reported in few case reports only. We report a case of CMV penumonitis initially presenting as unexplained pyrexia which responded well to intravenous Ganciclovir. This case report re-iterates the suspicion of CMV reactivation in lymphoma patients receiving bendamustine who present with unexplained pyrexia or chest symptoms.

Introduction

were normal. Dengue and Malaria

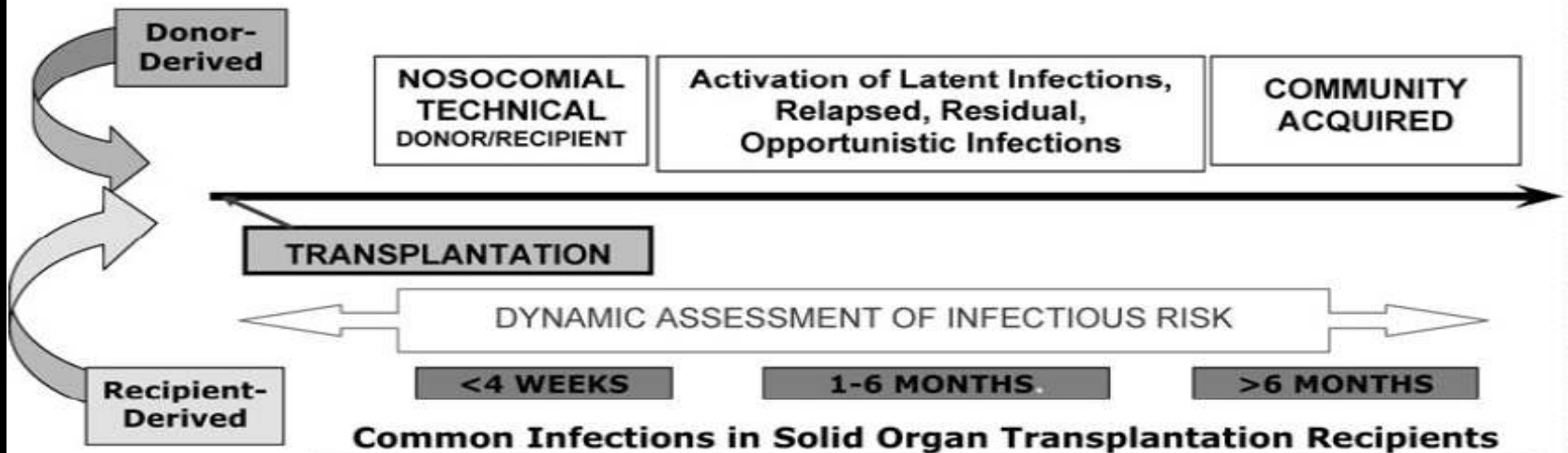
was discharged from chest clinic a month later.

Discussion

Bendamustine has shown a favourable risk profile and comparable efficacy as compared to standard R CHOP regimen for indolent lymphoma in particular there is decrease incidence of alopecia.[1] However bendamustine is known to cause more severe CD4 lymphopenia which can predispose patients to opportunistic infections like CMV.[2] Our patient had grade 3

The Timeline of Post-Transplant Infections

Modified from [1-3]



Common Infections in Solid Organ Transplantation Recipients

Antimicrobial-resistant species:
- MRSA
- VRE
- Candida species (non-albicans)

Aspiration
Line Infection
Wound Infection
Anastamotic Leaks/Ischemia
C. difficile colitis

Donor-Derived (Uncommon):
HSV, LCMV, rabies, West Nile

Recipient-Derived (colonization):
Aspergillus, Pseudomonas

With PCP and antiviral (CMV, HBV) Prophylaxis:
- BK Polyomavirus Nephropathy
- C. difficile colitis
- Hepatitis C virus
- Adenovirus, influenza
- *Cryptococcus neoformans*
- *M. tuberculosis*

