Meningitis y Encefalitis

Microbiología II, Cátedra 2
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Meningitis Bacteriana

- Es el proceso inflamatorio que compromete las meninges blandas (piamadre - aracnoides) que se identifica por las modificaciones LCR (turbidez , aumento de proteínas , disminución de glucosa ,aumento de las células con > % PMN) .

- Generalmente va acompañado por compromiso del Encéfalo.

Morbimortalidad

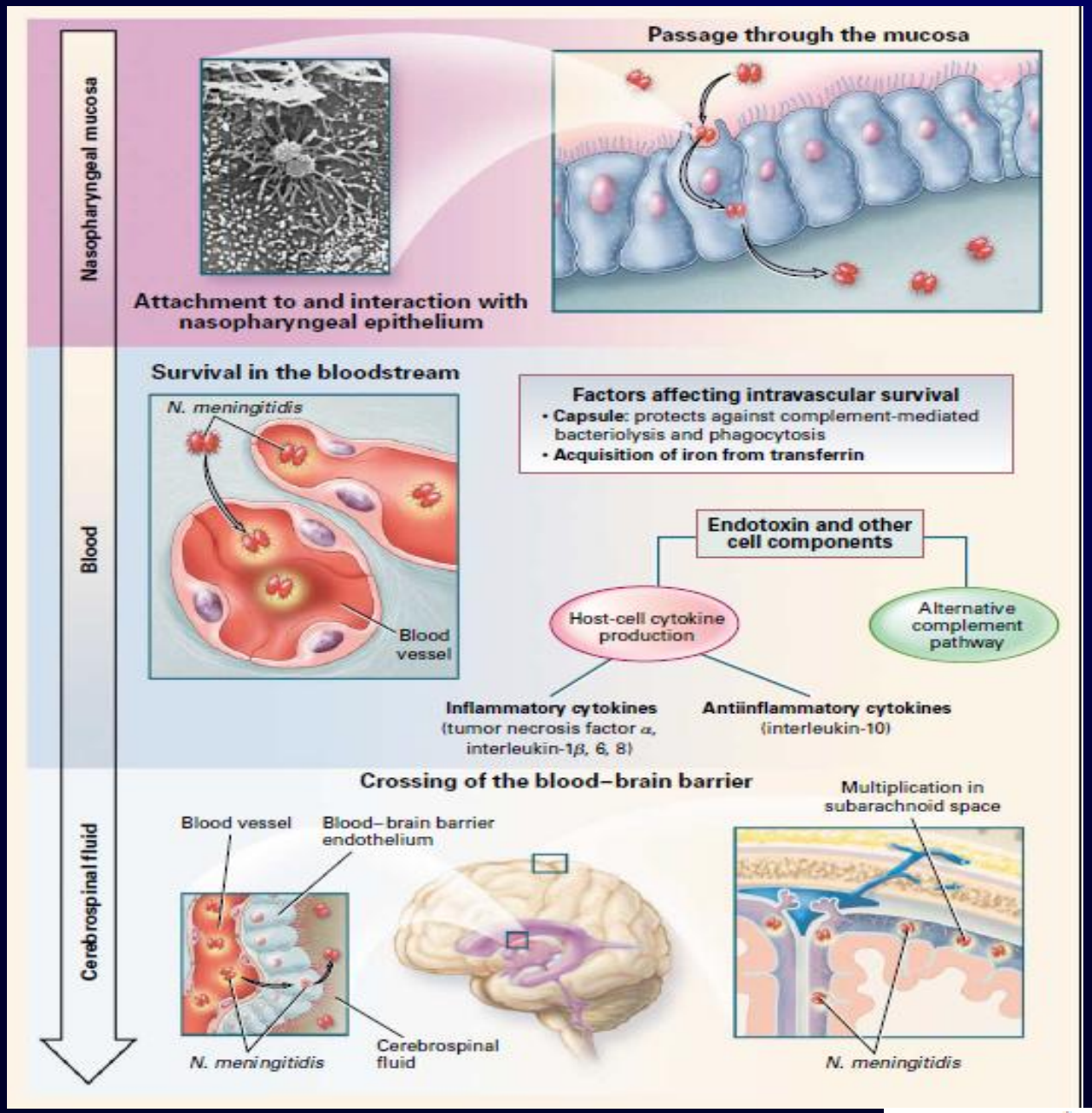
- Mortalidad: 5- 40%
- Secuelas: ~30% de sobrevivientes
- Secuelas neurológicas:
  - Daño auditivo: invasión directa del oído interno por la inflamación del espacio subaracnoideo
  - Hidrocéfalia obstructiva
  - Daño cerebral (déficit motor, retardo mental, convulsiones)

Meningitis bacteriana

Llegada de la bacteria al LCR

- Desde las vénulas de la nasofaringe (infección o colonización faríngea)
- Vía sanguínea (bacteriemia) mas frecuente
- Directa a través de un foco contiguo (foco adyacente intracraneano o de superficie: defectos congénitos de la duramadre, fracturas de craneo,sinusitis,absceso de cerebro)
- Inoculación por trauma o neurocirugía o procedimiento diagnósticos en el SNC.
- Metástasis sépticas (endocarditis bacteriana)
- Acompañando a otros microorganismo en la diseminación hematogena (síndrome de hiperinfectacion/diseminación por *strongyloides stercolaris)*

