

# Hepatitis per virus del grup herpes

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# Hepatitis per virus del grup herpes

- Virus DNA
- Grans 150-250 nm
- Provoquen destrucció directe dels teixits
- Tropicisme cel·lular específic:
  - EBV----- limfòcits
  - HSV, HZV ----- teixit epitelial
- Infecció latent després primoinfecció
  - malaltia per infecció primària, reactivació, reinfecció



# Hepatitis per virus del grup herpes

- No són virus hepatotrops
- Poden causar hepatitis però no és freqüent
- Tenen un efecte citopàtic directe sobre l'hepatòcit
- Poden causar hepatitis en primoinfecció o en reactivació
- La gravetat de la hepatitis depèn del tipus d'infecció i de l'estat immunitari del malalt
  - > primoinfecció, > immunodeprimits (reactivació)
- És important el diagnòstic precoç per a iniciar tractament específic, condiciona el pronòstic



# Classification of human herpesviruses

<b>Subfamily</b>	<b>Taxonomic name</b>	<b>Common name</b>
Alpha-herpesvirinae	HHV-1	Herpes simplex virus 1 (HSV-1)
	HHV-2	Herpes simplex virus 2 (HSV-2)
	HHV-3	Varicella-zoster virus (VZV)
Beta-herpesvirinae	HHV-5	Human cytomegalovirus (HCMV)
	HHV-6	HHV-6 variant A or B
	HHV-7	HHV-7
Gamma-herpesvirinae	HHV-4	Epstein-Barr virus (EBV)
	HHV-8	Kaposi's sarcoma-associated herpesvirus (KSHV)

*HHV, human herpesvirus.*



# Virus de la família *Herpesviridae* causants d'hepatitis

- Virus de l'Herpes Simple (HSV1, HSV2)
- Virus Varicel·la-zoster (VZV)
- Citomegalovirus (CMV)
- Virus Epstein-Barr (EBV)
- Herpesvirus humà 6 (HHV6)



# Infeccions causades pels virus de l'Herpes

VIRUS HERPES	IMMUNOCOMPETENTS		IMMUNODEPRIMITS
	<u>Infecció primària</u>	<u>Reactivació</u>	
<b>Herpes simple 1</b>	Gingivoestomatitis Queratoconjuntivitis Herpes cutani Herpes genital Encefalitis <b>Hepatitis</b> Infecció neonatal	Herpes labial Queratoconjuntivitis Herpes cutani Encefalitis	Herpes labial Queratoconjuntivitis Herpes cutani Afectació visceral: Encefalitis, mielitis, <b>hepatitis</b> , pneumonitis, retinitis, disseminada
<b>Herpes simple 2</b>	Gingivoestomatitis Queratoconjuntivitis Herpes cutani Herpes genital Encefalitis Meningitis <b>Hepatitis</b> Infecció neonatal	Herpes genital Herpes cutani Meningitis	Herpes labial Queratoconjuntivitis Herpes cutani Afectació visceral: Encefalitis, mielitis, <b>hepatitis</b> , pneumonitis, retinitis, disseminada
<b>Varicel·la-zòster</b>	Varicel·la <b>Hepatitis</b> Infecció neonatal	Herpes zòster	Herpes zòster Afectació visceral: encefalitis, meningitis, mielitis, <b>hepatitis</b> , pneumonitis, retinitis, artritis, disseminada
<b>Citomegalovirus</b>	Mononucleosis <b>Hepatitis</b> Infecció congènita		Mononucleosis Afectació visceral: <b>hepatitis</b> , pneumonitis, retinitis, gastroenterocolitis, disseminada
<b>Epstein-Barr</b>	Mononucleosis, <b>Hepatitis</b> Encefalitis		Síndrome limfoproliferativa post trasplantament, <b>hepatitis</b>
<b>Herpes humà 6</b>	<i>Roseola infantum</i> Febre i otitis mitja Encefalitis <b>Hepatitis</b>		Pneumonitis, encefalitis, <b>hepatitis</b> , aplàsia medul·lar



Pacient de 29 anys

- Ex-fumadora
- Part vaginal 9 mesos abans
- Infecció per SARS Cov2 3 mesos abans

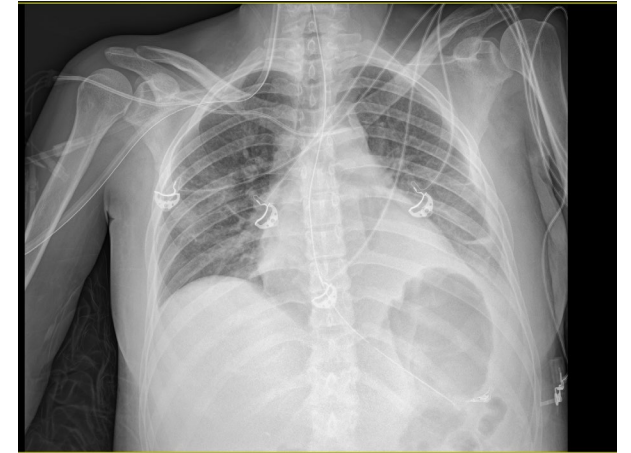
#### MALALTIA ACTUAL

- Una setmana
- Febre
- Astènia, anorèxia
- Dolor abdominal
- Bradipsíquia

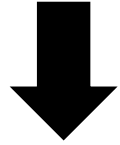
#### EXPLORACIÓ FÍSICA

- Regular estat general
- Icterícia conjuntival
- Bradipsíquia
- Dolor a la palpació abdominal

