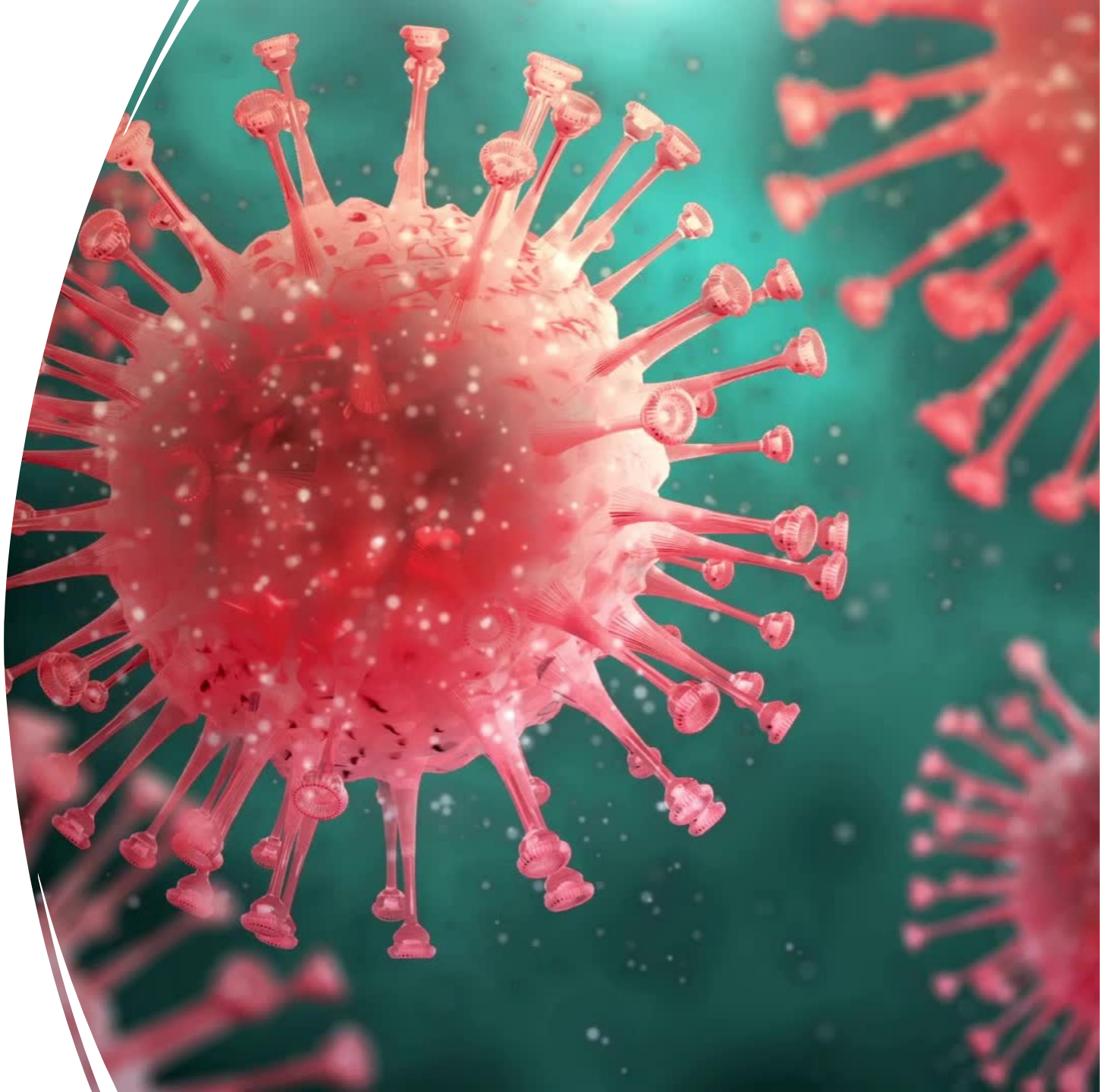
CMV y gestación

Judit Platero, Obdulia Alejos, Juan Parra, Carla Berengua, Elisenda Moliner

09 / 01 /2024



Índice

Introducción

- Principal causa de infección congénita en países desarrollados
- Principal causa de pérdida auditiva neurosensorial
- 85% de los RN son asintomáticos → 15% secuelas permanentes

0,2 - 2 % de los RN vivos

Escasa concienciación del personal médico y de las gestantes

Ausencia de programas de cribaje gestacional y neonatal

Desconocimiento de la evidencia actual sobre el tratamiento

Ausencia de vacunas

Epidemiología

TABLE 1
Prevalence at birth in different settings and burden of nonprimary CMV infection

Variables	Leruez-Ville et al, 2017[23]	Puhakka et al, 2018[20]	Mussi Pinhata et al, 2018[25]
Country	France	Finland	Brazil
CMV seroprevalence in pregnant women	60%	72%	98%
Neonates screened, n	11,715	19,868	1721
Prevalence of congenital CMV infection	0.37%	0.2%	0,5%
Proportion of congenital CMV infection following maternal primary infection	52%	47%	10%
Proportion of congenital CMV infection following maternal nonprimary infection	48%	53%	90%

CMV, cytomegalovirus.

Leruez-Ville. Cytomegalovirus infection during pregnancy. Am J Obstet Gynecol 2020.

Epidemiología

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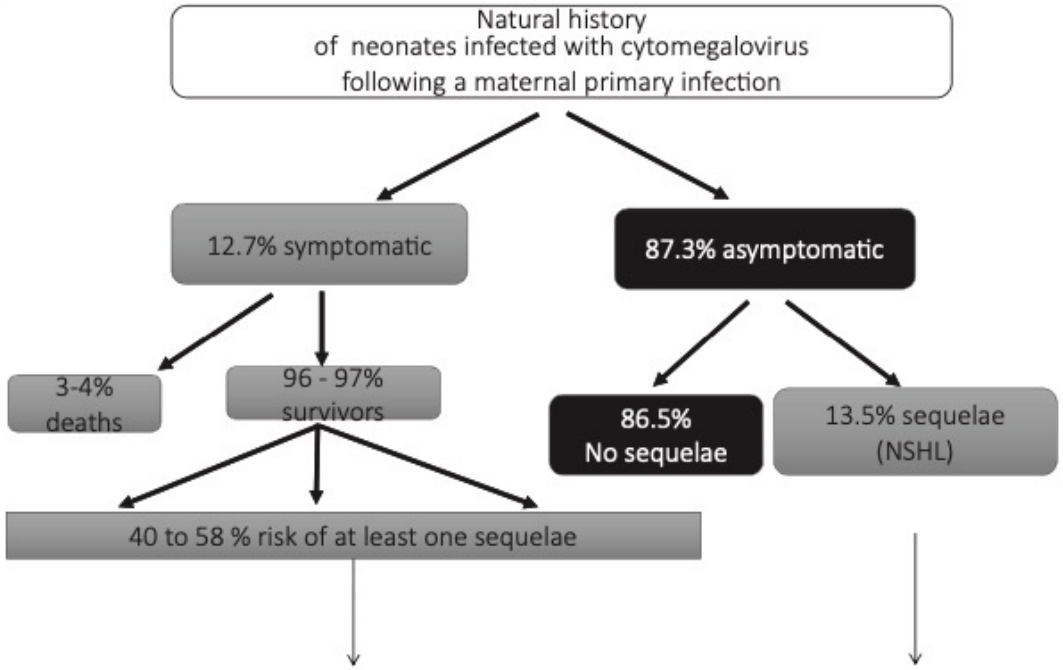
CMV, cytomegalovirus.

Leruez-Ville. Cytomegalovirus infection during pregnancy. Am J Obstet Gynecol 2020.

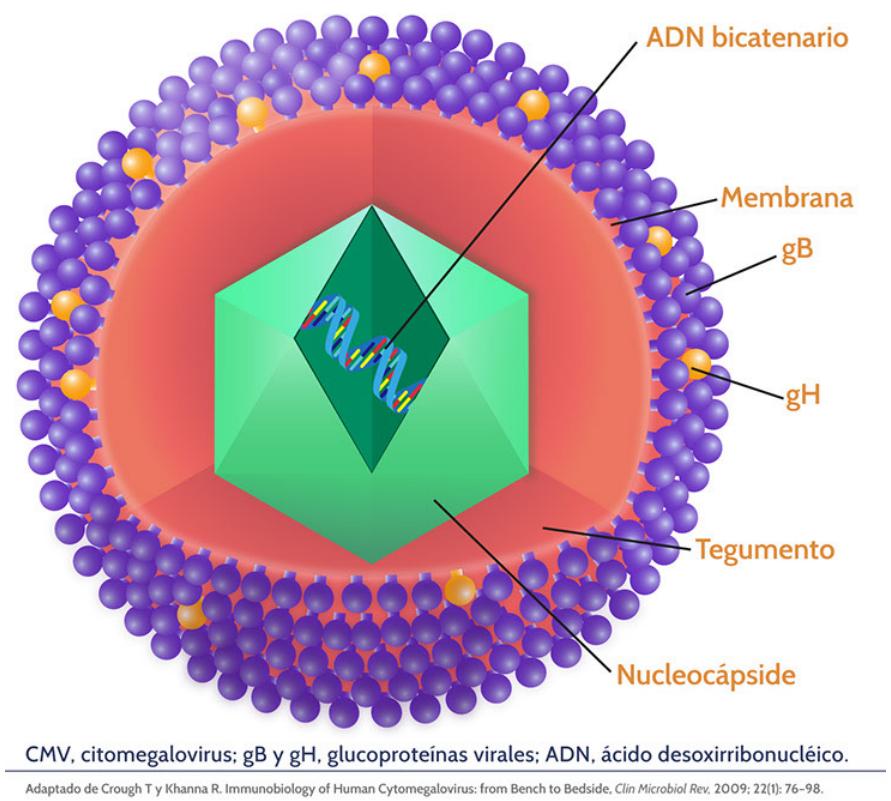
FIGURE 1
Natural history of congenital infection following maternal primary infection with CMV



In this study children with isolated hearing loss are classified in the asymptomatic group. The proportion of long-term sequelae in neonates infected following maternal first-trimester infection are based on the hypothesis that maternal primary infection and transmission are equally frequent in the 3 trimesters of pregnancy. Adapted from Dollard et al (2007).[27]

Leruez-Ville. Cytomegalovirus infection during pregnancy. Am J Obstet Gynecol 2020.