Anastamotic complications

Without Prophylaxis Add:
Pneumocystis
Herpesviruses (HSV, VZV, CMV, EBV)
Hepatitis B virus
Listeria, Nocardia, Toxoplasma
Strongyloides, Leishmania, T. cruzi

Community Acquired Pneumonia
Urinary Tract infection
Aspergillus, Atypical moulds, *Mucor* species
Nocardia, Rhodococcus species
Late Viral:
- CMV (Colitis/Retinitis)
- Hepatitis (HBV, HCV)
- HSV encephalitis
- Community acquired (SARS, West Nile)
- JC polyomavirus (PML)

Skin Cancer, Lymphoma (PTLD)

Kortikosteroid ve latent viral enfeksiyon

- Tek başlarına viral reaktivasyona neden olmazlar ancak diğer ilaçlarla sinerji yaparlar
  - Kortikosteroid + **Azotiopürin**=yüksek CMV reaktivasyon riski
  - Kortikosterodlerin erken azaltılması CMV riskini düşürmekte
  - Siklosporin ve Takrolimus – primer immunosupresif ila steroidle birlikte reaktivasyonu arttırırlar

İmmünsüpresif tedavi- CMV reaktivasyonu

- Mycophenolate mofetil (Cellcept)
  - CMV hastalığı riskini arttırır
- Sirolimus (rapamycin), everolimus (mTOR inhibitors)
  - CMV hastalığı riski göreceli olarak daha düşük
- ORTHOCLONE OKT-3 (muromonab-CD3)
  - rejeksiyonu önlemek için kullanılır
  - ciddi CMV hastalığı insidansını arttırır
  - CMV hepatiti ve dissemine CMV'ye neden olur

HIV- Late

EKMUD Çukurova Günleri

24 Şubat 2018
Antakya, Ottoman Otel
HIV ve Fırsatçı Enfeksiyonların Yönetimi

Açılış Konuşması: *Prof. Dr. Yusuf Önlen*

Saat: 10.30 - 12.00, Oturum 1. Oturum Başkanları: *Prof. Dr. Mustafa Namıduru, Prof. Dr. Yusuf Önlen*

- HIV enfeksiyonu ve immün system ilişkisi
  Doç. Dr. Aslıhan Ulu
- IRIS
  Prof. Dr. Yeşim Taşova
- Tüberküloz
  Doç. Dr. Behice Kurtaran

Öğle Yemeği

Saat: 14.00 - 15.20, 2. Oturum Başkanları: *Gülden Ersöz, Sabahattin Ocak*

- CMV enfeksiyonu
  Prof. Dr. İlkay Karaoğlan
- Toksoplazmoz
  Yard. Doç. Dr. A Seza İnal
- Pnömosistis enfeksiyonu
  Doç. Dr. Selma Ateş
- Diğer paraziter enfeksiyonlar
  Doç. Dr. Recep Tekin

Ara

Saat: 15.40 - 17.00, 3. Oturum Başkanları: *Prof. Dr. Özlem Kandemir, Prof. Dr. Mustafa Kemal Çefen*

- Kriptokokkoz
  Doç. Dr. Süheyla Kömür
- Diğer fırsatçı fungal enfeksiyonlar
  Doç. Dr. Funda Yetkin
- Poliomavirüsler
  Yard. Doç. Dr. Selçuk Nazik
- Enfeksiyon ile karışabilecek enfeksiyon dışı durumlar
  Yard. Doç. Dr. Ferit Kuşçu

Kanser ve tedavi ile ilişkili viral enfeksiyonların risk kategorisi

Risk durumu	Hastalık/ Tedavi	Enfeksiyon/Aktivasyon
Düşük	Solid tm kemoterapi	HSV
Orta	Lenfoma Multiple myelom KLL Pürin analogları	HSV VZV
Yüksek	Akut lösemi	HSV, CMV
	Alemtuzumab	HSV, VZV, CMV
	Bortezomib	VZV