Enfermedad Meningococica



N Engl J Med, Vol. 344, No. 18 · May 3, 2001

Meningitis Bacteriana

Diseminación de *Neisseria meningitidis*

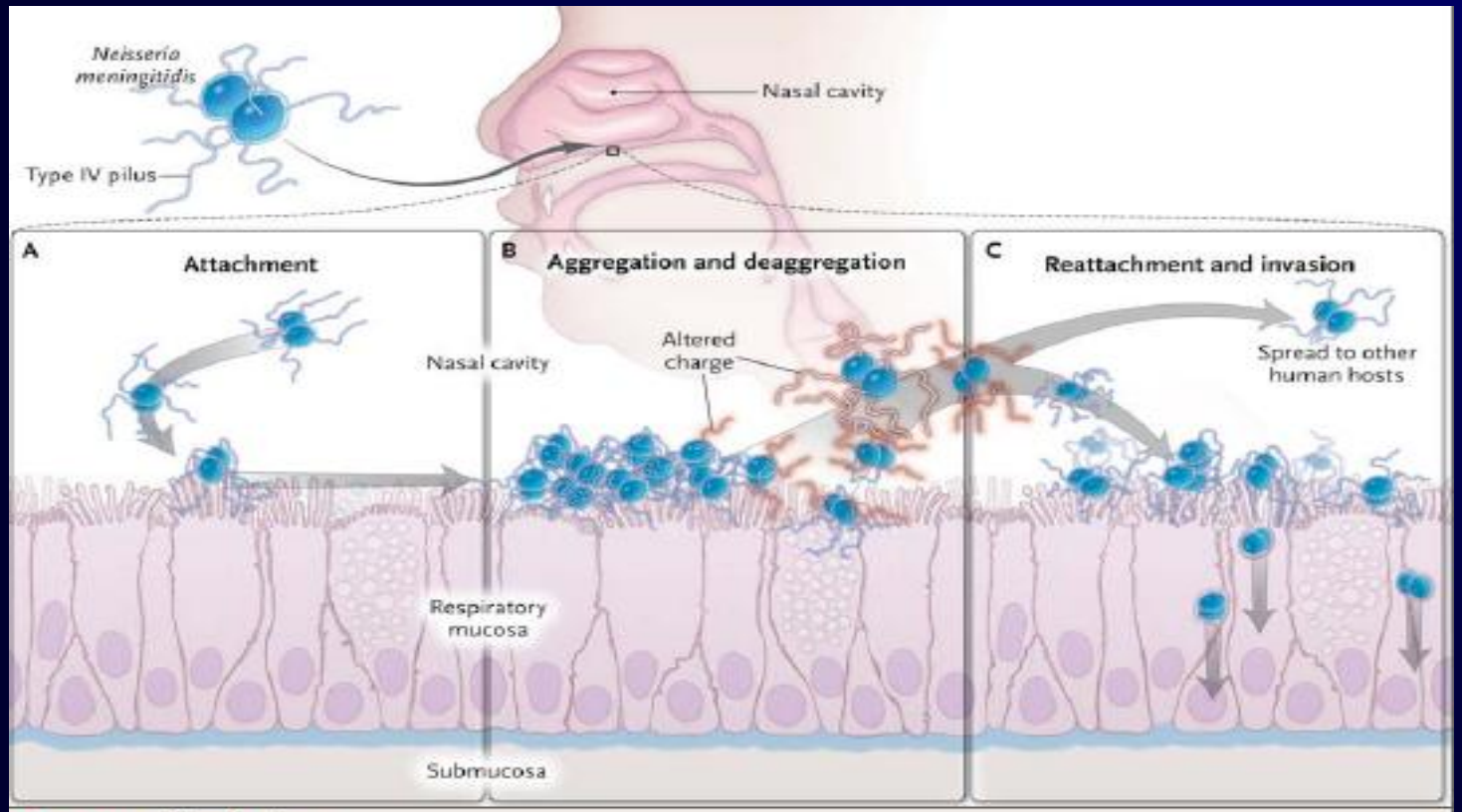


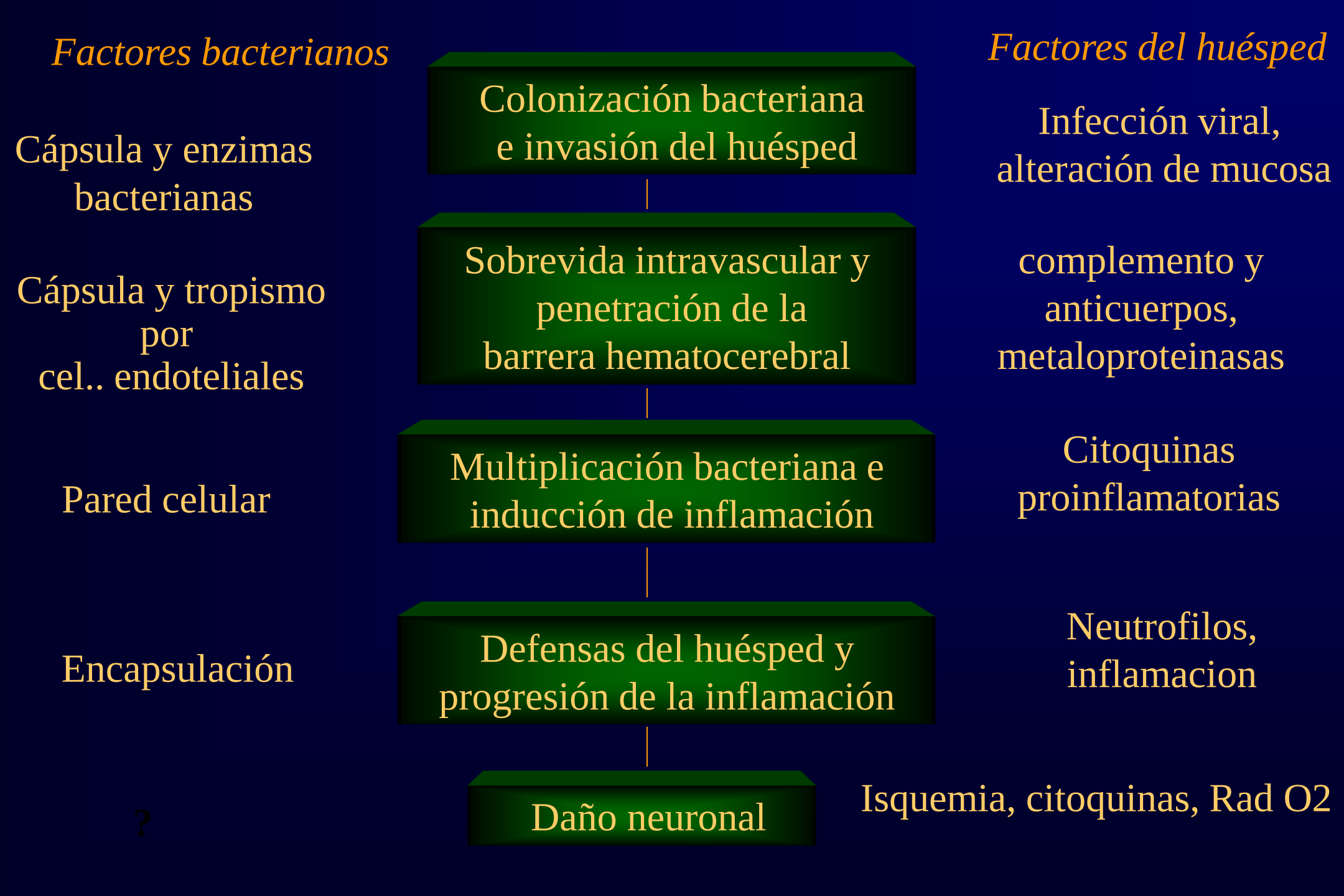
Figure 1. Prodding the Pilus.

Chamot-Rooke et al.[1] recently found that the initial step in the colonization of respiratory mucosa is attachment facilitated by type IV pili (Panel A). After attachment, the bacteria multiply and aggregate, but within 4 hours the expression of pilin phosphotransferase is enhanced; this enzyme modifies pili through phosphoglycerol, which alters the charge of pilin, the structural subunit of the pilus (Panel B). The altered charge, in turn, promotes the deaggregation of bacteria, which can then attach to new mucosal cells (including those of other human contacts) and invade the mucosal epithelium for systemic spread (Panel C).

N ENGL J MED 364;16 NEJM.ORG APRIL 21, 2011

Invasión no hematógena del SNC

- Ocurre en Situaciones en que se compromete la integridad de las barreras que rodean al cerebro:
  - -Otitis media
  - -Mastoiditis
  - -Sinusitis
  - -Malformaciones
  - -Trauma
  - -Neurocirugía


Factores bacterianos
Factores del huésped
Colonización bacteriana e invasión del huésped
Infección viral, alteración de mucosa
Cápsula y enzimas bacterianas
Sobrevida intravascular y penetración de la barrera hematocerebral
complemento y anticuerpos, metaloproteinasas
Cápsula y tropismo por cel.. endoteliales
Multiplicación bacteriana e inducción de inflamación
Citoquinas proinflamatorias
Pared celular
Defensas del huésped y progresión de la inflamación
Neutrofilos, inflamacion
Encapsulación
Daño neuronal
Isquemia, citoquinas, Rad O2
?

MENINGITIS BACTERIANA
PROCESO INFLAMATORIO

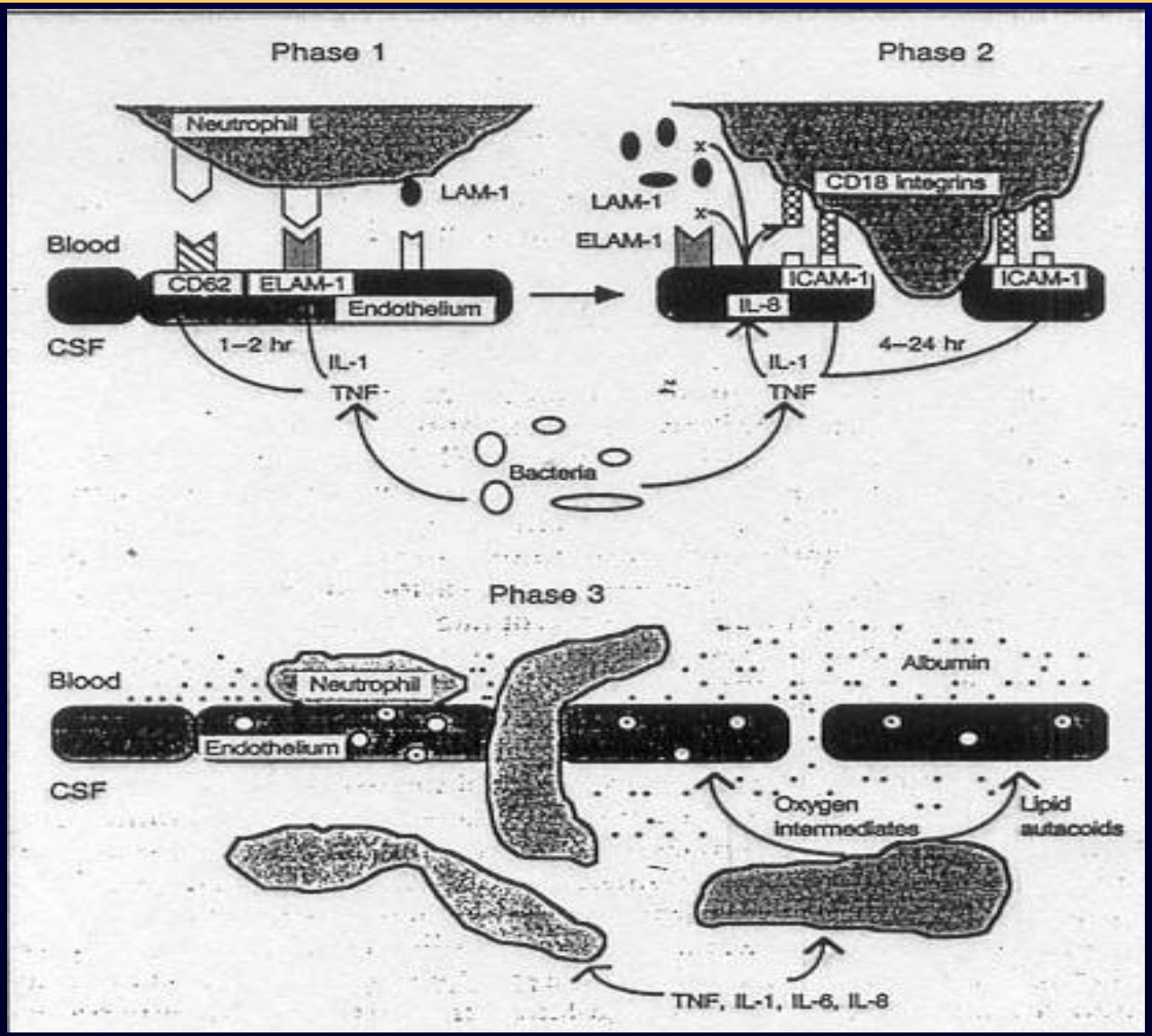
- La bacteria , los productos de la pared celular (acido teicoico y el pectidoglicano en bacterias Gram +) el lipido A (bacterias Gram -) ,liberados durante la multiplicación celular o por la lisis bacteriana producida por los ATB bactericidas inducen la producción de citocinas
- Las interleucina 1 - 6 - 8 y TNF alfa , secretadas por las celulas presentes en el SNC (endotelio / astroglia y macrófagos meníngeos), liberadas al LCR inducen el proceso inflamatorio y el daño de la barrera hemato-cerebral.