Virología



CMV, citomegalovirus; gB y gH, glucoproteínas virales; ADN, ácido desoxirribonucléico.

Adaptado de Crough T y Khanna R. Immunobiology of Human Cytomegalovirus: from Bench to Bedside, *Clin Microbiol Rev*, 2009; 22(1): 76–98.

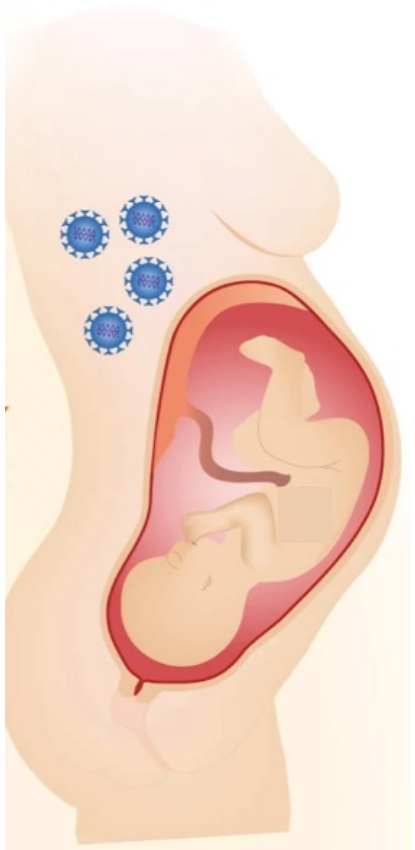
Periodo incubación: 3-4 semanas

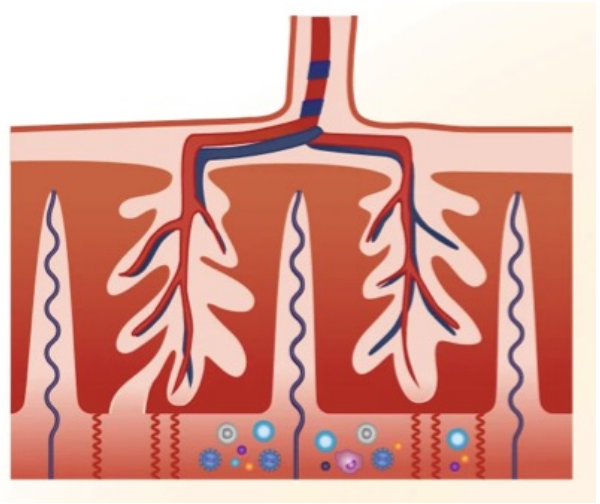
Capacidad de **latencia celular y reactivación**

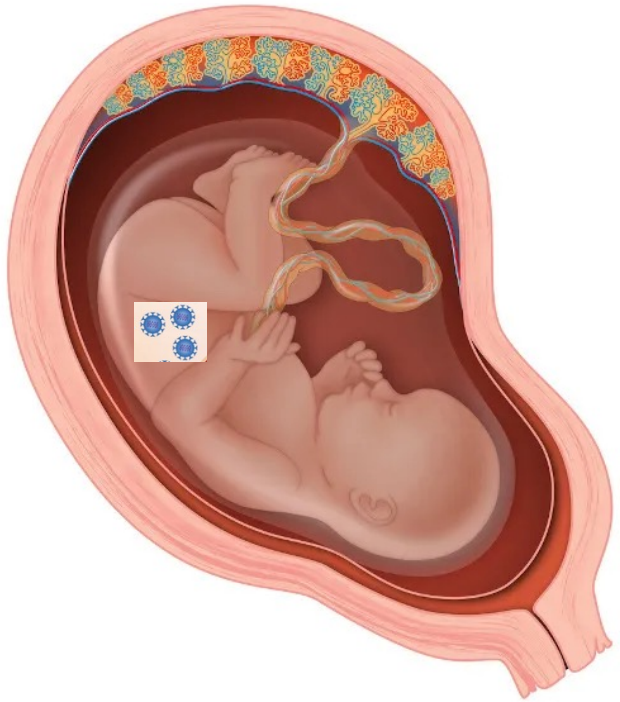
INFECCIÓN PRIMARIA (PRIMOINFECCIÓN)	INFECCIÓN SECUNDARIA (REACTIVACIÓN O REINFECCIÓN)
Pico de viremia a las 7-12 sem	Nivel bajo de replicación