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PLOS | ONE

Reactivation of Multiple Viruses in Patients with Sepsis

Andrew H. Walton[1], Jared T. Muenzer[2], David Rasche[1], Jonathan S. Boomer[3], Bryan Sato[4], Bernard H. Brownstein[1], Alexandre Pachot[5], Terrence L. Brooks[3], Elena Deych[3], William D. Shannon[3], Jonathan M. Green[3], Gregory A. Storch[2], Richard S. Hotchkiss[1]*

1 Department of Anesthesiology, Washington University School of Medicine, St. Louis, Missouri, United States of America, **2** Department of Pediatrics, Washington University School of Medicine, St. Louis, Missouri, United States of America, **3** Department of Medicine, Washington University School of Medicine, St. Louis, Missouri, United States of America, **4** Department of Surgery, Washington University School of Medicine, St. Louis, Missouri, United States of America, **5** Medical Diagnostic Discovery Department, BioMérieux Inc., Marcy 1'Etoile, France

Abstract

A current controversy is whether patients with sepsis progress to an immunosuppressed state. We hypothesized that reactivation of latent viruses occurred with prolonged sepsis thereby providing evidence of clinically-relevant immunosuppression and potentially providing a means to serially-monitor patients' immune status. Secondly, if viral loads are markedly elevated, they may contribute to morbidity and mortality. This study determined if reactivation of herpesviruses, polyomaviruses, and the anellovirus TTV occurred in sepsis and correlated with severity. Serial whole blood and plasma samples from 560 critically-ill septic, 161 critically-ill non-septic, and 164 healthy age-matched patients were analyzed by quantitative-polymerase-chain-reaction for cytomegalovirus (CMV), Epstein-Barr (EBV), herpes-simplex (HSV), human herpes virus-6 (HHV-6), and TTV. Polyomaviruses BK and JC were quantitated in urine. Detectable virus was analyzed with respect to secondary fungal and opportunistic bacterial infections, ICU duration, severity of illness, and survival. Patients with protracted sepsis had markedly increased frequency of detectable virus. Cumulative viral DNA detection rates in blood were: CMV (24.2%), EBV (53.2%), HSV (14.1%), HHV-6 (10.4%), and TTV (77.5%). 42.7% of septic patients had presence of two or more viruses. The 50% detection rate for herpesviruses was 5–8 days after sepsis onset. A small subgroup of septic patients had markedly elevated viral loads ($>10^4$–10^6 DNA copies/ml blood) for CMV, EBV, and HSV. Excluding TTV, DNAemia was uncommon in critically-ill non-septic patients and in age-matched healthy controls. Compared to septic patients without DNAemia, septic patients with viremia had increased fungal and opportunistic bacterial infections. Patients with detectable CMV in plasma had higher 90-day mortality compared to CMV-negative patients; $p<0.05$. Reactivation of latent viruses is common with prolonged sepsis, with frequencies similar to those occurring in transplant patients on immunosuppressive therapy and consistent with development of an immunosuppressive state. Whether reactivated latent viruses contribute to morbidity and mortality in sepsis remains unknown.

Citation: Walton AH, Muenzer JT, Rasche D, Boomer JS, Sato B, et al. (2014) Reactivation of Multiple Viruses in Patients with Sepsis. PLoS ONE 9(6): e98819. doi:10.

- Sepsisteki hastada latent viral enfeksiyonların reaktivasyonu artmakta

- Sekonder bakteriyel, fungal enfeksiyon oranı viremisi olanlarda daha yüksek

Walton AH, Muenzer JT, Rasche D, Boomer JS, Sato B, et al. (2014) Reactivation of Multiple Viruses in Patients with Sepsis. PLoS ONE 9(6): e98819.