MENINGITIS BACTERIANA

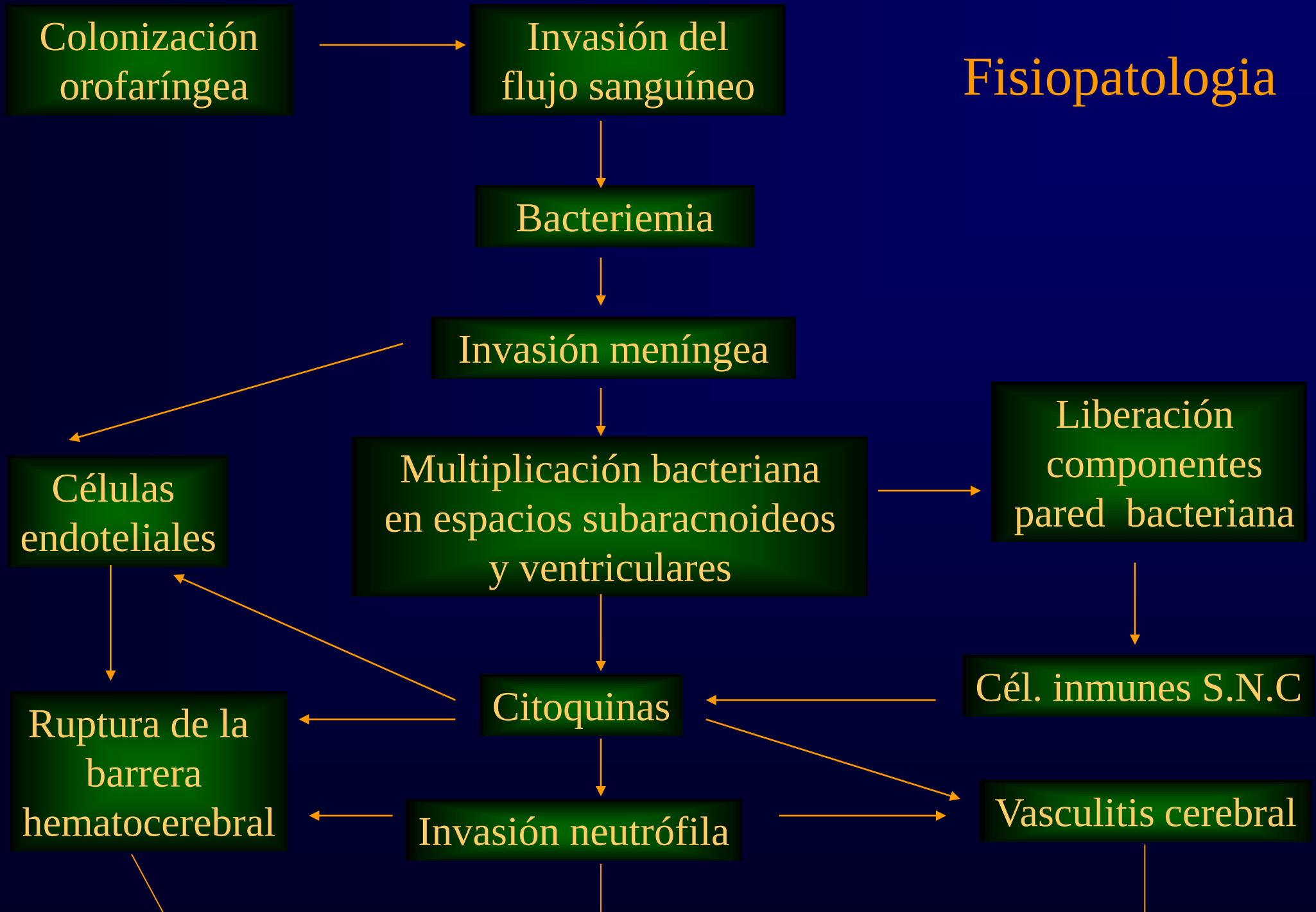
- Con la barrera hemato-cerebral intacta el transporte vesicular (proteinas) a través de la celulas endoteliales es minimo y la unión entre las celulas adyacentes es fuerte .
- Al generarse el proceso inflamatorio se daña la barrera hemato/cerebral , lo que produce aumento del transporte vesículas cargadas con albumina a través de las celulas endoteliales de las arteriolas meníngeas y se produce separación de las uniones intercelulares de las celulas endoteliales de las venulas meníngeas, dando origen al pasaje de albumina / celulas hacia el LCR .