Virología

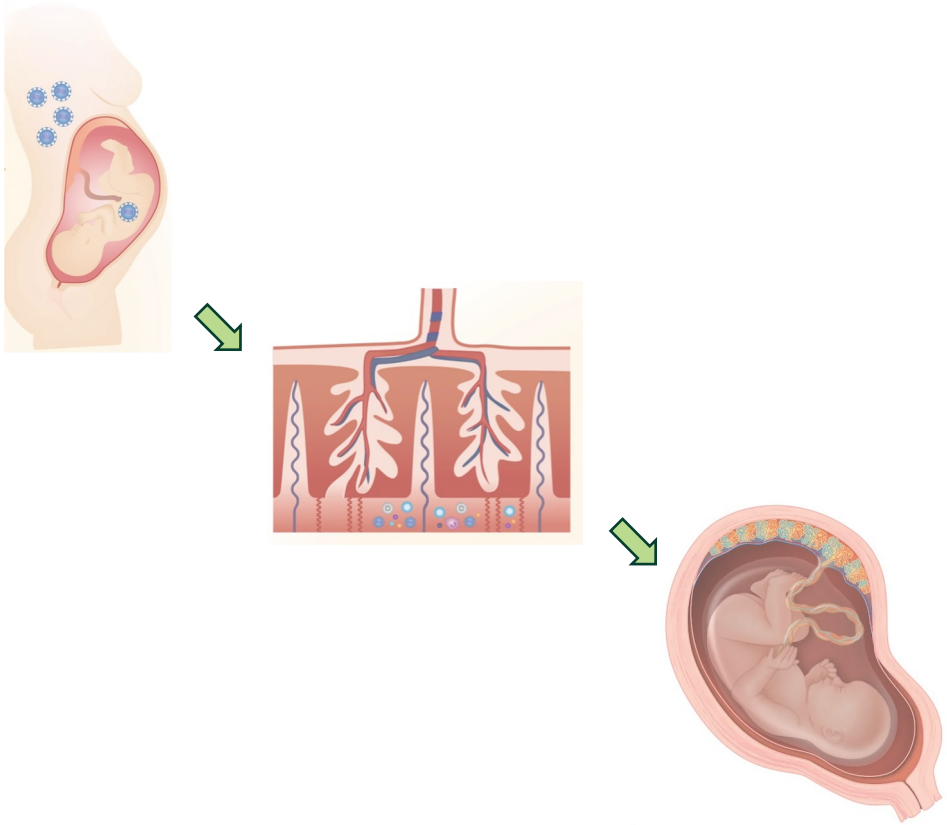
7 semanas

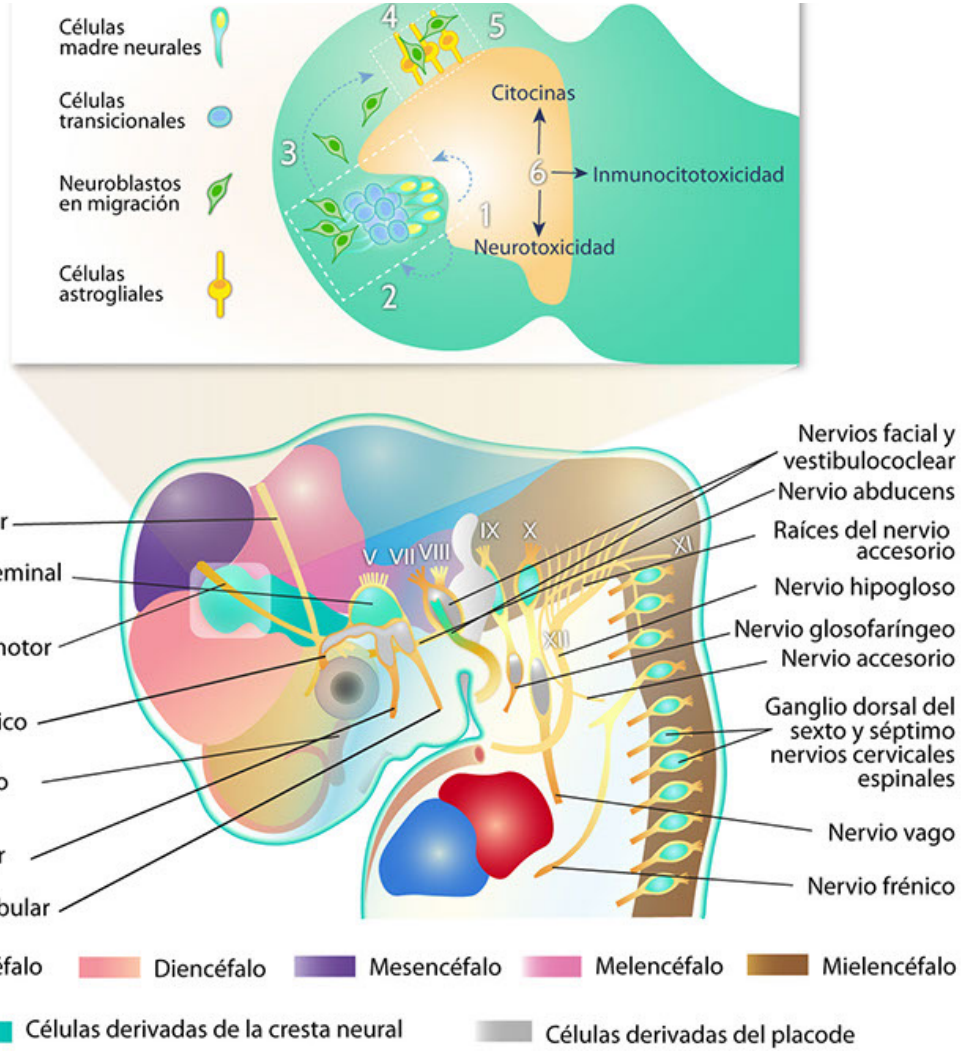






Virología




Células madre neurales
Células transicionales
Neuroblastos en migración
Células astrogliales
Citocinas
Inmunocitotoxicidad
Neurotoxicidad
Nervio troclear
Ganglión trigeminal
Nervio oculomotor
Nervio oftálmico
Bulbo olfatorio
Nervio maxilar
Nervio mandibular
Nervios facial y vestibulococlear
Nervio abducens
Raíces del nervio accesorio
Nervio hipogloso
Nervio glosofaríngeo
Nervio accesorio
Ganglio dorsal del sexto y séptimo nervios cervicales espinales
Nervio vago
Nervio frénico
Telencéfalo
Diencéfalo
Mesencéfalo
Melencéfalo
Mielencéfalo
Células derivadas de la cresta neural
Células derivadas del placode

Transmisión

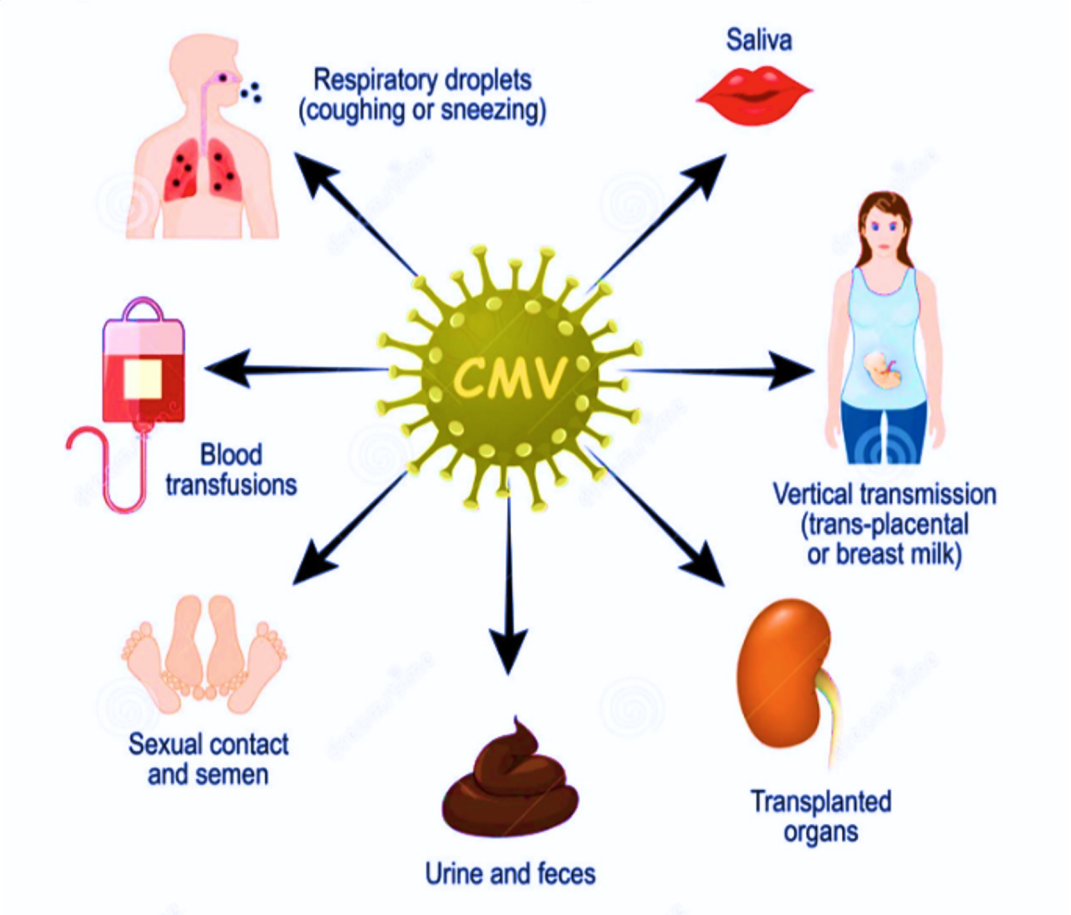


Table 1. Comparison of the Proportions of Infected Neonates Following a Primary Infection in the First Trimester

Inter-pregnancy Interval	Number of cCMV Following Maternal PI in T1	Number of Neonates	RR (95% CI)
0–1 year	2	240	8.9 (2.0–39.8)
1–2 years	9	369	26 (10.8–62.3)
2–3 years	1	213	5 (.65–38.4)
>3 years	0	149	NA
0–2 years	11	609	19 (8.37–44.18)
0 to >3 years	12	971	24 (9.07–64.1)

Leruez-Ville et al., CID 2020

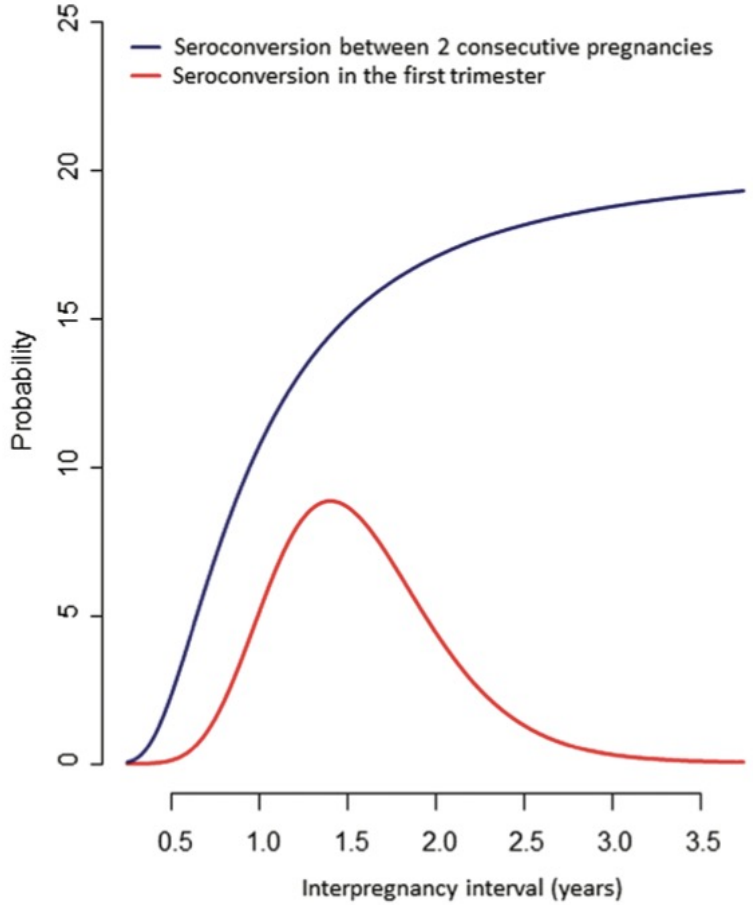


Figure 2. Model of the seroconversion rate and the primary infection rate in the first trimester, according to the inter-pregnancy interval.

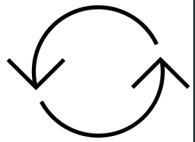
Importancia medidas higiénicas

ÚNICA MEDIDA PREVENTIVA

- Buena **higiene personal (lavado de manos)**
- **Evitar dar besos en la boca o en la mejilla** en menores de 6 años
- Evitar **compartir comida, bebidas o utensilios orales**
- **Limpiar las superficies** en contacto con orina o saliva de niños

7,6 % → 1,2 %

Transmisión



INFECCIÓN SECUNDARIA

0,5 – 3%

MOMENTO DE LA INFECCIÓN	TV	Afectación neurológica o IME	Recién nacido sintomático	Hallazgos ecográficos	Pérdida auditiva y alteración neurodesarrollo
Pregestacional (10-12 sem preFUR)	5,5 %	No datos	No datos	No datos	No datos
Perigestacional (4 sem pre – 6 sem postFUR)	21%	28,8%	1,3 %	30%	No datos
1r Trimestre	36,8%	19,3 %	9,1%	10%	22,8%
2n Trimestre	40,3 %	0,9 %	0,3%	0,3%	0,1%
3r Trimestre	66,2 %	0,4%	0,4%	0,5%	0%

Chatzakis et al., AJOG 2020

Transmisión

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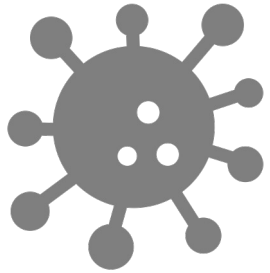
1r Trimestre	36,8%	19,3 %	9,1%	10%	22,8%
2n Trimestre	40,3 %	0,9 %	0,3%	0,3%	0,1%
3r Trimestre	66,2 %	0,4%	0,4%	0,5%	0%