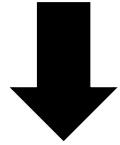
ANALÍTICA	
Creatinina	272 $\mu\text{mol/L}$
Filtrat glomerular	20 mL/min
ALT	3.912 U/L (<32)
AST	14.796 U/L (<31)
LDH	16.765 U/L (<213)
Bilirubina	50 $\mu\text{mol/L}$ (<8)
Hb	10
Plaquetes	23.000
Leucocits	4.500
TPT	2,58
Fibrinogen	0,92
Factor V	33%



**EVOLUCIÓ**  
**Crisi comicial**



**RNM cerebral normal**  
**PL normal**



**Sense sedació**  
Intent obertura ocular als estímuls  
~~Encefalopatia grau IV~~

CMV. Detecció quantitativa per PCR en temps real .....	Indetectable IU/ml
Varicela zoster. PCR en temps real .....	Negatiu
Virus Epstein-Barr. Detecció per PCR en temps real .....	Indetectable IU/ml
<b>Virus herpes simple. PCR en temps real .....</b>	<b>Herpes simplex tipus 1</b>
Herpes virus humà 6. PCR en temps real .....	Negatiu





# Hepatitis per virus Herpes simple

## Característiques

- Seroprevalença alta (50-90% HSV1, 20-60% HSV2)
- Hepatitis com a manifestació poc freqüent
- Hepatitis lleu ----- hepatitis fulminat
- No hepatitis crònica
- HEPATITIS GREU TÉ TRACTAMENT!!!!
- Mortalitat molt elevada!!!!



# Hepatitis per virus Herpes simple

## Característiques

### CLÍNICA

- Febre + augment de transaminases
- Lesions cutànies < 50%
- Grups de risc
  - Embarassades (primoinfecció 3er trimestre)
  - En immunodeprimits per reactivació
  - Nou nats malaltia disseminada amb predomini afectació sistema nerviós central

### PRONÒSTIC

- 74 % hepatitis per herpes desenvolupen hepatitis fulminant
- Mortalitat 90%
- Causa 1% de les hepatitis fulminants



# Herpes Simplex Virus Hepatitis: An Analysis of the Published Literature and Institutional Cases

*Liver transpl 2007*

## 137 cases of HSV hepatitis

- Clinical presentation
  - Fever 98%
  - Cutaneous lesions <50%
- 58% first diagnosed at autopsy
- diagnosis suspected clinically prior to tissue confirmation 23%
- Mortality 74%

**TABLE 2. Demographics and Clinical Presentation of HSV Hepatitis**

	Number (%)
Mean age (yr)	34 ± 15
Gender	
Male	51/137 (38)
Female	82/137 (62)
Immune status	
Immunocompetent	33/137 (24)
Immunosuppressed, total	73/137 (53)
Immunosuppressed, transplant	41/137 (30)
Immunosuppressed, nontransplant	32/137 (23)
Pregnant	32/137 (23)
Fever	98/100 (98)
Herpetic lesions (initial or during hospitalization)	
None	69/123 (56)
Mucocutaneous	33/123 (27)
Disseminated	21/123 (17)
Mean peak ALT or AST (U/L)	4927 ± 4099
Mean peak total bilirubin (mg/dL)	6.0 ± 8.1
Leukopenia	50/70 (71.4)
Thrombocytopenia	59/63 (93.6)
Coagulopathy	93/111(83.7)
Acute renal failure	34/52 (65.3)
Hepatic encephalopathy	57/71 (80)
HSV serotype	
Type I	36/93 (38.7)
Type II	57/93 (61.3)

**Abbreviations:** ALT, alanine aminotransferase; AST, aspartate aminotransferase.

**TABLE 3. Diagnosis and Outcomes of HSV Hepatitis**

	Number (%)
Method of initial diagnosis	
Autopsy	79/137 (57.6)
Liver biopsy	43/137 (31.4)
Explanted liver	4/137 (2.9)
Clinical criteria	11/137 (8.0)
Clinical suspicion on initial presentation	31/137 (22.6)
Confirmed by liver biopsy	10/137 (7.3)
Confirmed by explanted liver	2/137 (1.5)
Confirmed by autopsy	8/137 (5.8)
Confirmed by clinical criteria	11/137 (8.0)
Acyclovir treatment	49/134 (36.6)
Reason for acyclovir treatment	
Clinical suspicion	23/49 (46.9)
Serological confirmation	4/49 (8.2)
Liver biopsy confirmation	22/49 (44.9)
Death	
Overall	99/133 (74.4)
Liver transplant	4/7 (57.1)



# Herpes Simplex Virus Hepatitis: An Analysis of the Published Literature and Institutional Cases

Liver transpl 2007

74% of cases progressed to death or liver transplantation  
51% in acyclovir treated patients vs. 88% in the untreated subjects

*\*Based on the frequent delay in HSV diagnosis and significantly improved outcomes, empiric acyclovir therapy for patients presenting with ALF of unknown etiology is recommended until HSV hepatitis is excluded.*

TABLE 4. Acyclovir-Treated and Untreated Group Comparison

	Acyclovir	No acyclovir
Mean age (yr)*	32.9 ± 11.3	40 ± 18.1
Male gender (%)	15/49 (30.1)	35/84 (41.6)
Coagulopathy (%)	35/44 (79.5)	57/66 (86.4)
Immunocompromised (%)	25/49 (51)	45/84 (53.6)
Encephalopathy (%)	21/25 (84)	36/46 (78.3)
Rash (%)	19/44 (43.2)	35/78 (44.8)
Mean ALT or AST (U/L)	4398 ± 3668	5263 ± 4375
Mean bilirubin (mg/dL)	7.8 ± 10.8	3.7 ± 4.1
Mean platelet (10 <sup>3</sup> /μL)	68 ± 62	52 ± 39
Death/LT† (%)	25/49 (51)	74/84 (88.1)

Abbreviations: ALT, alanine aminotransferase; AST, aspartate aminotransferase.