Meningitis bacteriana

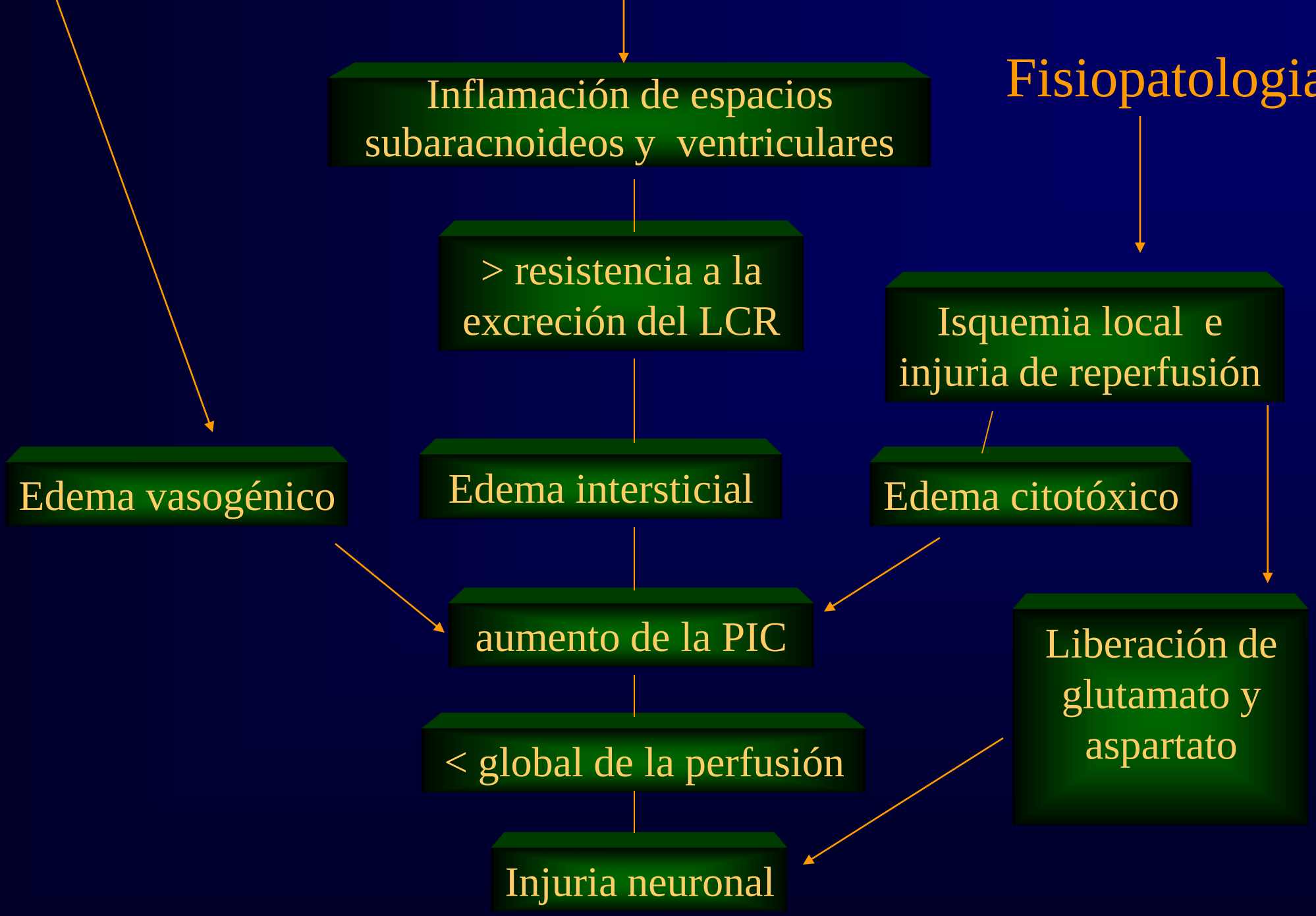
Fisiopatologia



Fisiopatologia

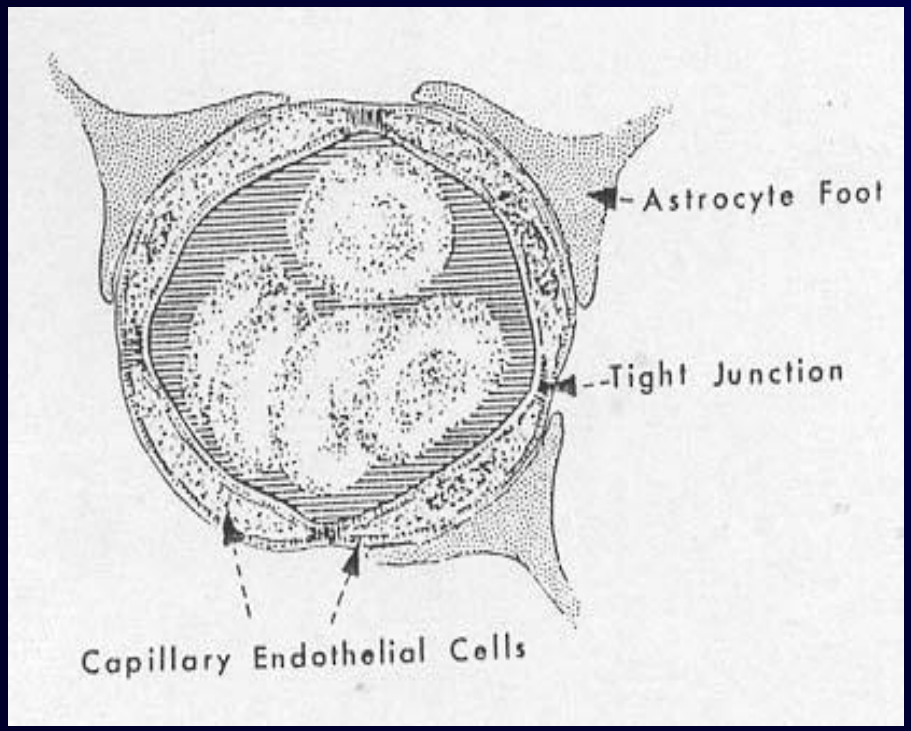


Fisiopatologia



Meningitis Bacteriana

Edema Vasogenico



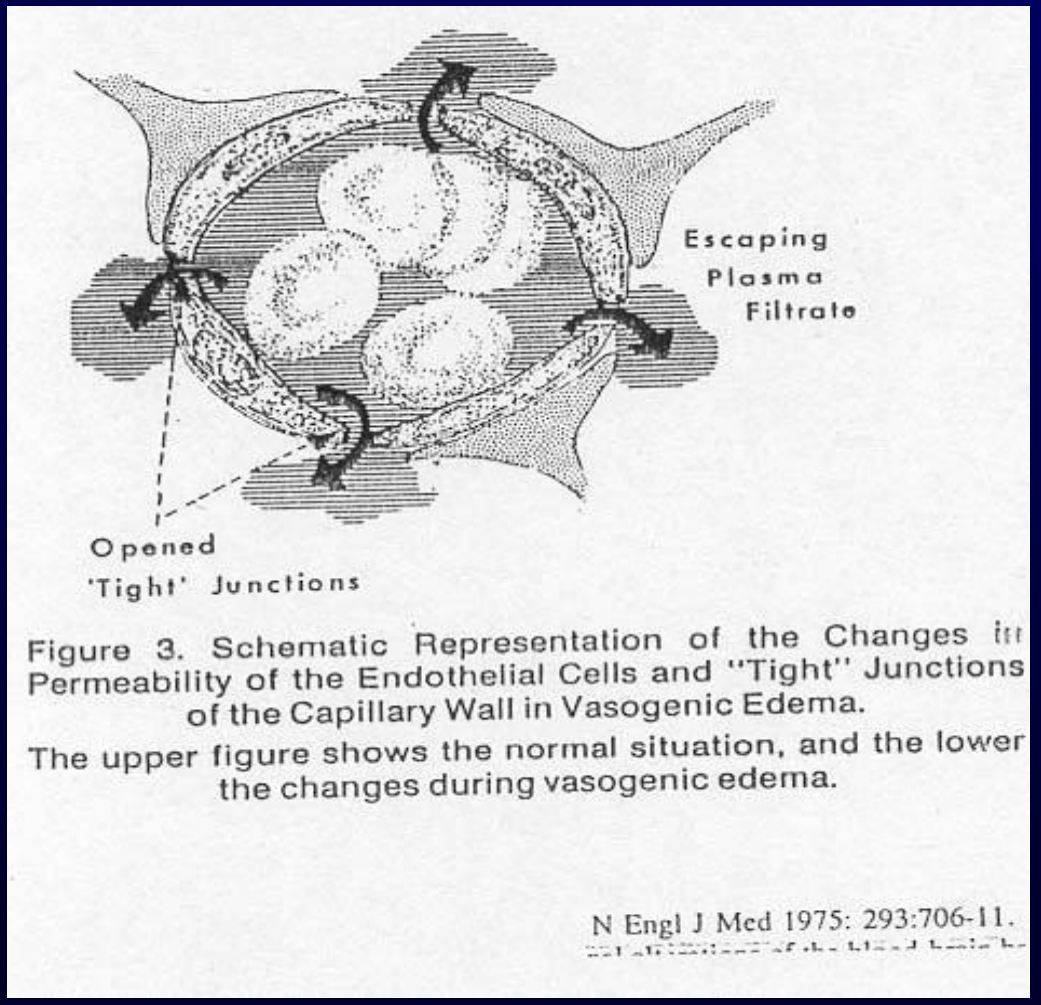


Figure 3. Schematic Representation of the Changes in Permeability of the Endothelial Cells and "Tight" Junctions of the Capillary Wall in Vasogenic Edema.

The upper figure shows the normal situation, and the lower the changes during vasogenic edema.

N Engl J Med 1975: 293:706-11.