Chatzakis et al., AJOG 2020

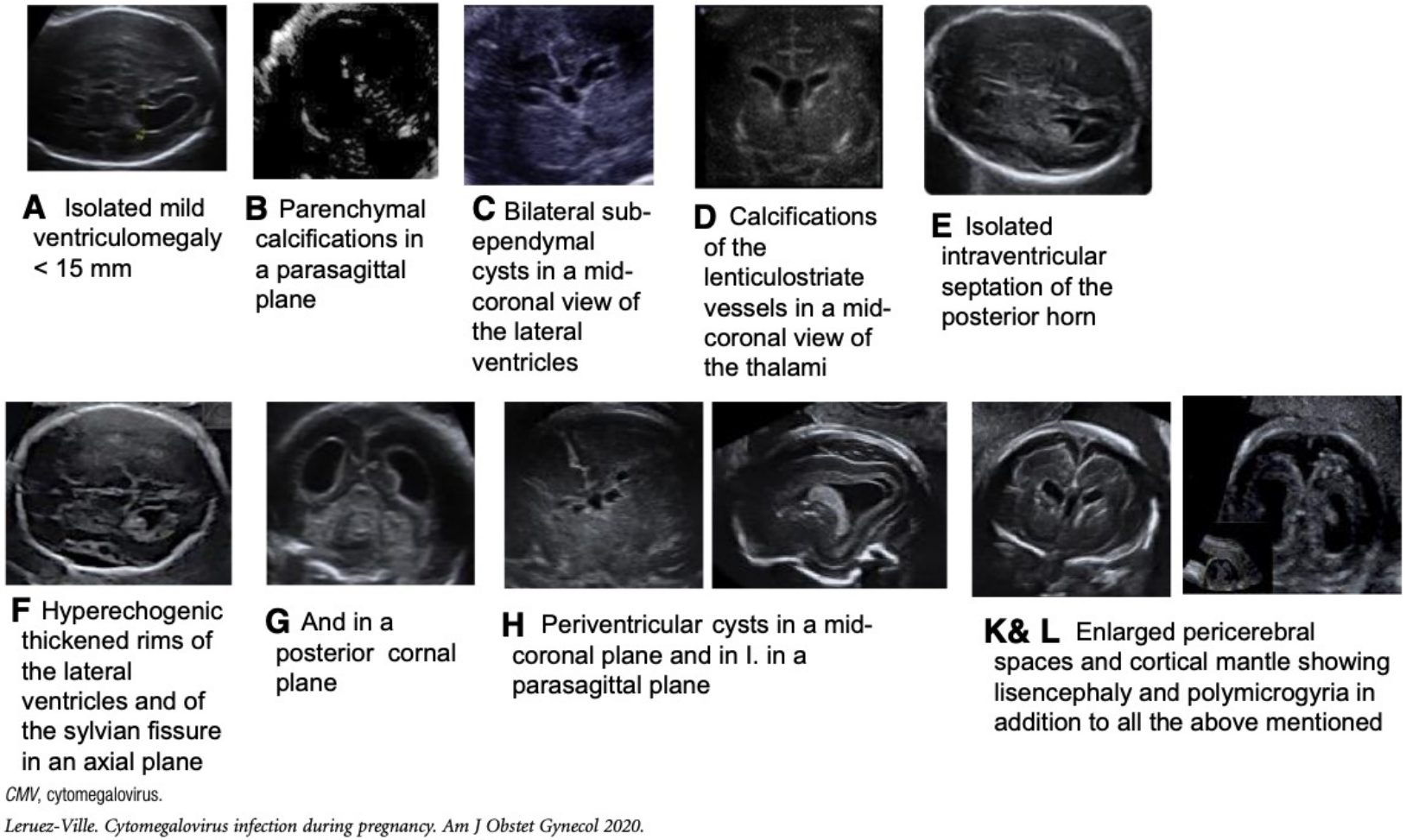
Clínica - GESTANTE

ASINTOMÁTICO



Ecografía - FETO

SNC



A Isolated mild ventriculomegaly < 15 mm

B Parenchymal calcifications in a parasagittal plane

C Bilateral sub-ependymal cysts in a mid-coronal view of the lateral ventricles

D Calcifications of the lenticulostriate vessels in a mid-coronal view of the thalami

E Isolated intraventricular septation of the posterior horn

F Hyperechogenic thickened rims of the lateral ventricles and of the sylvian fissure in an axial plane

G And in a posterior cornal plane

H Periventricular cysts in a mid-coronal plane and in I. in a parasagittal plane

K& L Enlarged pericerebral spaces and cortical mantle showing lisencephaly and polymicrogyria in addition to all the above mentioned

CMV, cytomegalovirus.

Leruez-Ville. Cytomegalovirus infection during pregnancy. Am J Obstet Gynecol 2020.

TABLE 2
Ultrasound findings in fetal infection with CMV in the literature

Variables	Liesnard et al, 2000[17]	Enders et al, 2001[193]	Lipitz et al, 2002[35]	Azam et al, 2001[194]	Gouarin et al, 2002[195]	Benoist et al, 2008[98]	Guerra et al, 2008[196]	Lipitz et al, 2010[100]	Picone et al, 2013[19]	Leyder et al, 2016[197]	Enders et al, 2017[84]	Total
Number of cases of congenital CMV infection	55	57	51	20	30	73	154	38	60	61	38	637
Overall ultrasound findings	14	39	11	5	15	37	23	9	23	30	16	222 (35%)
SGA	5	12	6	0	10	7	4	2	8	1	1	**56 (9%)**
Hydrops	0	4	2	0	0	1	1	0	0	0	0	8 (1.2%)
Ascitis	0	15	0	2	1	3	0	0	5	0	1	27 (4.2%)
Pericardial effusion	0	3	0	0	0	1	0	0	3	1	0	8 (1.2%)
Pleural effusion	0	0	1	0	0	0	0	0	0	0	0	1 (<1%)
Skin edema	0	2	0	0	0	0	0	0	0	0	0	2 (<1%)
Hyperechogenic bowel	8	2	3	1	6	19	10	5	8	11	9	**82 (13%)**
Hepatomegaly splenomegaly	1	3	0	1	0	10	1	1	3	1	3	24 (3.8%)
Liver calcifications	**0**	**0**	**1**	**0**	**0**	2	0	0	1	2	2	8 (1.2%)
Placentomegaly	0	2	0	1	0	2	0	0	3	2	3	13 (2.0%)
Oligohydramnios /hydramnios	1	5	4	0	0	5	0	0	0	4	3	22 (3.4%)
Polyhydramnios	1	1	1	0	0	1	0	0	1	0	0	5 (<1%)
Others extracerebral findings[a]	0	2	0	0	0	2	1	0	3	0	2	11 (1.7%)
Microcephaly	2	11	0	1	5	7	0	0	9	2	0	**37 (6%)**
Hydrocephaly	2	9	0	0	2	13	0	0	0	0	0	26 (3.6%)
Ventriculomegaly	1	7	4	1	3	2	10	0	6	2	3	**39 (6.1%)**
Cerebral calcification(s)	0	NA	2	0	9	13	0	0	9	4	0	**37 (6.3%)** (37/580)
Hyperechogenic periventricular halo	0	0	0	0	0	0	1	0	4	4	10	19 (3%)
Subependymal cysts	0	0	0	0	0	5	0	1	5	0	0	11 (1.7%)
Abnormal gyration	0	0	0	0	0	1	0	0	4	0	0	5 (<1%)
LSV	0	0	0	0	0	0	0	1	2	0	0	3 (<1%)
Other brain structural abnormalities[b]	1	10	1	0	0	3	0	3	1	6	0	36 (5.6%)

The most frequent symptoms are indicated in bold.

CMV, cytomegalovirus; *LSV*, lenticulostriate vessel; *SGA*, small for gestional age.

[a] Others extracerebral findings are hyperechogenic kidneys, hydronephrosis, cardiomegaly, and club foot; [b] Other brain structures abnormalities are temporal cyst; irregular ventricular wall, holoprosencephaly, cystic occipital lesion; small cyst in parietal lobe periventricular cysts, cerebral; and cerebellar hypoplasia, choroid plexus cyst,

Leruez-Ville. Cytomegalovirus infection during pregnancy. Am J Obstet Gynecol 2020.