\*P = 0.03.

†P < 0.001.



# Case Report Acute Herpes Simplex Virus Hepatitis in Pregnancy

OBSTETRICS & GYNECOLOGY  
2020

## Teaching Points

1. HSV should remain in the differential diagnosis for any pregnant or peripartum patient presenting with acute hepatitis.
2. Primary HSV hepatitis can present without the pathognomonic rash
3. Acute febrile hepatitis in pregnancy warrants a low threshold to initiate empirical treatment for HSV with intravenous acyclovir while awaiting confirmatory test results



# Herpes Simplex Hepatitis in Adults

## *A Search for Muco-Cutaneous Clues*

*J Clin Gastroenterol 2004*

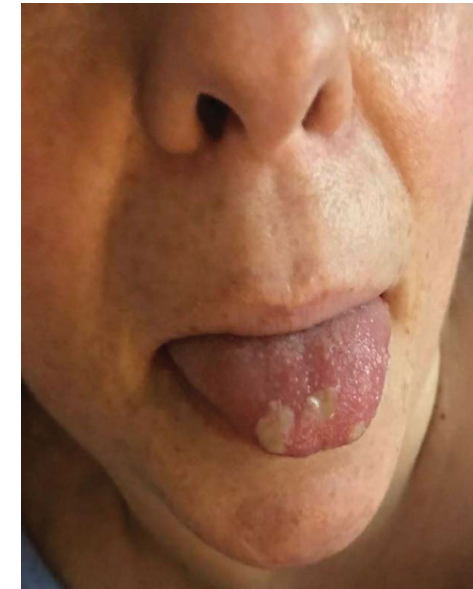
**A:** Was HS hepatitis considered in the work-up of the fulminant hepatitis in these patients?

**B:** Did the treating physician search for m-c lesions as clues to the diagnosis?

**C:** Was there evidence of m-c disease?

**D:** If m-c herpes infection was detected in these patients, was HS considered to be the most likely etiology of the hepatitis?

Case	A	B	C	D
1*	No	No	Yes	N/A‡
2	No	No	NK†	No
3	No	No	Yes	No
4	No	No	Yes	N/A‡



\*The reason that the patient underwent laprotomy was because of the clinical concern of intraabdominal sepsis. The biopsy diagnosis of Herpes simplex was fortuitous.

†Not known as these surfaces were not examined ante or postmortem.

‡Not applicable as the m-c lesions were identified at post-mortem.



# Hepatitis per virus Herpes simple

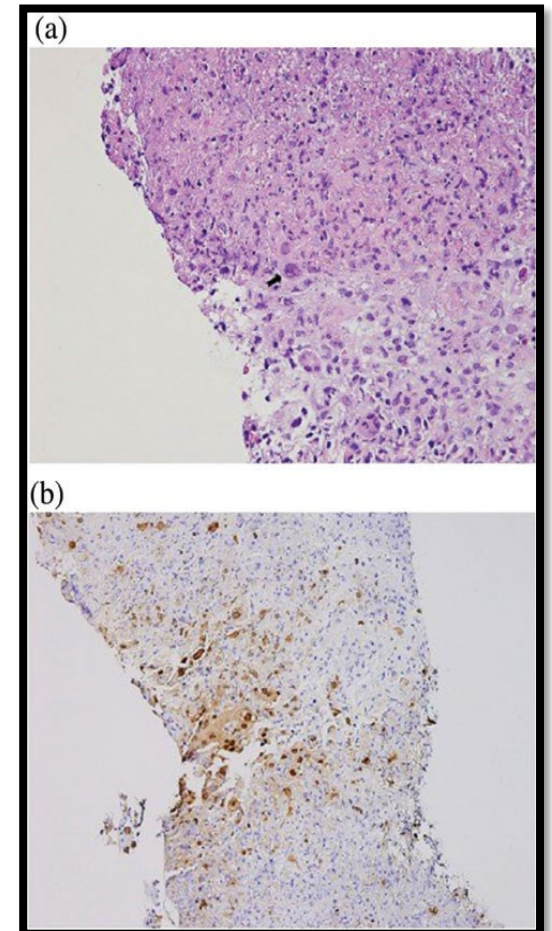
## DIAGNÒSTIC

- DE SOSPITA: HEPATITIS FEBRIL!!!!
- No factors de risc establerts
- Serologies falsos positius i negatius. PCR HSV en sang
- Biòpsia hepàtica: inclusions virals característiques + necrosi centrolobulillars
  - PCR HSV

Immunohistochemical analysis of the liver biopsy of Herpes simplex virus hepatitis.

(a) Hepatocellular necrosis. Within the necrotic debris, viral eosinophilic, ground-glass nuclear inclusions can be seen as well as multinucleated cells with nuclear molding (arrow).

(b) Immunostaining for HSV-2 highlights the infected cells.