Meningitis Bacteriana

Edema Citotoxico

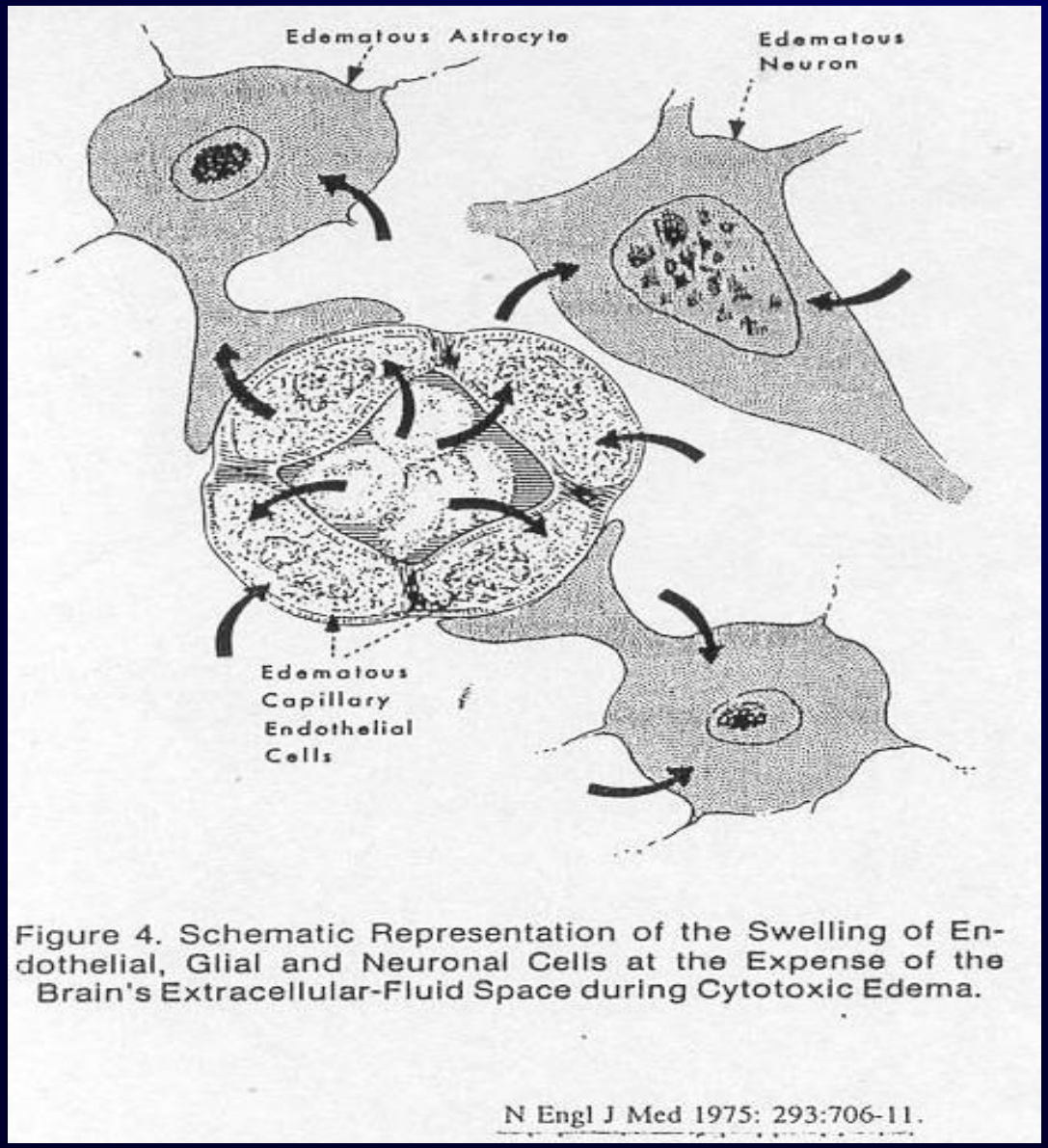
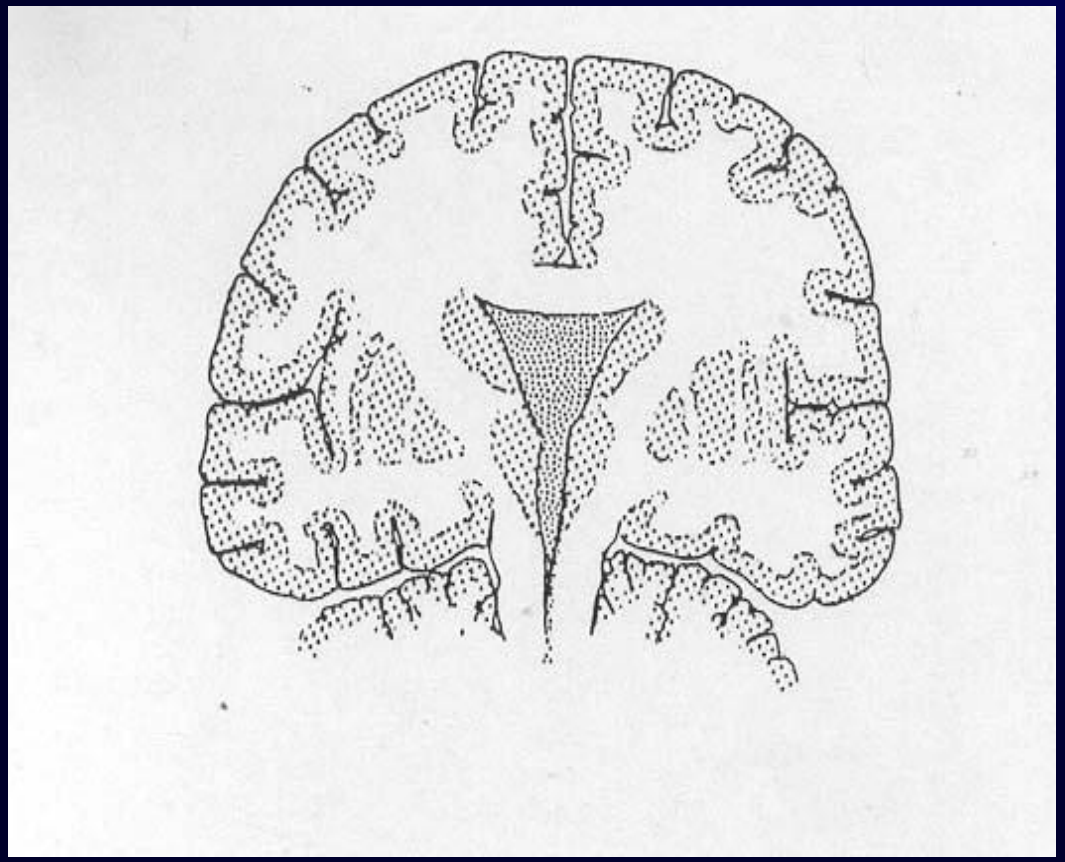


Figure 4. Schematic Representation of the Swelling of Endothelial, Glial and Neuronal Cells at the Expense of the Brain's Extracellular-Fluid Space during Cytotoxic Edema.

N Engl J Med 1975: 293:706-11.

Meningitis Bacteriana

Edema del SNC (intersticial)



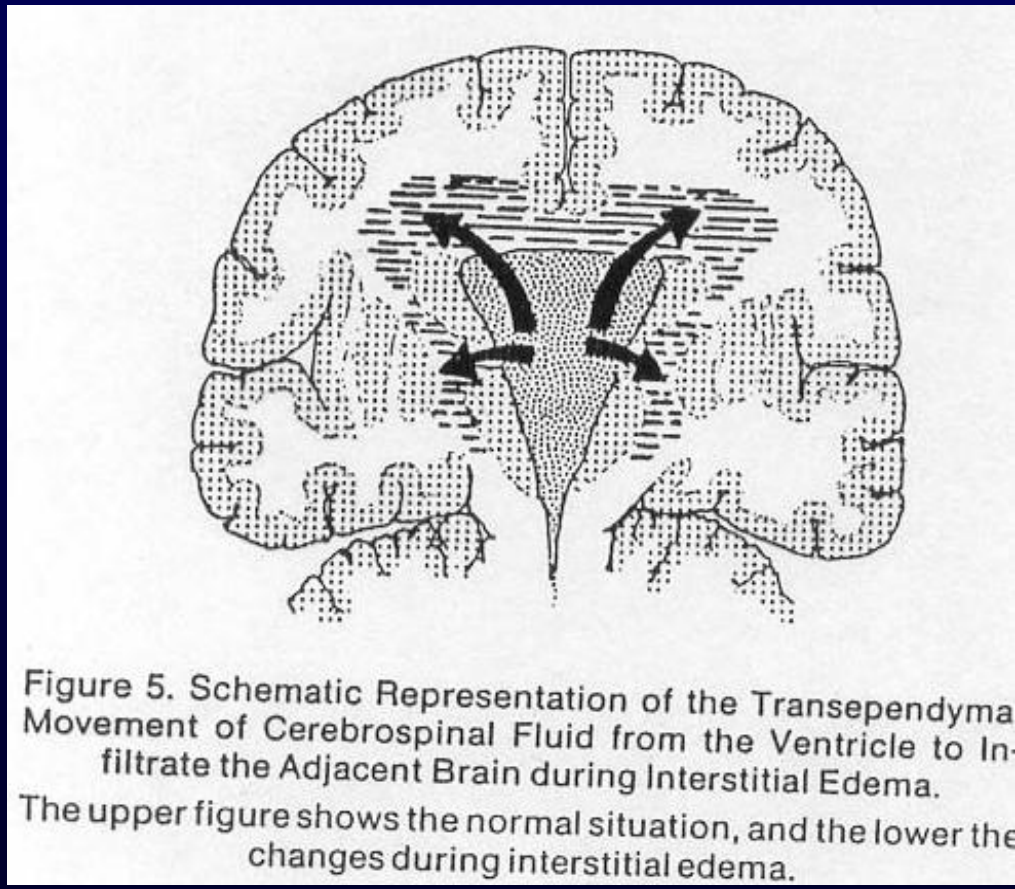


Figure 5. Schematic Representation of the Transependyma
Movement of Cerebrospinal Fluid from the Ventricle to In-
filtrate the Adjacent Brain during Interstitial Edema.
The upper figure shows the normal situation, and the lower the
changes during interstitial edema.

Meningitis bacteriana

Complicaciones del edema del SNC

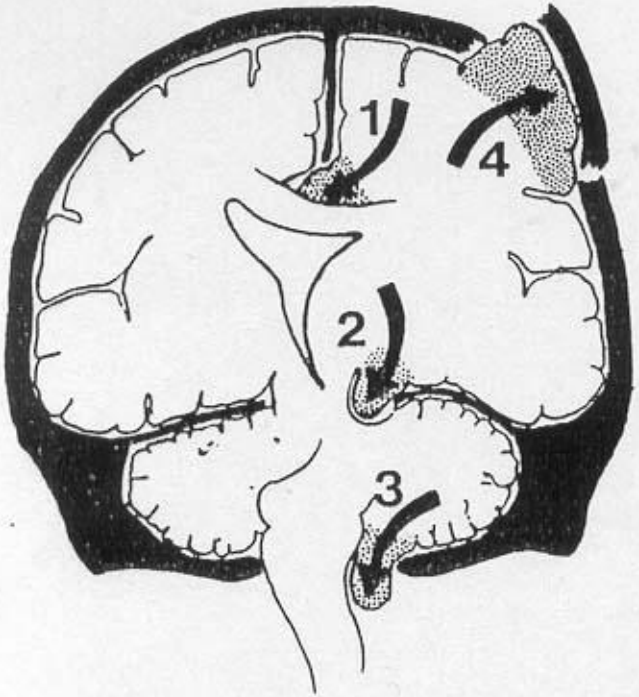


Figure 1. Brain Herniations — Cingulate (1), Temporal (Uncal) (2), Cerebellar (3) and Transcalvarial (Postoperative or Traumatic) (4).

N Engl J Med 1975: 293:706-11.