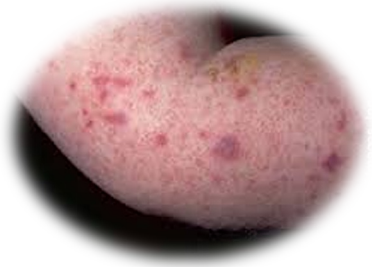
PEG / CIR

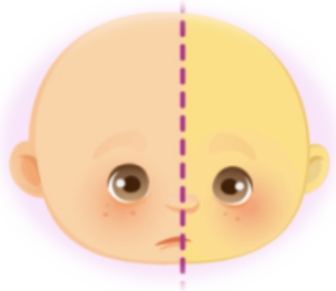
Hiperecogenicidad intestinal

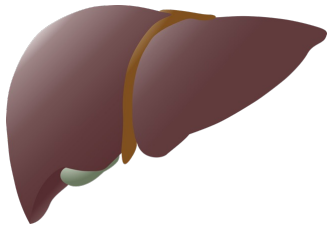
Microcefalia

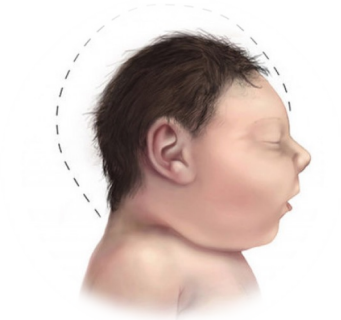
Clínica – Recién nacido

≈ 15 %









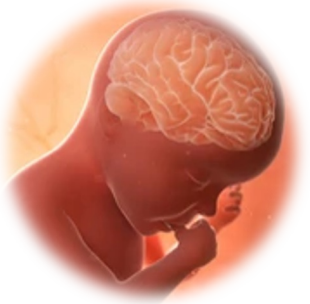


Tabla 4. Definiciones operacionales, hallazgos clínicos y de laboratorio más frecuentes en RN con CMVc

Signos clínicos	Definición/Comentar	Frecuencia de presentación
Petequias o púrpura Exantema tipo "*blueberry muffin*"	Al nacer o en las primeras horas de vida, pueden persistir por varias semanas Secundario a focos de eritropoyesis extramedular intradérmica	50-75%
Ictericia	Puede estar presente desde el primer día de vida	40-70%
Hepato-esplenomegalia	Buscar dirigidamente al examen físico	60%
Pequeño para la edad gestacional	Peso de nacimiento menor al p10	40-50%
Microcefalia	Perímetro cefálico < 2 DS para la EG	21-50%
Signos neurológicos	Letargia e hipotonía Crisis convulsivas Reflejo de succión pobre	30% 7-20% 5-10%
Coriorretinitis	Evaluado dirigidamente por oftalmólogo	10-20%
Hallazgos de laboratorio		
Aumento de transaminasas	GPT > 80 UI/L	83%
Hiperbilirrubinemia conjugada	Bilirrubinemia directa > 2 mg/dL	81%
Hemograma	Trombocitopenia: recuento plaquetas < 100.000/mm^3 Anemia: hematocrito < 40% 0-7 días, < 35% entre los 8-14 días y < 30% entre los 15 a 28 días de vida Neutropenia: RAN < 1.500 céls/mm^3 Neutropenia profunda: RAN < 500 céls/μL	70% 5-10%
LCR	Proteinorraquia > 120 g/dL Presencia de una RPC-CMV positiva en LCR	46% 6-20%*

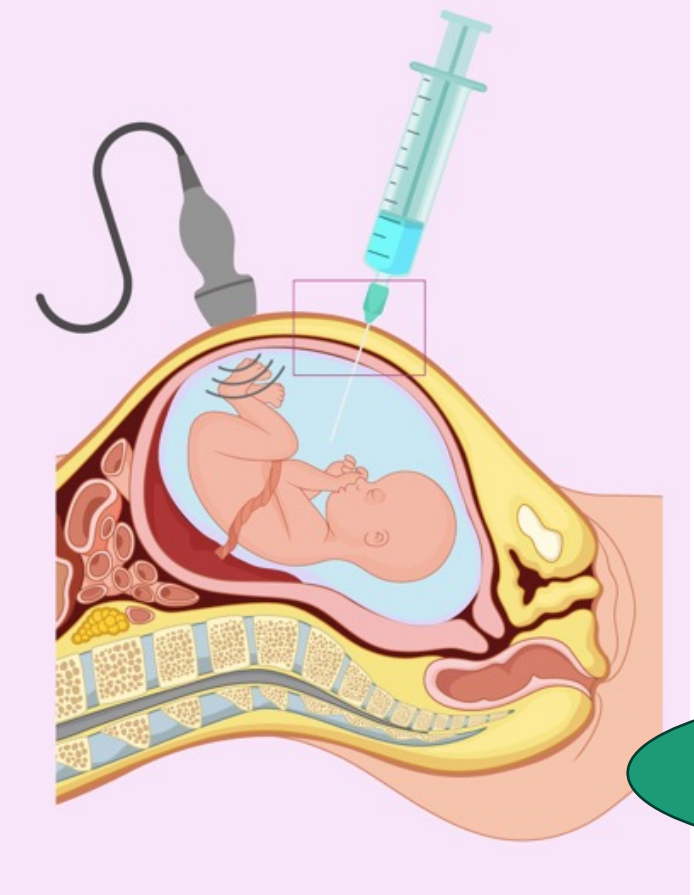
Abreviaturas: CMV: citomegalovirus; RPC: reacción de polimerasa en cadena; LCR: líquido cefalorraquídeo, RAN: recuento absoluto de neutrófilos. Adaptado de: Boppana SB y cols, Clin Infect Dis. 2013;57 (Suppl 4):S178-81. Boppana SB y cols. Pediatr Infect Dis J 1992; 11:93–9.*

Diagnóstico - gestante

AVIDEZ INTERMEDIA ?

ANTICUERPOS CMV	Avidez IgG	Interpretación
IgM + y IgG -	No aplicable	Puede ser un **falso positivo** (90%) a causa de otro virus, enfermedad autoinmune o métodos de laboratorio
IgM + y IgG +	Bajo	**Infección reciente (< 3-4 meses)** - La seroconversión es el diagnóstico de infección primaria
	Alto	**Infección secundaria vs pasada (>4-5 meses)** - Un aumento significativo (> x2) de los títulos de IgG entre dos muestras separadas 2-3 semanas sugiere reactivación o reinfección
IgM – y IgG +	Alto	**Infección pasada (>4-5 meses)** (vs infección secundaria) - El no aumento de forma significativa de los títulos de IgG nos sugiere descartar una reactivación o reinfección
	Bajo	Poco claro, ya que todos los estudios de validación de la avidez son con IgM positiva

Diagnóstico - feto



- Sospecha **serológica** (IgM y IgG +)
- **Sintomatología** de la gestante compatible no atribuible a otra infección
- **Contacto de riesgo**
- **Hallazgos ecográficos o de la RMN**
- **CIR precoz** (PFE <p3 y <28 SG)
- **Pliegue nucal aumentado persistente** (>p99 y >16 SG) con cariotipo / array normal

8 sem infección
≥ 17 SG

S 92%
E 98-100%

Cribado serológico universal

1. ENFERMEDAD

- Clínicamente importante ✓
- Prevalente ✓
- Bien definida ✓

2. CRIBADO

- Válido ✓
- Inocuo ✓

3. INTERVENCIÓN

- Efectiva
- Seguro
- Aplicable

Tratamiento – prevención secundaria

Randomized Controlled Trial > Lancet. 2020 Sep 12;396(10253):779-785.
doi: 10.1016/S0140-6736(20)31868-7.

Valaciclovir to prevent vertical transmission of cytomegalovirus after maternal primary infection during pregnancy: a randomised, double-blind, placebo-controlled trial

Keren Shahar-Nissan [1], Joseph Pardo [2], Orit Peled [3], Irit Krause [3], Efraim Bilavsky [3], Arnon Wiznitzer [2], Eran Hadar [2], Jacob Amir [2]

Valaciclovir 8 gr / día
(posología: 4gr/12h)

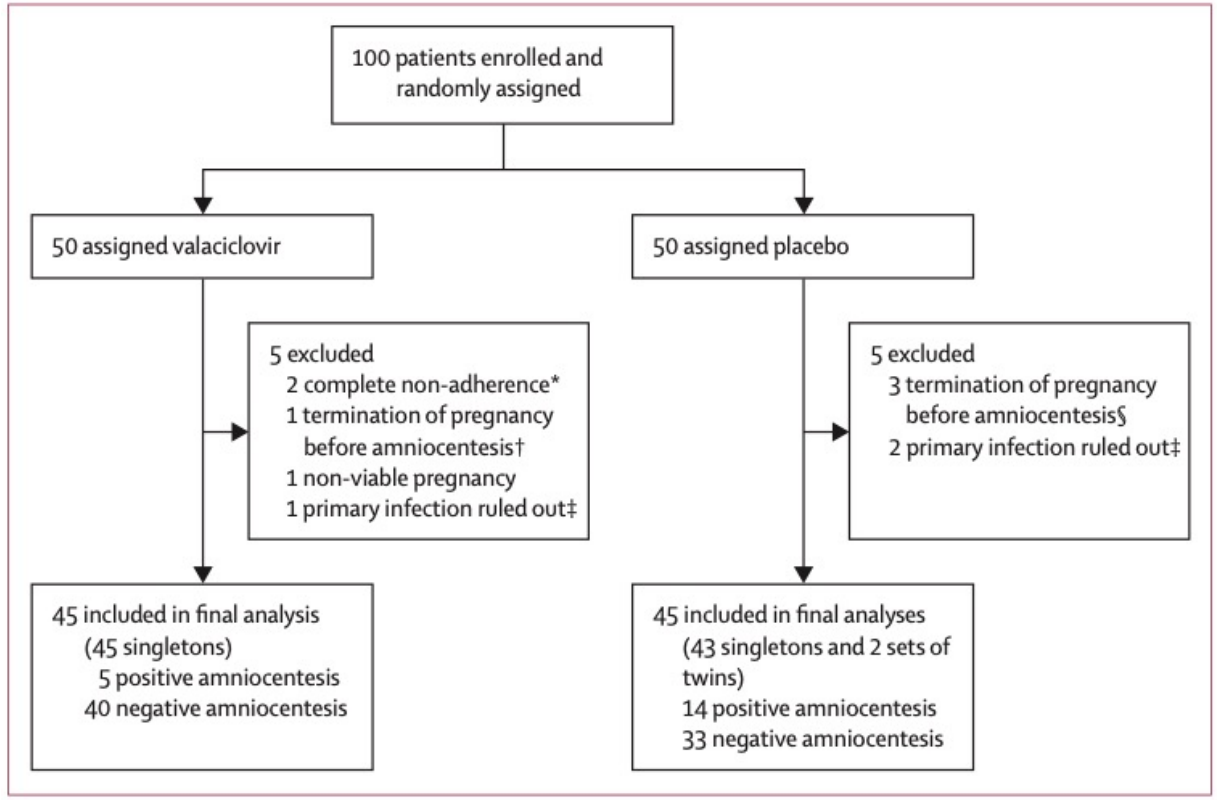


Figure 1: **Trial profile**
*Refusal to swallow the study drug. †Because of fetal anomalies suggesting a genetic disease (pathological report confirmed trisomy 18). ‡Falsely interpreted cytomegalovirus serology. §Without findings consistent with fetal cytomegalovirus infection.