# Hepatitis per virus Herpes simple

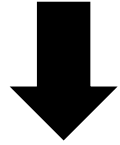
## TRACTAMENT

- Tractament ACICLOVIR
  - Alternatives: foscarnet
- Tractament precoç amb aciclovir millora el pronòstic

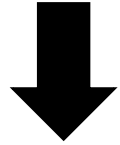
*Considerar aciclovir empíric  
en hepatitis agudes greus  
febrils*



**EVOLUCIÓ**  
**Crisi comicial**



**RNM cerebral normal**  
**PL normal**

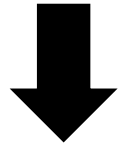


**Sense sedació**  
**Intent obertura ocular als**  
**estímuls**  
**Encefalopatia grau IV**

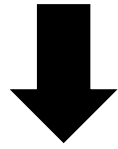
**Virus herpes simple. PCR en temps real ..... Herpes simplex tipus 1**



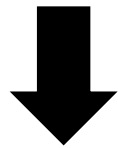
**EVOLUCIÓ**  
**Crisi comicial**



**RNM cerebral normal**  
**PL normal**



**Sense sedació**  
**Intent obertura ocular als**  
**estímuls**  
**Encefalopatia grau IV**



**S'inclou en emergència 0**  
**per a trasplantament**  
**hepàtic**



### ANATOMIA PATOLÒGICA

- EXTENSAS ÀREAS DE **NECROSIS** QUE AFECTAN AL **80% DE LOS HEPATOCITOS**.
- NO SE IDENTIFICAN INCLUSIONES VIRALES Y LAS TINCIONES INMUNOHISTOQUÍMICAS PARA HERPES SIMPLE I Y II SON NEGATIVAS
- **PCR con resultado positivo para Herpes simplex tipo 1**

# Hepatitis per virus varicel·la-zòster

## Característiques

- Primoinfecció (varicel·la) amb augment autolimitat de transaminases
- Reactivació amb malaltia disseminada en immunodeprimits
  - malaltia hematològica, receptors de trasplantament de moll d'os, HIV, trasplantament d'òrgan sòlid
  - Es pot presentar com hepatitis greu

## CLINICA

- Dolor abdominal, febre, alteració transaminases.
- Pot precedir les lesions cutànies.



# Varicella-zoster virus hepatitis – a rare complication of primary infection in immunocompetent children?

*Clin Exp HEPATOL 2024*

Immunocompetent children hospitalized due to varicella 2019 -2022 (excluding the period of COVID-19 pandemic)

- Elevation of ALT during varicella in 1 of 10
- The course of this hepatitis is predominantly mild.

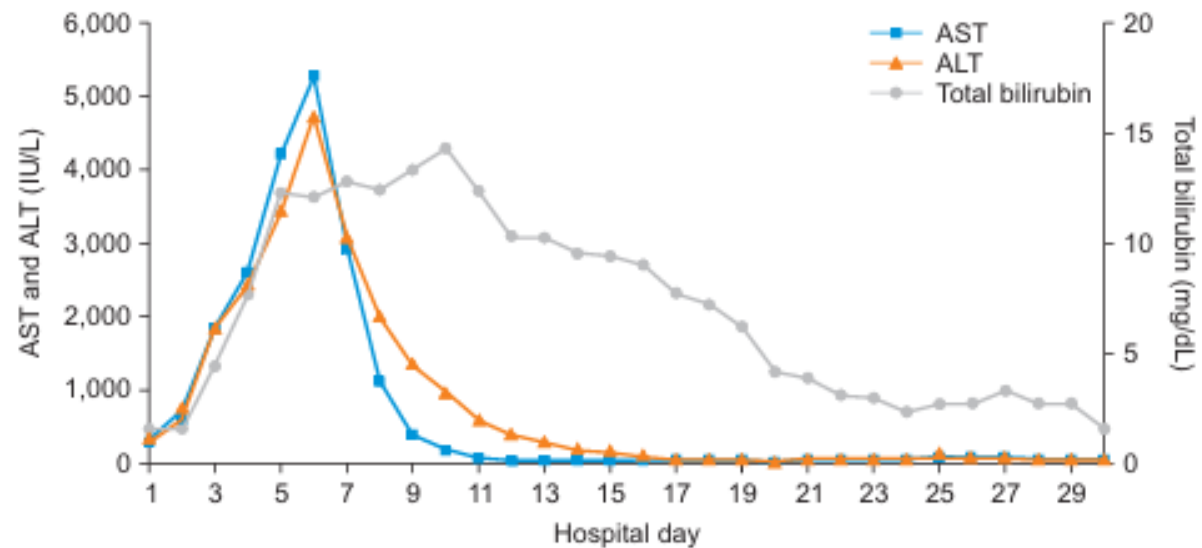
**Table 2.** Clinical presentation in the group with and without elevation of alanine aminotransferase during primary varicella-zoster infection

Parameter	Total (N = 216)	Normal ALT (n = 192)	Elevated ALT (n = 24)	P value
General condition, n (%)				
Good	52 (24)	50 (26)	2 (8.3)	0.05
Fair	136 (63)	117 (60.9)	19 (79.2)	0.08
Serious	28 (13)	25 (13.0)	3 (12.5)	0.94
Median time of... (in days)				
Lesions	6	6	7.5	0.01
Fever	3	3	4	0.10
Hospitalization	4	4	5	0.40



# Fulminant hepatitis and myocarditis associated with varicella zoster virus infection in a kidney transplant recipient: a case report