Meningitis Bacteriana

- Síndrome meníngeo:

  - Rigidez de nuca - Signos de Kernig y Brudzinski
- Síndrome de hipertensión endocraneana

  - Cefalea intensa

  - Vómitos
- Síndrome febril : Hipertermia- escalofríos
- Síndrome neurológico:

  - Alteración del estado de conciencia

  - Déficit motor - convulsiones

Meningitis Bacteriana

- Estudios complementarios:
- L.C.R. Fisico-quimico-citologico, directo y cultivo . Valores normales: Proteínas hasta 0.45 g/L , glucemia > o = a la mitad de la glucemia y hasta 5 leucocitos (100 % linfocitos)
- T.A.C. de cerebro
- Hemocultivos
- Laboratorio sangre periférica, gases en sangre arterial
- Rx tórax

Meningitis Bacteriana

Hallazgos anormales del LCR por tipo de microorganismo

Tipo	WBC(mm2)	Diff.. (%)	Proteinas (mg/ml)	Glucosa(mg/ml)
NML	< 10	>50 linf	< 50	30-70
Bact.	400-100,000	>90 PMN	80- 500	< 35
Viral	5- 500	>50 linf	30-150	NML/baja
Fungal	40 400	>50 linf	40-150	NML/baja
M.TB	100-1,000	>50 linf	40- 400	NML/baja

Meningitis Bacteriana

Diagnóstico ,tests rapidos

- ✓Tests de detección de ag. bacteriano
- ✓69% seguros cuando los cultivos son positivos
- ✓Útiles cuando los ATB fueron dados antes de que el cultivo
- ✓ del LCR se haya realizado
- ✓Puede reaccionar con otros organismos
- ✓Otros tests
- ✓Contrainmunoelectroforesis (CIE) fijación del látex
- ✓(organismos encapsulados)

Abstract: 95.071

Citation: Abstract Book of the 9th International Congress on Infectious Diseases, Buenos Aires, Argentina, April 2000, page 222

Bacterial Meningitis

Intensive Care Department of Critical Infectious Patients, Francisco J. Muñiz Hospital of Infectious Diseases

Material and Methods: The research was done on 431 patients who had caught bacterial meningitis and who were admitted at the intensive care unit

Results: The etiological vectors were the following ones: in 171 patients (39%), *Neisseria meningitidis;* in 140 patients (32%), *Streptococcus pneumoniae;* in 15 patients (3.4%), *Staphylococcus aureus,* and in 1% of the cases.In those cases where *Neisseria meningitidis* was the etiological vector, the infection arose as sepsis in 118 of them (69%), fulminant sepsis reaching 16%. The mortality amounted to 7.6 and 53 per cent respectively, 88% of which was due to multiorganic failure syndrome.

As for the cases where the infection was caused by *Streptococcus pneumoniae,* one third of these patients suffered from convulsive syndrome, and the remaining two thirds showed motive disorders, 79% of whom having their pyramidal way involved. Rostral-caudal deterioration -a result of non-controlled endocranial hypertension- was the cause of death in 74.3% of the 39 cases of decease.The minimal inhibiting concentration for penicillin of the 101 strains of *Streptococcus pneumoniae* studied was less than 0.06 in 81% of them, the remaining 19% showing reduced sensitivity to this antibiotic.

MENINGITIS BACTERIANA

- Período : 6 / 93 - 5 / 99
- Total de pacientes : 431
- Promedio de edad : 40 (14 - 86)
- Sexo : F= 202 M= 229
- Diagnóstico etiológico : 304 / 431 (70.5%)
- Mortalidad : 84 / 431 (19.4 %)

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ETIOLOGIA - 431

- *Neisseria meningitidis* : 171 / 431 (39.6%) - M: 23 (13%)
- *Streptococcus pneumoniae*:140 / 431 (32.4%)-M:39(28%)
- *Staphylococcus aureus* : 15 / 431 (3%) - M: 5 (33%)
- *Listeria monocytogenes* : 6 / 431 (1.4%) - M: (50%)
- *Haemophilus B*: 2 / 431 (0.6%) - M: 0
- *E.coli* : 3 / 431 (0.7%) - M: (100%)
- *Streptococcus viridans* : 2/ M: (50%)
- *Enterococcus* : 1 - M: (100%)
- *Aeromona sp* : 1 - M: (100%)
- *Salmonella sp* : 1- M: 100%
- *Streptococcus B-hemolitico* : 1 - M: 100%
- Sin diagnóstico etiológico : 88 / 431 (20%) - M: (6%)

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Meningitis Bacteriana – Factores de alto riesgo

Factores de riesgo	*N.meningitidis* (171)	*S.pneumoniae* (140)	Otras etiol (33)	Sin diag.etiol (88)	Totales - % (431)
LCR prot <1g	26	6	7	21	60
1-2G	72	6	7	25	110(25%)
>2g	73	**128 (91%)**	19	41	261**(60%)**
Glucosa no dosable	72	**96(68.5%)**	13	24	205(48%)
dosable	99	44	20	63	226(52%)
Células <1000	20	32	11	31	94
1000-2000	-	8	6	3	17
>2000	151	**100 (71%)**	16	53	320**(74%)**
S. convulsivo	-	45 **(32%)**	9	9	63 (15%)
Glasgow <8	26	**40**	8	5	79 **(18%)**
8-12	53	**67** **(76.4%)**	16	32	161**(37%)**
>12	92	33	16	50	191(44%)

ENFERMEDAD MENINGOCOCICA

FORMAS CLINICAS

- Sepsis meningococica fulminante: (sepsis meningococica mas exantema purpurico / shock / Glasgow < 8)
- Sepsis meningococica
- Meningitis aislada.

ENF. MENINGOCOCICA
FORMAS CLINICAS

- Sepsis meningococica:(hemocultivo (+) o deteccion de antigeno en sangre (+) para *N.meningitidis* o exantema purpurico mas cultivo (+) o deteccion de Ag en LCR para *N.meningitidis*).
- Meningitis aislada: (cultivo (+) o deteccion de Ag en LCR para *N.meningitidis* asociada a las alteraciones del FQ del LCR)

Meningitis Bacteriana
N.meningitidis Mortalidad / F.Clinica / SPSM

- Sepsis Meningococcica Fulminante: 21/100 mortalidad 12/21(57 %)
  Score < 8 : 8/21 (38%) mortalidad : 0 -- Score > o igual 8:13/21 (62%) mortalidad 12/13 (92.3%).
  SFMO atribuible a la infección por *N.meningitidis*
- Sepsis Meningococica: 63/100 mortalidad 2/63 (3%).
  Score < o igual a 6 en los 63 pacientes mortalidad no atribuible a la infección por *N.meningitis*
- Meningitis aislada 16/100 mortalidad 1/16 (6%)
  Score < o igual de 4 en todos los pacientes, mortalidad no atribuible a la infección por *N.meningitidis*

Meningitis Neumococica

CARACTERISTICAS NEUROLOGICAS

- Convulsiones: 38/107 (35.5%)
- Score de Glasgow (ingreso): < 8 = 30/107 (28%) / 8 - 12 = 52/107 (48%) / > 12 25/107 (23%)
- Deficit focal : 78/107 (73%)
- Paresia pares craneales : 18/107 (16.7%) VII : 10 – III : 5 -- VI : 3
- Deficit motor : 60/78 (77%)

Hemiparesia (FBC) : 11 -- (BC) : 17 Monoparesia : 10 / Deterioro rostro-caudal : 22 < 24 hs (ingreso) 7 -- >24 hs (I) : 15 (68%).

MENINGITIS BACTERIANA

Neisseria meningitidis Diagnostico

- Meningitis Meningococica Definida: **114/145 (79%)**
- **Cultivo LCR (+) : 82/114 (72%)** COA (ag) LCR: 32/114 (28%)
- Hemocultivos (+) : 13/114 (11.4%)
- Sero tipo : **B = 78 (68%)** C = 34 (30%) A = 2 (2%).

Meningitis Neumococica

DIAGNOSTICO BACTERIOLOGICO

- Cultivo LCR : 89 / 107 (83%)
- Deteccion de Ag en LCR (COA): 18 / 107 (17%)
- Hemocultivos (+) : 29 / 107 (27%)

CIM S.pneumoniae a Penicilina 53 cepas
< 0.006 ug/ml : 43 (81%) -- 0.1 - 1 ug/ml : 8 (15%)
1 - 2 ug/ml : 2 (4%) -- > 2 ug/ml : --
19 % de las cepas muestran sensibilidad
disminuida a Penicilina

MENINGITIS BACTERIANA

Neisseria meningitidis mortalidad : 23/171 (13%)
SFMO: 90.4% <96 hs ingreso: 50 Deterioro rostro caudal: 2.

Streptococcus pneumoniae mortalidad : 39/140 (28%)
Deterioro rostro-caudal: 71% SFMO : 26%

Meningitis no *N.meningitidis* no *S.pneumoniae* mortalidad: 16/32 (50%)
SFMO 80% < 96 hs 75% Deterioro rostro-caudal : 3

Una serie de 50 pacientes con infección por *N.meningitidis* 20 recibieron dexametasona previo al Atb , el score de Glasgow a las 12 hs aumento en 66% de los pacientes (P = 0.027) vs el 33% en el otro grupo 30/50

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MENINGITIS BACTERIANA

Diagnostico y tratamiento empirico, según edad

- Edad < 3 meses : *S.agalactiae* , *E.coli* , *L.monocytogenes* . Ampicilina + Cefalosporinas de 3°
- Edad > 3 meses y < 18 años : *N.meningitidis* , *S.pneumoniae* , *H.influenzae* . Cefalosporinas de 3°
- Edad 18 - 50 años : *S.pneumoniae* , *N.meningitidis*. Cefalosporinas de 3°
- Edad > 50 años : *S.pneumoniae* , *L.monocytogenes* bacilos gram (-) , < % *N.meningitidis* . Ampicilina + Cefalosporinas de 3° .
- Deterioro de la inmunidad celular : *L.monocytogenes* , bacilos gram (-) . Ampicilina + Ceftazidime.