Tratamiento – prevención secundaria

Efectivo

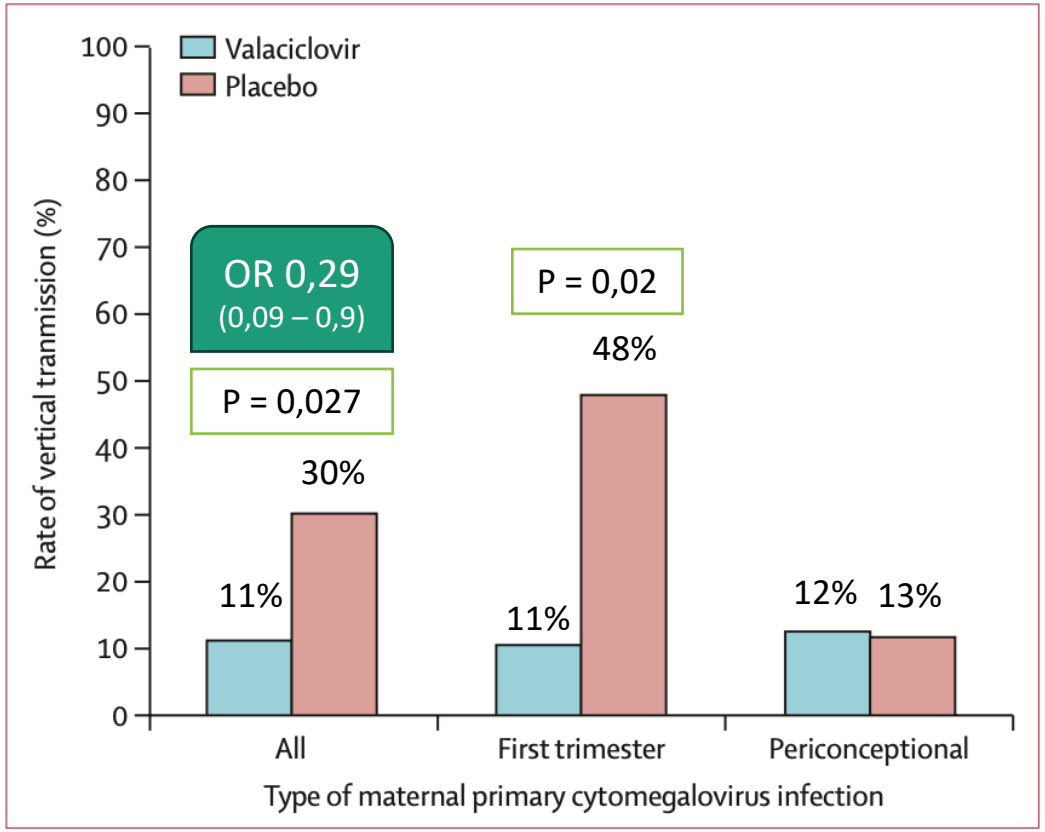


Figure 2: **Rate of vertical transmission among study participants**

POSTNATAL

VALACICLOVIR

1 pérdida auditiva

1 quiste subependimario

PLACEBO

5 pérdida auditiva

OR 0,38
(0,09 – 1,56)

Tratamiento – prevención secundaria

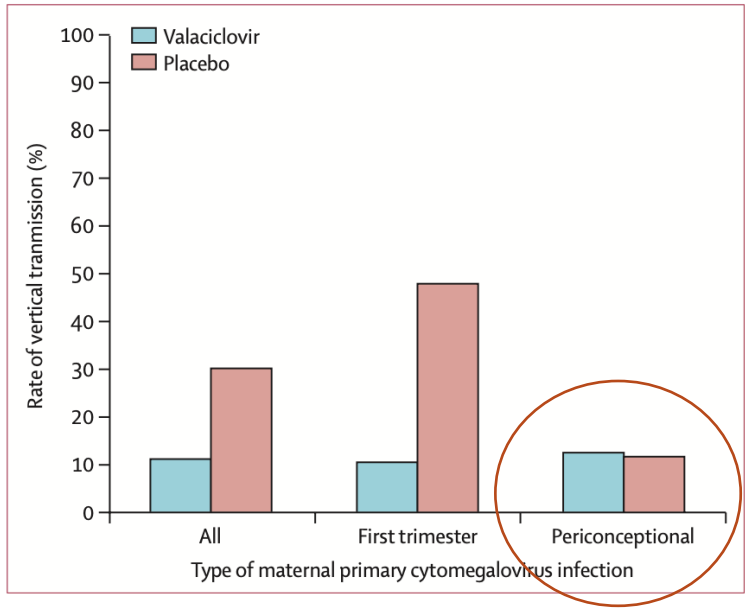


Figure 2: **Rate of vertical transmission among study participants**

	Placebo			Valaciclovir			Total		
	First trimester (n=23)	Periconceptual (n=24)	p value	First trimester (n=19)	Periconceptual (n=26)	p value	First trimester (n=42)	Periconceptual (n=50)	p value
Time, days	41·09 (12·89)	66·50 (18·00)	<0·0001	43·84 (14·16)	60·58 (19·29)	0·0026	42·33 (13·38)	63·42 (18·73)	<0·0001

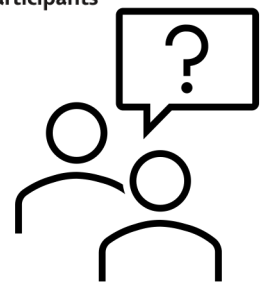
Data are mean (SD), unless otherwise indicated.

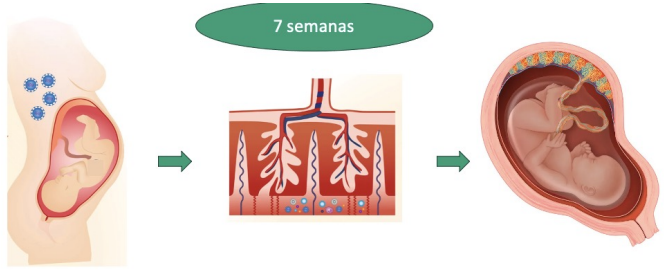
Table 2: **Time from maternal infection to treatment initiation, by timing of maternal infection**

	Placebo				Valaciclovir			
	Negative (n=33)	Positive (n=14)	Total (n=47)	p value	Negative (n=40)	Positive (n=5)	Total (n=45)	p value
Time, days	58·76 (21·36)	43 (11·27)	54·06 (20·16)	0·013	50·75 (17·63)	75·60 (16·71)	53·51 (19·06)	0·0047

Data are mean (SD), unless otherwise indicated.

Table 3: **Time from maternal infection to treatment initiation, by amniocentesis result**





Tratamiento – prevención secundaria

Efectivo

Ultrasound Obstet Gynecol 2021; 58: 576–581
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Secondary prevention of congenital cytomegalovirus infection with valacyclovir following maternal primary infection in early pregnancy

V. FAURE-BARDON[1,2,3], J. FOURGEAUD[2,3,4], J. STIRNEMANN[1,2,3], M. LEREUZ-VILLE[2,3,4] and Y. VILLE[1,2,3]

Table 1 Characteristics of 65 pregnant women with primary infection with cytomegalovirus in early pregnancy who were treated with valacyclovir (VACV) and 65 matched, untreated controls

Characteristic	*Untreated controls*	*Treated with VACV*	P*
Periconceptional MPI	26 (40)	28 (43)	0.85
GA at amniocentesis (weeks)	18.30 (17.60–19.30)	17.60 (17.10–18.10)	< 0.001
Duration of VACV therapy (days)	—	35 (26–54)	—
GA at initiation of VACV therapy (weeks)	—	12.71 (10.00–13.86)	—
Vertical transmission rate†			
Overall	19 (29)	8 (12)	0.029
Following periconceptional MPI	2/26 (8)	1/28 (4)	0.60
Following first-trimester MPI	17/39 (44)	7/37 (19)	0.027

Data are given as *n* (%), median (interquartile range) or *n*/*N* (%). *Wilcoxon rank-sum test or Fisher's exact test. †Transmission defined by positive result on polymerase chain reaction analysis of amniotic fluid. GA, gestational age; MPI, maternal primary infection.

Efectivo

Tratamiento – prevención secundaria

Revised protocol for secondary prevention of congenital cytomegalovirus infection with valaciclovir following infection in early pregnancy

Amir et al., 2023 | *Clinical Infectious Diseases*

IDSA Infectious Diseases Society of America

A previous randomized placebo-controlled study found valaciclovir to be effective in reducing the rate of vertical cytomegalovirus transmission in mother infected in the first trimester, but not in the periconception period. The aim of the present study was to evaluate valaciclovir efficacy with earlier treatment initiation.

- **Treatment was initiated up to 9 weeks from the presumed time of infection in women infected during the periconception period. The primary endpoint was the rate of vertical cytomegalovirus transmission.**

Among 178 women who completed valaciclovir treatment, amniocentesis was positive for cytomegalovirus in 14 women (7.9%) compared with 14 of 47 (30%) in the placebo arm ($P < .001$). The proportion of positive amniocentesis in the valaciclovir was significantly lower than the placebo arm both among women infected in the first trimester (14/119 vs 11/23; odds ratio [OR] = 0.15; 95% confidence interval [CI]: .05–.45, $P < .001$), as well as among those infected in the periconception period (0/59 vs 3/24, OR = 0; 95% CI 0–.97, $P = .02$).