*Korean J Transplant 2022*



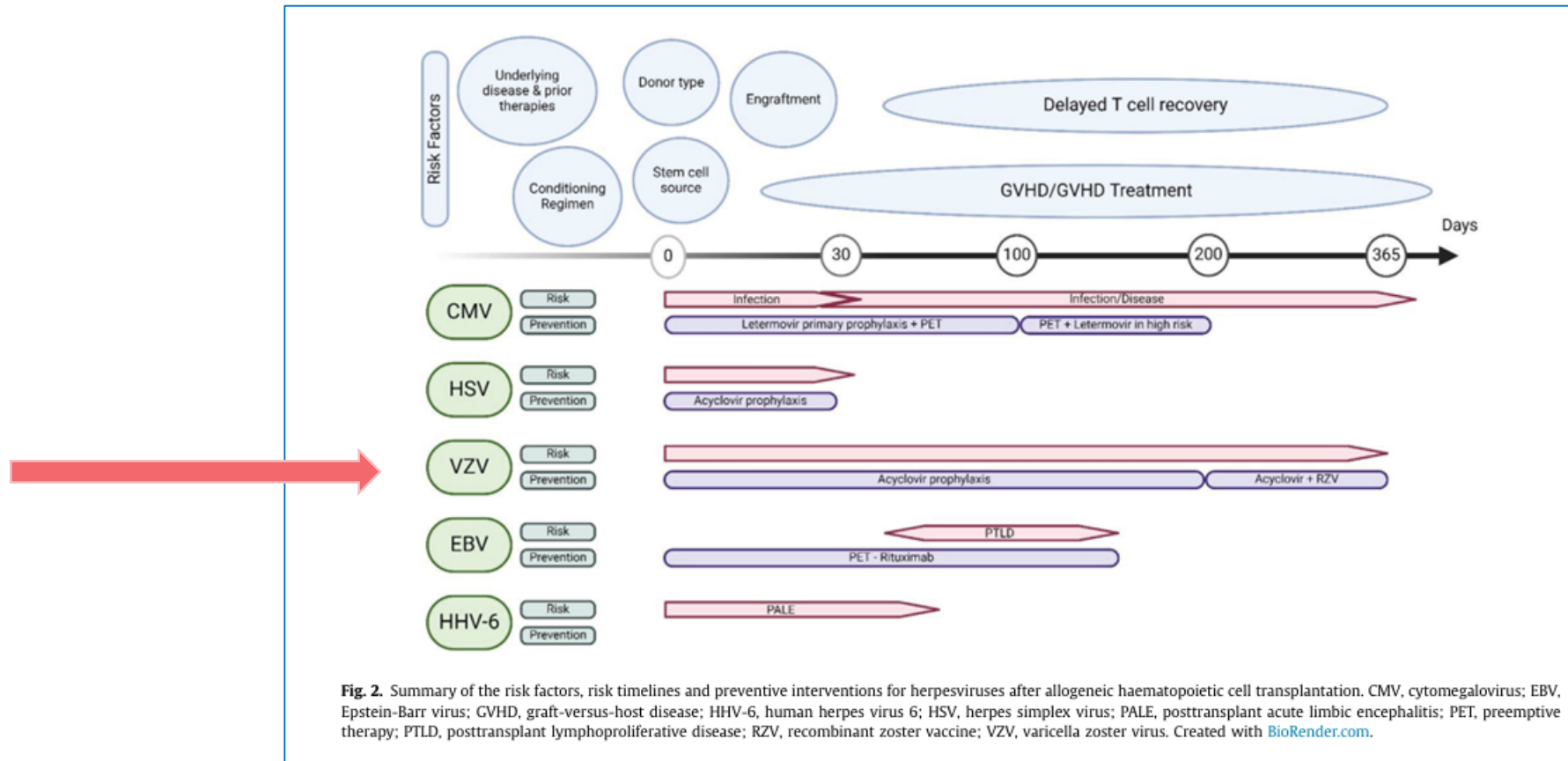
**Fig. 1.** Changes in aspartate aminotransferase (AST), alanine aminotransferase (ALT), and total bilirubin levels during hospitalization. Acyclovir was administered on the fourth day of hospitalization and intravenous immunoglobulin was administered on the fifth day of hospitalization.



# Narrative review

## Advances and prospect in herpesviruses infections after haematopoietic cell transplantation: closer to the finish line?

CMI 2025



# Hepatitis per virus varicel.la-zòster

## DIAGNÒSTIC

- Biòpsia hepàtica. Inclusions característiques
- PCR de les lesions cutànies
- PCR en sang

## TRACTAMENT

- Tractament ACICLOVIR
  - Alternativa foscarnet



Pacient de 68 anys

- THO x CH enòlica 4 mesos abans
- Serologia CMV D+/R-
- Profilaxi valganciclovir 3 mesos
- Immunosupressió: tacrolimus + micofenolat

#### MALALTIA ACTUAL

- 10 dies
- Febreta
- Astènia, anorèxia

PCR CMV 7.800 còpies

ANALÍTICA	
ALT	350 U/L (<32)
AST	625 U/L (<31)
Bilirubina	70 µmol/L (<8)
Plaquetes	23.000
Leucos	3.200
TPT	1,5

REBUIG?



HEPATITIS PER CMV?



# Hepatitis per citomegalovirus

## Característiques

- Seroprevalença 70-80% en adults
- La majoria asimptomàtics: augment de transaminases autolimitades en primoinfecció
  - Mononucleosis: febre + limfomonocitosi + hepatitis lleu (ALT>AST)
- Casos greus en immunodeprimits: malaltia disseminada.
  - Receptors de trasplantament hepàtic.
    - Més risc D+/R-. Inducció amb timoglobulina. Sense profilaxi o després de la profilaxi
    - 2-3 mesos post trasplantament
    - Febre + augment transaminases i bilirubina
- Malaltia congènita en nou nats: hepatitis, anèmia hemolítica, PTT, afectació SNC



# The Wide Spectrum of Presentations of Cytomegalovirus Infection in Immunocompetent Hosts: An Exhaustive Narrative Review

Pathogens 2024

Table 1. The spectrum of liver, and pancreatic disease in CMV-infected immunocompetent patients.

<b>B. Liver and Pancreaticobiliary involvement</b> (liver involvement: common)
Hepatitis ± jaundice (common) (predominantly hepatocellular; rarely cholestatic)
Hepatomegaly (common, median, 9%)
Fulminant hepatitis * (rare)
Hepatitis presenting with ascites (high gradient) and portal hypertension (rare)
Acute pancreatitis (probably rare)
Cholangitis (rare)
* Associated mortality has been reported. ^ May be associated with inflammatory bowel disease (IBD)—preceding, concurrent, or complicating its course (see text).