MENINGITIS BACTERIANA

Neisseria meningitidis 75 cepas

- **CIM < de 0.1 ug/ml : 54/75 (72%)**
- **CIM > de 0.1 < 0.5 ug/ml : 14/75 (18.6%)**
- **CIM > de 0.5 < 1 ug/ml : 7/75 (9.3%)**
- **CIM > 1 ug/ml : ---**

CIM a PENICILINA G Na

CIM Penicilina < 1 ug/ml
100% de las cepas .

Meningitis Bacteriana

Streptococcus pneumoniae 101 cepas

< 0.06 ug/ml : 82 (81%)

0.1 - 1 ug/ml : 17 (17%)

> 1 - < 2 ug/ml : 1 (0.9%)

> 2 ug/ml : 1 (0.9%)

19 % de las cepas muestran sensibilidad disminuida y 2% resistencia a penicilina

CIM a ceftriaxona 31 cepas

< 0.5 ug/ml : 29 (93.5%)

> 0.5 ug/ml : 2 (6.5%)

Meningitis Bacteriana

Tratamiento según diagnostico microbiologico inicial

- ✓ LCR patológico - Síndrome purpurico - Gram cocos (-) o COA (+) *Neisseria meningitidis* : Penicilina G Na. Con ATB previo , pruebas rápidas y directo (-) iniciar Cefalosporinas de 3 ,evaluar en 48hs.
- ✓ LCR patológico - Gram cocos (+) y/o COA (+) *Streptococcus pneumoniae* : Cefalosporinas de 3ª.
- ✓ LCR patológico y/o hemorrágico - Exantema maculopapuloso en partes distales y conjuntiva - Gram y pruebas rápidas (-) sin ATB previo sospechar foco endovascular *Staphylococcus aureus* Vancomicina + Cefalosporinas de 3ª + Rifampicina.
- ✓ LCR patológico - (edad >50 /etilismo /Enf.Debilitante / DBT) independiente del Gram iniciar Cefalosporinas de 3ª + Ampicilina. En ausencia de las características descriptas,sin ATB previo / pruebas rápidas y directo en LCR (-) iniciar igual esquema antimicrobiano. *Listeria monocytogenes*

Encefalitis

- Generalmente son meningoencefalitis
- La mayoria son de origen viral
- % permanecen sin diagnostico
- La mortalidad depende del agente etiologico

TABLE 91-3 Possible Etiologic Agents of Encephalitis Based on Epidemiology and Risk Factors

EPIDEMIOLOGY OR RISK FACTOR	POSSIBLE INFECTIOUS AGENTS
Travel	
Central and South America	Rabies virus; eastern equine encephalitis virus; western equine encephalitis virus; Venezuelan equine encephalitis virus; St. Louis encephalitis virus; Rocio virus
Australia	Murray Valley encephalitis virus; Japanese encephalitis virus; Hendra virus
Southeast Asia, China	Japanese encephalitis virus; tick-borne encephalitis; Nipah virus; Me Tri virus; Semliki Forest virus
India, Nepal	Rabies virus; Japanese encephalitis virus; Chikungunya virus
Africa	Rabies virus; WNV; Rift Valley fever virus
Middle East	WNV
Europe	WNV; tick-borne encephalitis; louping ill virus; Toscana virus
Russia	Tick-borne encephalitis; Powassan virus
Insect Contact	
Mosquitoes	Eastern equine encephalitis virus; western equine encephalitis virus; Venezuelan equine encephalitis virus; St. Louis encephalitis virus; Murray Valley encephalitis virus; Japanese encephalitis virus; WNV; California encephalitis group; Chikungunya virus; Me Tri virus
Ticks	Tick-borne encephalitis; Powassan virus; louping ill virus
Animal Contact	
Old World monkeys	Herpesvirus B
Birds	WNV; eastern equine encephalitis virus; western equine encephalitis virus; Venezuelan equine encephalitis virus; St. Louis encephalitis virus; Murray Valley encephalitis virus; Japanese encephalitis virus
Rodents	Eastern equine encephalitis virus (South America); Venezuelan equine encephalitis virus; tick-borne encephalitis; Powassan virus (woodchucks); La Crosse virus (chipmunks and squirrels); LCMV; monkeypox
Horses	Eastern equine encephalitis virus; western equine encephalitis virus; Venezuelan equine encephalitis virus; Hendra virus
Swine	Japanese encephalitis virus; Nipah virus
Dogs	Rabies virus
Bats	Rabies virus; Nipah virus
Raccoons	Rabies virus
Skunks	Rabies virus
Sheep and goats	Louping ill virus
Human Contact	
Person-to-person transmission	HSV (neonatal); VZV; Venezuelan equine encephalitis virus (rare); poliovirus; enteroviruses; measles virus; mumps virus; rubella virus; EBV; HHV-6; herpesvirus B; WNV (transfusion, transplantation, breast-feeding); HIV; rabies virus (transplantation); influenza virus

MANDELL, DOUGLAS, AND BENNETT'S PRINCIPLES AND PRACTICE OF INFECTIOUS DISEASES, EIGHTH EDITION ISBN: 978-1-4557-4801-3

Season	
Late summer/early fall	All agents transmitted by mosquitoes and ticks (see above); enteroviruses
Winter	Influenza virus; LCMV
Recreational Activities	
Sexual contact	HIV
Swimming	Enteroviruses
Camping/hunting	All agents transmitted by mosquitoes and ticks (see above)
Spelunking	Rabies virus
Occupation	
Physicians and health care workers	VZV; HIV; influenza virus
Veterinarians	Rabies virus
Laboratory workers	WNV; HIV
Workers exposed to Old World primates	Herpesvirus B
Workers exposed to horses	Hendra virus
Ingestions	
Unpasteurized milk	Tick-borne encephalitis
Age	
Neonates	HSV-2; CMV; rubella virus
Infants and children	Eastern equine encephalitis virus; Murray Valley encephalitis virus (rapid in infants); influenza virus; La Crosse virus
Elderly	Eastern equine encephalitis virus; St. Louis encephalitis virus; WNV
Other	
Unvaccinated	VZV; Japanese encephalitis virus; poliovirus; measles virus; mumps virus; rubella virus
Recent vaccination	ADEM
Transfusion and transplantation	CMV; EBV; WNV; HIV; tick-borne encephalitis virus; rabies virus; LCMV
Immunocompromised	VZV; CMV; HHV-6; WNV; HIV; JC virus
Agammaglobulinemia	Enteroviruses

ADEM, acute disseminated encephalomyelitis; CMV, cytomegalovirus; EBV, Epstein-Barr virus; HHV, human herpesvirus; HIV, human immunodeficiency virus; HSV, herpes simplex virus; LCMV, lymphocytic choriomeningitis virus; VZV, varicella-zoster virus; WNV, West Nile virus.

Modified from Tunkel AR, Glaser CA, Bloch KC, et al. The management of encephalitis: clinical practice guidelines by the Infectious Disease Society of America. Clin Infect Dis. *2008;47:303-327.*

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Encefalitis virales o Meningoencefalitis

Patogénesis

- Encefalitis viral aguda
- Postinfecciosas o encefalomielitis
- Infecciones virales lentas del SNC
- Enfermedades degenerativas crónicas del SNC de presunto origen viral.
- Llegada al SNC vía hematogena mas común (sitio de replicación viral lugar de inoculación o enantema,viremia transitoria, segunda viremía o amplificación viral sistema retículo endotelial, bazo hígado ganglios, virema secundaria acceso del virus a otros sitios como SNC) otra vía de acceso es la neuronal (herpes, rabia)

Encefalitis Viral

The New England Journal of Medicine 1990;324,4:242

- Encefalitis viral ,el blanco son los capilares corticales de sustancia gris y de la unión sust gris / blanca , infiltrado linfocitico perivascular resulta de la transferencia pasiva del virus a través del endotelio por daño endotelial , consecuencia de replicación viral activa en endotelio capilar.
- Otra entrada al SNC : vía neuronal periférica por vía axonal retrograda, Herpes simplex 1-2 (reactivación de la infección periférica latente en bulbo olfatorio o ganglio trigeminal ,o reactivación de infección latente en mismo cerebro) 2/3 encefalitis herpética son reactivaciones y un tercio son primo infecciones (migración viral desde las mucosas por vía axonal del nervio olfatorio o el trigémino ,explicaria el tropismo por áreas frontobasales y temporales (edad 20 o < años). *An.Med.Interna (2005)22:10;pp 473-477*
- Otra trasmisión intraneuronal es el acceso al SNC es virus rabia, con compromiso del sistema límbico ,luego que llega replica en la cuerpo neuronal y se trasmite por paso de célula a célula o transmisión extracelular.
- Encefalitis post infecciosas puede resultar de un fenómeno autoinmune iniciado por la replicación viral