This study provides further evidence of the efficacy of valaciclovir in preventing vertical transmission of cytomegalovirus after primary maternal infection. Efficacy improved with earlier treatment.

Clinical Infectious Diseases — Full text not published yet, reference pending

Tratamiento – prevención secundaria

Efectivo

Ultrasound Obstet Gynecol 2023; 61: 436–444
Published online in Wiley Online Library (wileyonlinelibrary.com). DOI: 10.1002/uog.26136

Effectiveness and safety of prenatal valacyclovir for congenital cytomegalovirus infection: systematic review and meta-analysis

F. D'ANTONIO[1], D. MARINCEU[2], S. PRASAD[3] and A. KHALIL[3,4,5]

Table 4 Pooled odds ratios (OR) of risk of congenital cytomegalovirus infection in pregnancies treated compared to those not treated with prenatal valacyclovir (VCV) therapy, according to timing of maternal infection

Timing of infection	*Studies (n)[ref]*	*Fetuses affected: VCV vs no VCV (n/N)*	*Pooled OR (95% CI)*	I^2 *(%)*	P
All studies					
All maternal infections	3[7,8,11]	23/164 *vs* 49/161	0.37 (0.21–0.64)	0	< 0.001
Periconceptional infection	3[7,8,11]	5/67 *vs* 5/54	0.77 (0.21–2.80)	0	0.688
First-trimester infection	3[7,8,11]	17/91 *vs* 38/93	0.34 (0.15–0.74)	20.9	0.001
Second-trimester infection	1[8]	1/6 *vs* 6/13	0.020 (0.002–0.190)	—	0.001
Third-trimester infection	1[8]	0/0 *vs* 0/1	—	—	—
RCT					
All maternal infections	1[11]	5/45 *vs* 14/47	0.29 (0.10–0.90)	—	0.033
Periconceptional infection	1[11]	3/26 *vs* 3/24	0.91 (0.17–5.03)	—	0.917
First-trimester infection	1[11]	2/19 *vs* 11/23	0.13 (0.02–0.69)	—	0.002
Second-trimester infection	0	—	—	—	—
Third-trimester infection	0	—	—	—	—
Observational studies					
All maternal infections	2[7,8]	18/119 *vs* 35/114	0.40 (0.21–0.76)	0	0.001
Periconceptional infection	2[7,8]	2/41 *vs* 2/30	0.60 (0.08–4.42)	0	0.914
First-trimester infection	2[7,8]	15/72 *vs* 27/70	0.43 (0.20–0.90)	0	0.026
Second-trimester infection	1[8]	1/6 *vs* 6/13	0.020 (0.002–0.190)	—	0.001
Third-trimester infection	1[8]	0/0 *vs* 0/1	—	—	—

RCT, randomized controlled trial; ref, reference.

Tratamiento – prevención secundaria

Efectivo

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Effectiveness and safety of prenatal valacyclovir for congenital cytomegalovirus infection: systematic review and meta-analysis

F. D'ANTONIO[1], D. MARINCEU[2], S. PRASAD[3] and A. KHALIL[3,4,5]

Table 5 Pooled odds ratios (OR) of perinatal outcomes following maternal cytomegalovirus infection in pregnancies treated compared to those not treated with prenatal valacyclovir (VCV) therapy

Outcome	*Studies (n)[ref]*	*Fetuses affected: VCV vs no VCV (n/N)*	*Pooled OR (95% CI)*	I^2 *(%)*	P
Symptomatic infection	2[6,11]	11/65 *vs* 20/67	0.46 (0.18–1.14)	0	0.092
Asymptomatic infection	2[6,11]	54/65 *vs* 47/67	2.98 (1.18–7.55)	0	0.021
Perinatal death	2[6,11]	1/66 *vs* 1/71	1.15 (0.07–19.60)	0	0.923
Termination of pregnancy	2[6,11]	8/66 *vs* 18/71	0.40 (0.14–1.15)	0	0.089
Fetal anomaly at follow-up or at birth	3[6,8,11]	11/73 *vs* 16/91	1.04 (0.42–2.58)	0	0.934
Severe symptoms	2[6,11]	0/58 *vs* 0/57	0.91 (0.02–46.91)	—	0.965
Mild-to-moderate symptoms	2[6,11]	4/58 *vs* 0/57	4.62 (0.50–42.97)	0	0.179
Neurological symptoms	2[6,11]	2/58 *vs* 0/53	2.72 (0.27–27.41)	0	0.395
Hearing symptoms	2[6,11]	4/58 *vs* 5/53	0.93 (0.02–35.14)	0	0.970
Visual symptoms	2[6,11]	0/58 *vs* 0/53	0.91 (0.02–46.91)	—	0.965
Other symptoms	2[6,11]	2/58 *vs* 1/53	1.64 (0.13–21.10)	0	0.706

Tratamiento – prevención secundaria

Seguro

Ultrasound Obstet Gynecol 2023; **61**: 436–444
Published online in Wiley Online Library (wileyonlinelibrary.com). **DOI:** 10.1002/uog.26136

Effectiveness and safety of prenatal valacyclovir for congenital cytomegalovirus infection: systematic review and meta-analysis

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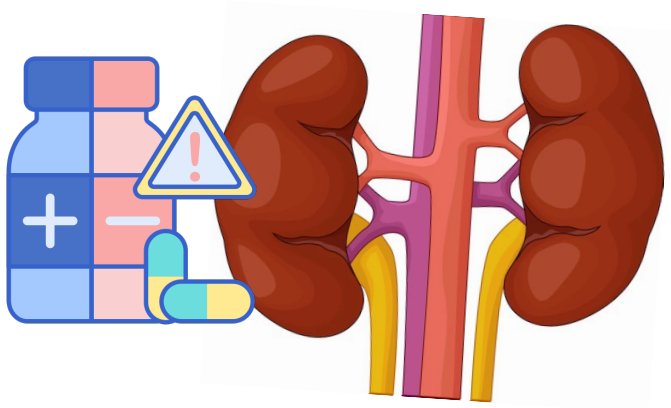

Posología: **2gr/6h**
AS hemograma, perfil renal y hepático
1º set + c/2 set

Table 6 Pooled proportions of incidence of significant maternal adverse events secondary to intake of valacyclovir in pregnancy

Event	*Studies (n)[ref]*	*Women affected (n/N)*	*Pooled proportion (% (95% CI))*	I^2 *(%)*
All severe adverse events	6[4–8,11]	5/210	3.17 (1.24–5.93)	0
Acute renal failure	6[4–8,11]	2/210	1.71 (0.41–3.39)	0
Acute hepatic failure	6[4–8,11]	0/210	0 (0–2.11)	0
Other effects	6[4–8,11]	3/210	1.91 (0.51–4.17)	0

Coste / Efectivo

Cribado serológico universal

Leaning towards *Cytomegalovirus* serological screening in pregnancy to prevent congenital infection: a cost-effectiveness perspective

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Table 2. Behavioural characteristics of pregnant women and the unit medical costs of CMV prenatal detection and treatment (tariffs from the French national health insurance system)

	Mean	Range	Calculations
Accounting for pregnant women's decision making			
Observed rates of termination of pregnancy in pregnant women with a confirmed diagnosis of fetal CMV	13%	6–19%	19/102 = 19%[25] 4/71 = 5.6%[31] 15/123 = 12%[32] Total 38/296 = 13%
Rate of uptake for amniocentesis among pregnant women	80%	NA	With no data available in the context of CMV, we used the rate of uptake for amniocentesis in the case of trisomy 21[33–37]
Unit cost in euros (tariffs from the French national health insurance system)			
CMV serology IgG and IgM	€22.95		
CMV IgG avidity testing	€27.00		
Amniocentesis	€68.58		
CMV PCR in amniotic fluid	€162.00		
Fetal ultrasound	€100.20		
Fetal cerebral MRI	€300.00		
Valaciclovir (8 g) per day (prescription price)	€11.84		
Consultation with a specialist physician	€30.00		

PCR, polymerase chain reaction.

Table 3. Costs and associated effectiveness of various strategies for prenatal CMV detection

Expected costs	No screening and no treatment		Screening			
			Treatment		No treatment	
	n	Cost (€)	*n*	Cost (€)	*n*	Cost (€)
CMV serology IgM + IgG at 7 and 12 weeks of pregnancy			1 000 000	35,891,100.00	1 000 000	35,891,100.00
Valaciclovir (8 g/day = 16 pills/day) from 10 to 20 weeks of gestation (70 days)			2222	1,841,593.60		
Amniocentesis and CMV PCR in amniotic fluid	103	23 749.74	2228	513,796.37	2228	513,796.37
Ultrasound and consultation every 2 weeks (nine in total)	101	118 351.80	245	287,202.46	639	748,754.07
MRI of fetal brain	101	30 300.00	245	73,528.53	639	191,693.31
Total costs		172 401.54		38,607,220.96		37,345,343.76
Expected outcomes	**Detected**	**Not detected**	**Detected**	**Not detected**	**Detected**	**Not detected**
No disabilities	20	320	123	19	319	19
Severe disabilities	66	211	100	15	262	15
Moderate disabilities	15	46	22	3	58	3
At least one disability	81	257	123	19	319	19
Total	101	577	245	37	639	37
Fetal congenital CMV screening detection rate	14.95%		94.15%		94.15%	
At the strategy level expected rate of newborns with congenital CMV and presenting						
Severe disabilities	100.0%		41.77%		100%	
Moderate disabilities	100.0%		41.77%		100%	
At least one disability	100.0%		41.77%		100%	

PCR, polymerase chain reaction.