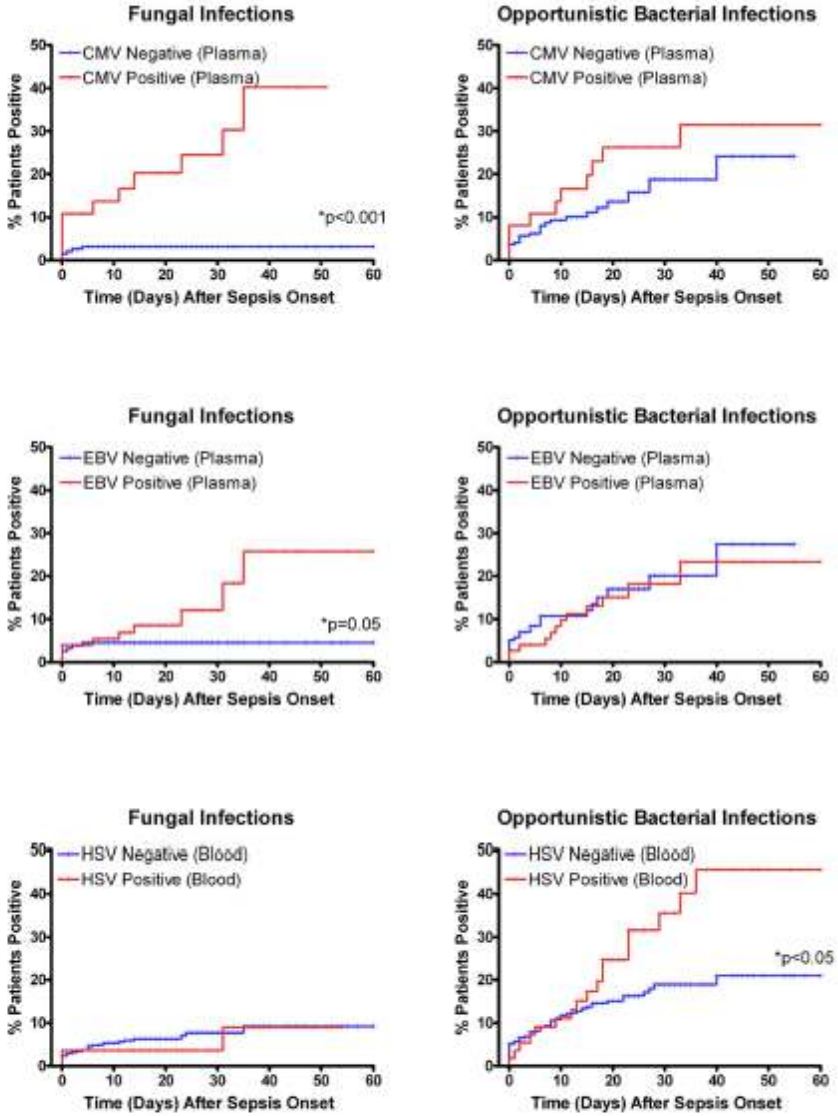

Figure 4. Impact of viral reactivation on fungal and opportunistic bacterial infections. Septic patients with CMV detected in either blood or plasma had increased fungal infections compared to CMV negative patients; only results for plasma are shown and are significant, $p<0.001$. Similarly, patients who had EBV detected in blood had increased fungal infections compared to viral negative patients, $p=0.05$. Patients who were HSV positive in blood had increased opportunistic bacterial infections due to *Stenotrophomonas*, *Acinetobacter*, or *Enterococcus* compared to viral negative patients, $p<0.05$. Censored subject (vertical hash marks) represent patients who were either discharged from the ICU or who died without events. Analysis was performed using all events but plot was truncated at 60 days for clarity. N = 35 patients with fungal infections, n = 86 patients with *Stenotrophomonas*, *Acinetobacter*, or *Enterococcus* infections.

doi:10.1371/journal.pone.0098819.g004

Ülseratif kolit

- Ağır ve tedaviye cevapsız alevlenmelerde CMV reaktivasyonu akla gelmeli

Latent viral enfeksiyonların önlenmesi

- Profilaksi (HSV, CMV..)
- Preempitif tedavi
- İmmünsüpresyonun azaltılması
- Aşı (VZV)
- Latent virüs genomunu hedefleyen yeni tedaviler..

Teşekkür ederim...