*While acute hepatitis is almost the sine qua non of active CMV infection, it is benign and self-limited in the majority of cases*



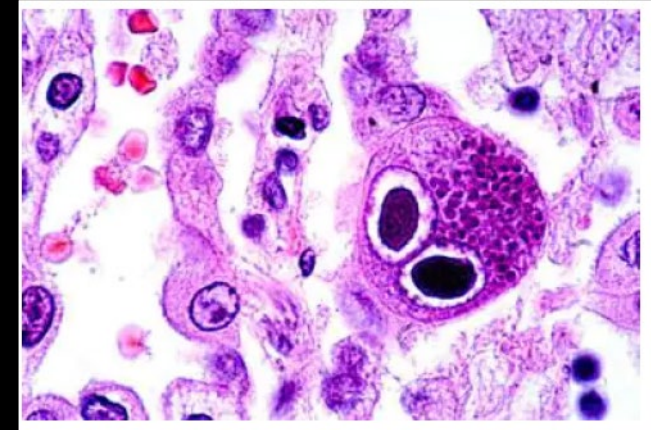
# Hepatitis per citomegalovirus

## DIAGNÒSTIC

- PCR CMV en sang (vigilar interpretació!)
- Biòpsia hepàtica-inclusions per CMV ('owl eyes')
  - No dx PCR per CMV positiva

## TRACTAMENT

- Tractament ganciclovir/valganciclovir
  - Alternatives foscarnet, maribavir, cidofovir



Pacient de 18 anys

#### MALALTIA ACTUAL

- Dues setmanes
- Febre fins a 39°C
- Astènia, anorèxia
- Dolor abdominal
- Nàusees i vòmits

#### EXPLORACIÓ FÍSICA

- Dolor a la palpació HD
- Pol de melsa

ECO abdominal: esplenomegàlia

ANALÍTICA	
ALT	<b>321 U/L (&lt;31)</b>
AST	<b>434 U/L (&lt;32)</b>
Bilirubina	19 µmol/L
Fosfatasa alcalina	268 U/L (<104)
GGT	150 U/L (<21)
Leucòcits	10.070
Limfòcits*	<b>6.140</b>

\* Morfologia sang perifèrica: Alguns limfòcits d'aspecte reactiu



# Hepatitis per Epstein-Barr

## Característiques

- Seroprevalença >90% en adults
- Tropisme pels limfòcits B
- Primoinfecció: la majoria asimptomàtics
- Mononucleosi:
  - febre (90%) + adenopaties cervicals (90%), + odinofàgia (80%) + EMG (50%)+ HMG (10%)
  - hepatitis lleu (70%-90%)
  - Icterícia (5-10%)



# Hepatitis per Epstein-Barr

## Característiques

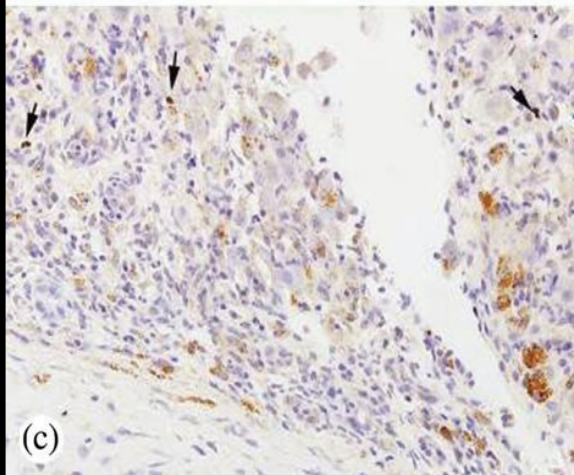
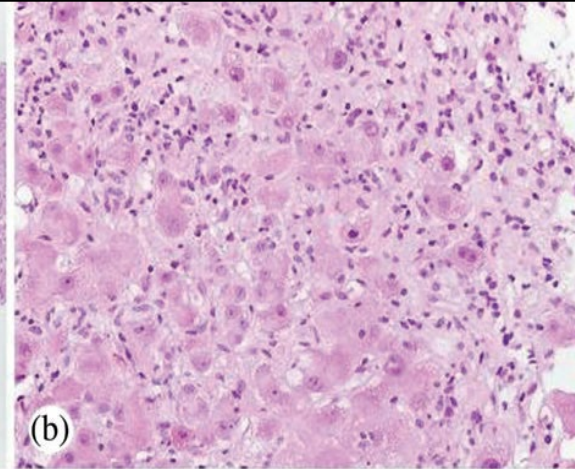
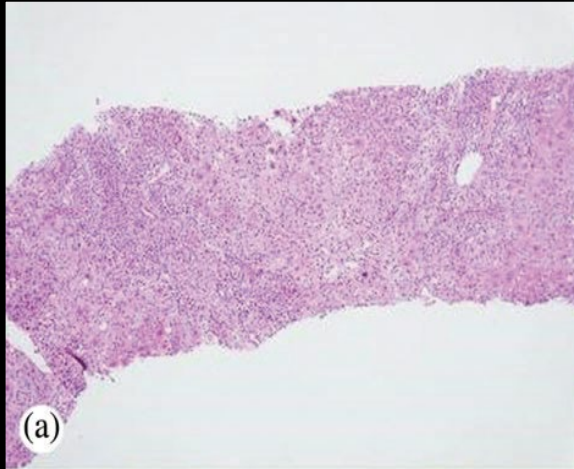
- Hepatitis per EBV es pot presentar sense clínica de síndrome de mononucleosi (+ freqüent en pacients de més edat)
- Alguns casos hepatitis fulminant <1%
- S'ha associat a hepatitis crònica, sembla més desencadenant que efecte directe del virus com hepatitis autoimmune, hepatitis colostàsica, “acute-on-chronic-liver failure”

Acute liver disorders	Acute hepatitis (with or without features of IM) Cholestasis or cholestatic hepatitis ALF
Chronic liver disorders	Chronic active hepatitis (may mimic AIH) Granulomatous hepatitis Vanishing bile duct syndrome Precipitation of AIH Precipitation of acute-on-chronic-liver failure
Liver transplant setting	PTLDs Non-PTLD EBV syndromes

*Gastroenterol Clin North Am. 2020*

. Non-PTLD EBV disease after LT: IM; organ-specific diseases, such as hepatitis; pneumonitis; gastrointestinal symptoms; and hematological manifestations, such as leukopenia, thrombocytopenia, hemolytic anemia, and hemophagocytosis.