Tratamiento – feto infectado

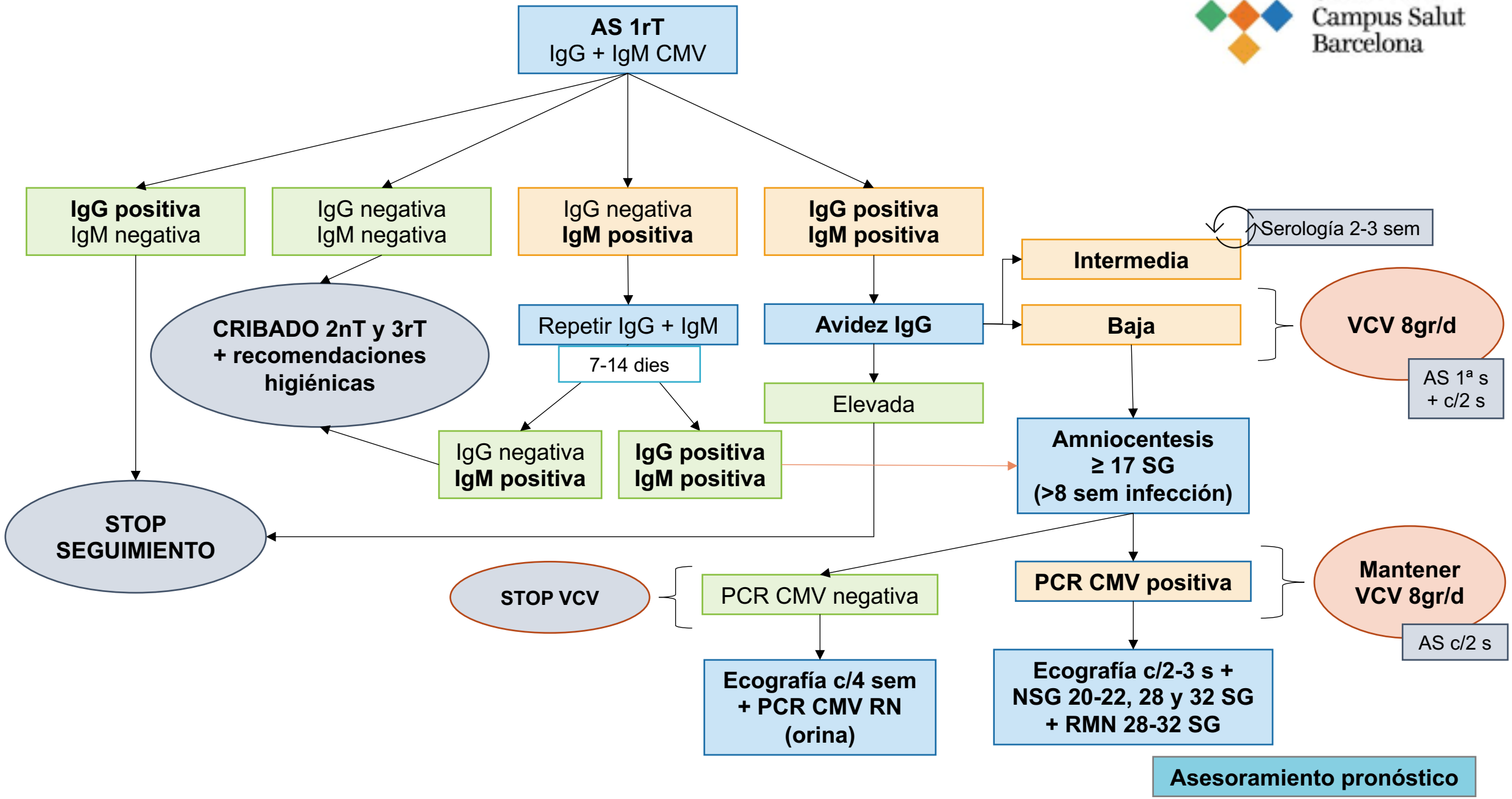
Valaciclovir 8 gr / día

Mal pronóstico

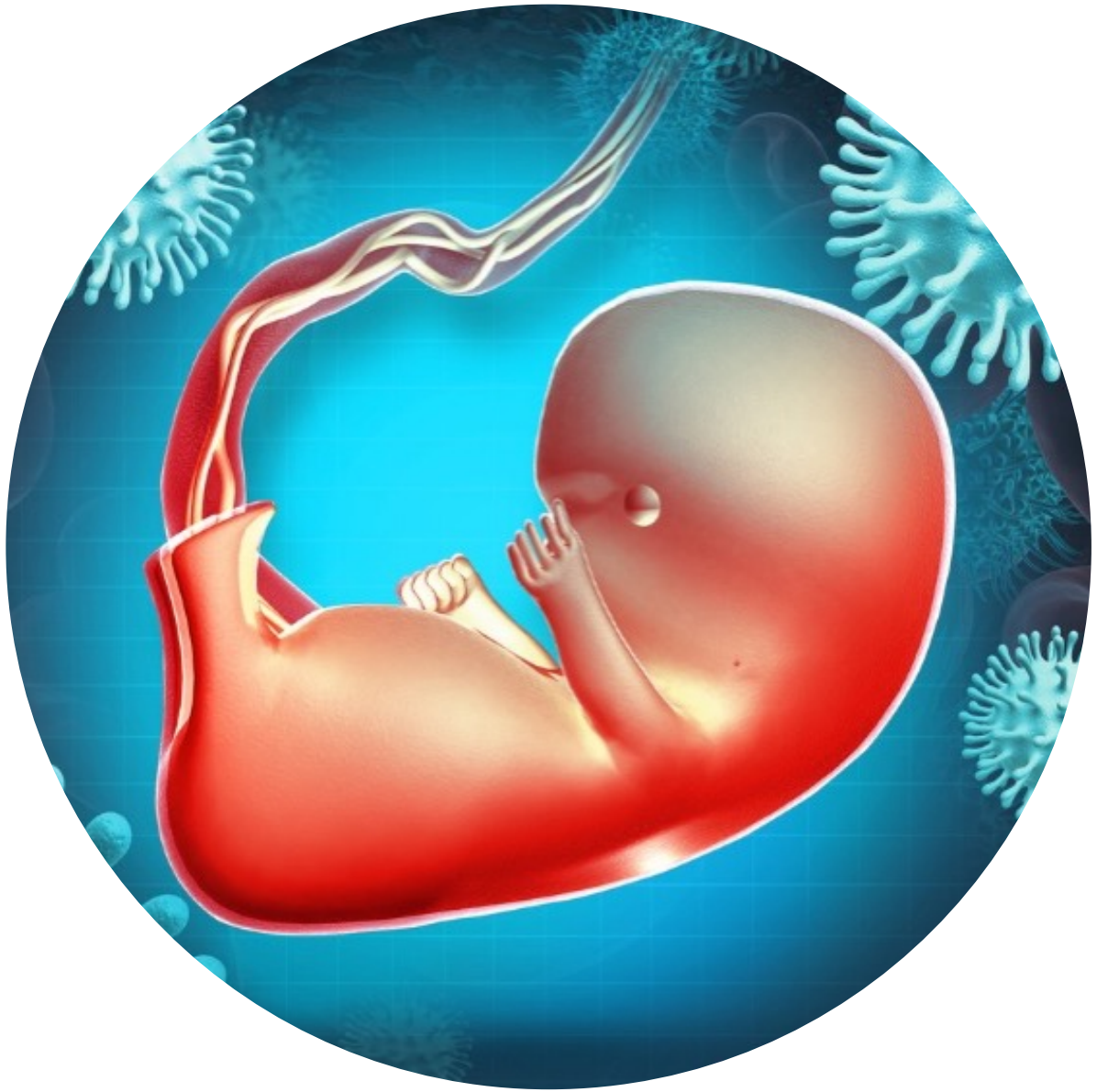
- Ventriculomegalia severa (>15mm), hidrocefalia
- Microcefalia (<-3DS)
- Aumento del espacio subaracnoideo
- Agenesia del cuerpo calloso
- Cerebelo hipoplásico
- Lesiones destructivas y hemorrágicas
- Anomalías de la sulcación y del patrón circunvolucional
- Hiperecogenicidad periventricular

Pronóstico incierto

- Ventriculomegalia leve (10-14,9mm)
- Calcificaciones aisladas
- Sinequias intraventriculares
- Vasos hiperecogénicos en los tálamos ("*candle lights*") → asocian exclusivamente a déficit auditivo.
- Pequeños quistes parenquimatosos aislados
- Incremento de la captación de señal en la sustancia blanca en la RMN


AS 1rT
IgG + IgM CMV
IgG positiva
IgM negativa
IgG negativa
IgM negativa
IgG negativa
IgM positiva
IgG positiva
IgM positiva
Serología 2-3 sem
Intermedia
Baja
VCV 8gr/d
AS 1ª s
+ c/2 s
CRIBADO 2nT y 3rT
+ recomendaciones
higiénicas
Repetir IgG + IgM
7-14 dies
Avidez IgG
Elevada
IgG negativa
IgM positiva
IgG positiva
IgM positiva
Amniocentesis
≥ 17 SG
(>8 sem infección)
STOP
SEGUIMIENTO
STOP VCV
PCR CMV negativa
PCR CMV positiva
Mantener
VCV 8gr/d
AS c/2 s
Ecografía c/4 sem
+ PCR CMV RN
(orina)
Ecografía c/2-3 s +
NSG 20-22, 28 y 32 SG
+ RMN 28-32 SG
Asesoramiento pronóstico

Gracias por la atención



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