### **Liver biopsy of Epstein–Barr virus hepatitis.**

(a)  $\times 100$ ; (b)  $\times 400$ . Liver showing 25% parenchyma necrosis with bridging necrosis, acidophilic bodies, mixed inflammatory infiltration and sinusoidal lymphocytosis. HE stain, magnification:

(c) EBV in situ hybridization showing occasional EBV-positive B lymphocytes ( $\times 400$ , arrows).

# Hepatitis per Epstein-Barr

## DIAGNÒSTIC

- Ac heteròfils
- Serologia (reaccions creuades CMV, hepatitis E)
- PCR EBV en sang

## TRACTAMENT

- De suport
- Casos greus: ganciclovir, valganciclovir +/- corticosteroids.





Pacient de 18 anys  
Hepatitis + febre + limfocitosi + EMG

**Plasma**  
**ESTUDI VIROLÒGIC**

Epstein-Barr (Mononucleosi): **Ac.heteròfils** (Paul Bunnell) (AG) .....**Positiu**  
Epstein-Barr, anticossos EBNA IgG (CLIA) .....Negatiu  
Epstein-Barr, anticossos VCA **IgM** (CLIA) .....**Positiu**  
**Virus Epstein-Barr: càrrega vírica** .....**4.419 UI/mL**



## Epidemiology, clinical features, laboratory examinations, diagnostic modalities and treatment of herpes-group viral hepatitis

Virus	Epidemiology	Clinical features	Laboratory examinations	Diagnostic modalities	Treatment
HSV	Immunocompetent and immunocompromised; second or third trimester of pregnancy;	Fever; nausea and vomiting; headache; abdominal pain of the right upper quadrant; mucocutaneous rash; encephalopathy	Elevated transaminase of 1000 × ULN; leukopenia; thrombocytopenia; coagulopathy	Serology IgM and IgG, liver biopsy; PCR DNA	Acyclovir, liver transplantation
EBV	Most patients aged >60 years; immunocompetent and immunocompromised	Mild hepatitis with IM syndrome; ALF; FHF; clinical jaundice; splenomegaly; hepatomegaly	Elevated aminotransferase levels of × 2–3 ULN, elevated ALP and bilirubin; lymphocytosis	Serology IgM, VCA, PCR, liver biopsy	Valganciclovir, ganciclovir + steroids, liver transplantation
CMV	Immunocompetent and immunocompromised	Asymptomatic to mononucleosis-like symptoms	Mildly elevated liver function test, ALT > AST, normal ALP and bilirubin	Positive IgM or 4-fold increase in IgG, PCR, viral culture, immunofluorescent assay of pp65 antigen positivity, liver biopsy, immunohistochemical stain for CMV antigen, Owl's eye intracellular inclusions. In immunocompetent: nuclear inclusions and immunohistochemical staining of antigen absent.	Valganciclovir, ganciclovir; cidofovir and foscarnet in case with ganciclovir resistance; liver transplantation

ALF, acute liver failure; ALP, alkaline phosphatase; ALT, alanine aminotransferase; AST, aspartate aminotransferase; CMV, cytomegalovirus; EBV, Epstein-Barr virus; FHF, fulminant hepatic failure; HSV, herpes simplex virus; IgG, immunoglobulin G; IgM, immunoglobulin M; IM, infectious mononucleosis; PCR, polymerase chain reaction; ULN, upper limit of normal; VCA, viral capsid antigen.



# Hepatitis per virus herpes humà 6

## Característiques

- Seroprevalença 95% en adults
- Primoinfecció abans dels 2 anys
- Sisena malaltia: rosèola infantum.
  - Febre 3 dies + exantema maculo papular 20% de casos
- Hepatitis en receptors de trasplantament de moll d'os i receptors de trasplantament d'òrgan sòlid (hepàtic).
- No criteris dx serològics clars (reactivació/ primoinfecció)
- PCR virus, biòpsia hepàtica
- S'ha utilitzat Ganciclovir/foscarnet



# Human herpesvirus 6 infections after liver transplantation

World J Gastroenterol 2009

Table 1 Clinical syndromes attributed to HHV-6 after liver transplantation

HHV-6 direct effects	Ref.	HHV-6 indirect effects	Ref.
Fever and rash	[36]	Increased incidence and severity of cytomegalovirus disease	[31,40,41]
Hepatitis	[33,36,49]	Earlier and more severe recurrence of hepatitis C virus	[42]
Myelosuppression	[37]	Higher incidence of fungal infections	[44]
Pneumonitis	[37]	Higher incidence of opportunistic Infection	[36]
Neurologic illness	[38,44,51]	Higher incidence of allograft rejection	[33,36,45,53]

HHV-6: Human herpesvirus 6.

# HHV-6 in liver transplantation: A literature review

Liver International.  
2018

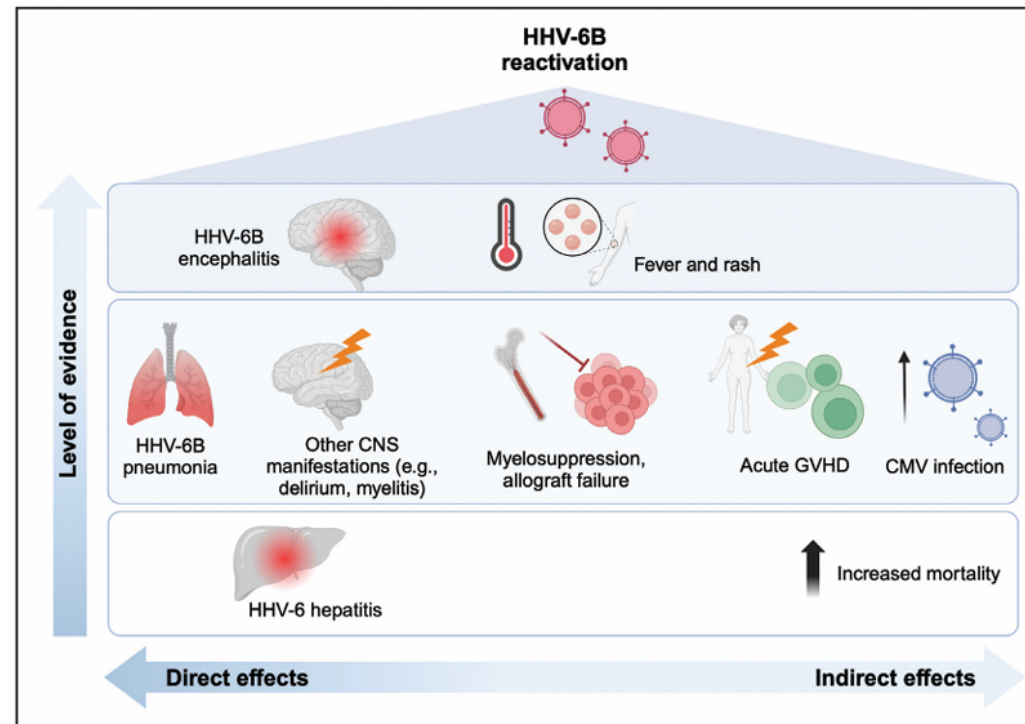
## Key points

- HHV-6 reactivation after liver transplantation is mostly asymptomatic but can be associated with fever, hepatitis and encephalitis.
- Tissue-invasive HHV-6 disease cannot be completely ruled out without a biopsy since infections can be localized in the tissue without remarkable DNA levels in blood. Quantitative assays are essential to distinguish active from latent HHV-6 DNA.
- When testing for the presence of HHV-6, ciHHV-6 in either donor or recipient must be considered.
- Symptomatic and tissue-invasive HHV-6 infections in liver transplant recipients can be successfully treated using ganciclovir, foscarnet or cidofovir.



# Human herpesvirus-6, HHV-8 and parvovirus B19 after allogeneic hematopoietic cell transplant: the lesser-known viral complications

*Curr Opin Infect Dis*  
2024



**FIGURE 1.** Clinical spectrum of HHV-6B reactivation in allogeneic HCT recipients. The horizontal axis represents direct effects (left) and indirect effects (right) mediated by HHV-6B. The vertical axis represents the level of evidence and strength of association varying from weak (bottom) to strong (top). Figure created with BioRender.com.



# Case report: Acute liver failure in children and the human herpes virus 6-? A factor in the recent epidemic

TABLE 1 Patient characteristics and clinical progression.

Patient demographics and clinical characteristics	Findings n=
Age at ALF presentation	6 to 11months
Gender	All female
Prodromal illness with URTI	3
Widespread erythematous blanching rash	2
HHV-6 viraemia pre-transplantation*	2
Progression to liver transplantation	3
Aciclovir prophylaxis	3
Immunosuppression:	
Basiliximab induction, maintenance Tacrolimus	2
Dacluliximab induction, maintenance Tacrolimus & Prednisolone	1
Graft dysfunction at 6-8 weeks post-LT	3
ACR diagnosed in liver allograft biopsy**	3
Immunosuppression used to treat ACR:	
Methylprednisolone	3
Basiliximab	3
Tacrolimus & Prednisolone	3
Mycophenolate mofetil (MMF)	2
Persistence of HHV-6 viraemia	3
Progression to chronic rejection, graft failure and re-transplantation	3
HHV-6 detected in allografts	3

*Front. Pediatr 2023*

Hepatitis fulminante por herpes virus tipo 6 en adultos inmunocompetentes



Fulminant hepatitis caused by herpes virus 6 in immunocompetent adults

[dx.doi.org/10.1016/j.gastrohep.2015.09.003](https://doi.org/10.1016/j.gastrohep.2015.09.003)



# Hepatitis per virus de la família Herpesviridae

- ✓ Poc freqüents
- ✓ Efecte citopàtic directe dels hepatocits
- ✓ En general hepatitis lleus: alteració autolimitada de transaminases en primoinfecció en immunocompetents (VVZ, CMV, EBV)
- ✓ En immunodeprimits en general, hepatitis durant reactivació i infecció disseminada (HVZ, CMV, EBV)
- ✓ En alguns casos poden evolucionar hepatitis fulminant amb mal pronòstic, sobretot HSV
  - ✓ Iniciar aciclovir empíric en hepatitis febril greu fins excloure diagnòstic
  - ✓ Embaraçades, immunocompetents i immunodeprimits.
- ✓ HHV6 molt poc freqüent. Pacient immunodeprimits i alguns casos d'hepatitis greu en nens i adults immunocompetents.



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# Gràcies