Encefalitis Viral - Causas

The New England Journal of Medicine 1990;324,4:242

- Encefalitis endémicas virus rabia y herpes simplex (causa mas frecuente de encefalitis esporádica ,focal aguda)
- Encefalitis epidémicas virus encefalitis japonesa (JE)
- Enfermedades prevenible con vacunas: virus sarampión , rubeola, parotiditis, varicela zoster, fiebre amarilla (encefalitis aguda y las complicaciones , encefalomielitis post infecciosas)
- Control de poliomielitis (vacuna), reducción de virus polio en SNC
- Otros picornavirus ; virus Coxsackie - Echo (meningitis a LCR claro o aséptica)
- Virus trasmitidos por picaduras de artrópodos (mosquitos) :

  St Louis, virus Nilo occidental (West Nile ,África) , encefalitis Equina del Este (EEE) ,del Oeste (EEO),Venezolana, Murray Valley virus (Australia), Roció virus (Brasil) , LaCrosse (UE) ,virus de encefalitis de California (encefalitis epidémica o esporádicas)
- Encefalomielitis post infecciosas (mas común asociadas a infecciones del aparato respiratorio superior) virus influenza
- Otro virus herpes (CMV,Epstein-Barr,Varicela-zoster), Virus HIV,Adenovirus

Encefalitis Viral ,Virus Herpes Simplex 1-2

The New England Journal of Medicine 1990;324,4:242

- Causa mas comun de encefalitis esporádica ,no epidémica , encefalitis aguda focal, huésped inmunocompetentes, no estacional
- Alta mortalidad > 70% , sin tratamiento antiviral
- La trasmisión o diseminación viral en SNC tiende a ser unitemporal (inicio) luego termina bitemporal (niños y adultos, > % herpes tipo 1 , transmisión neuronal), diferencia con la infección difusa del neonato (> % herpes tipo 2 , SFMO llegada por sangre al SNC)
- Recuperación del virus LCR neonato 50% aislamiento, adulto muy bajo
- Niños y adultos diagnostico por biopsia o deter material genético LCR viral PCR (sensibilidad del 98% especificidad >94%, falsos negativos muestra < 72hs del comienzo de síntomas o LCR hemorrágico)
- Determinación de anticuerpos en suero y LCR , suero negativo y LCR positivo síntesis en SNC (gran valor diag. con otros métodos negativos y diag. retrospect permanencia de anticuerpos en LCR meses /años) IgM en LCR infección primaria (1/3 casos de encef, 2/3 encef reactivaciones) el aumento de 4 veces el titulo de IgG el LCR en 3 semanas (reactivación de infección previa o recurrencia), la producción de anticuer en LCR baja sensibilidad fase precoz de enfermedad . *Arch.argent.pediatr.vol 110 no 4 jul./ago. 2012 – www.sap.org.ar*

Flavivirus Encephalitis

Tom Solomon, M.D., Ph.D.

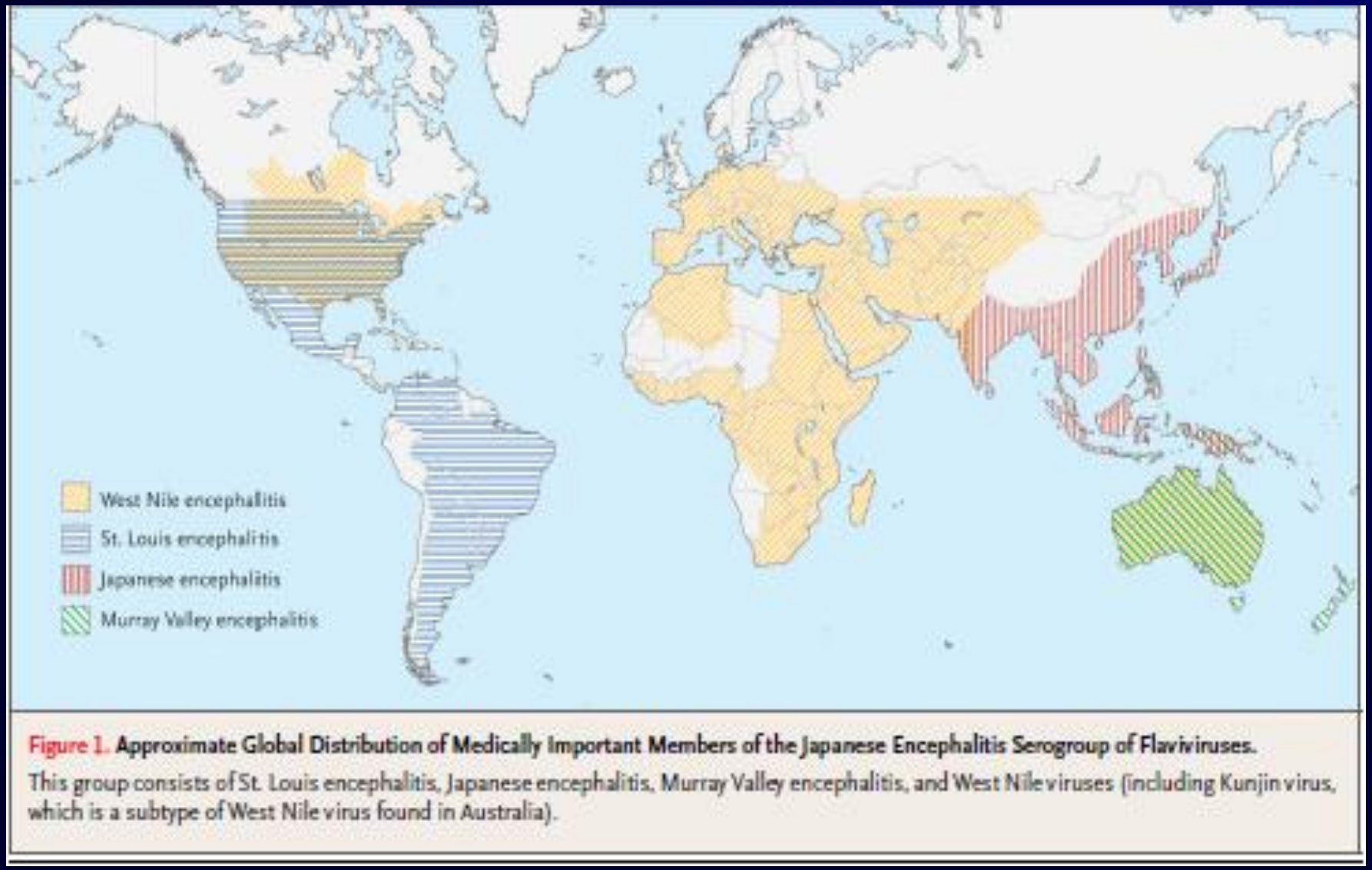

Figure 1. Approximate Global Distribution of Medically Important Members of the Japanese Encephalitis Serogroup of Flaviviruses.

This group consists of St. Louis encephalitis, Japanese encephalitis, Murray Valley encephalitis, and West Nile viruses (including Kunjin virus, which is a subtype of West Nile virus found in Australia).

The NEW ENGLAND JOURNAL of MEDICINE

N Engl J Med 2004;351:370-8.

Table 1. Epidemiologic Features of Flavivirus Encephalitis.*

Feature	Japanese Encephalitis	West Nile Encephalitis	St. Louis Encephalitis	Murray Valley Encephalitis
Geographic area	South Asia, Southeast Asia, China, Pacific Rim, North Australia	Africa, the Middle East, south Asia, Malaysia, Australia, southern Europe, North America	North America, Central America, and South America	Australia, New Guinea
Main vectors	*Culex tritaeniorhyncus*, *C. vishnui*, *C. gelidus*, *C. pipiens*	*C. pipiens*, *C. restuans*, *C. quinquefasciatus*, *C. tarsalis*	*C. pipiens*, *C. tarsalis*, *C. quinquefasciatus*	*C. annulirostris*, *C. quinquefasciatus*, *Aedes normanensis*
Main vertebrate hosts	Migrating birds, especially Asiatic cattle egret (*Bubulcus ibis coromandus*); domestic fowl, pigs	Birds of the family Corvidae (e.g., crows, blue jays) and other passerines (e.g., finches, blackbirds, warblers)	Pigeons, blue jays, sparrows	Birds, especially night heron (*Nycticorax caledonicus*); possibly feral pigs
Groups at risk	Children in areas of endemic disease and nonimmune adults	Elderly, immunosuppressed, and chronically ill persons	Elderly persons	Children and nonimmune adults
Approximate incidence	30,000–50,000 cases annually in Asia	Sporadic cases in Africa, larger outbreaks (300–3000) in the Middle East and North America	35 cases (median) annually with occasional outbreaks of up to 2800	40 cases in 25 years
Ratio of symptomatic to asymptomatic infections	1 in 25 (nonimmune adults) to 1 in 250–1000 (children)	1 in 5 (presenting with fever); 1 in 140–320 (presenting with central nervous system disease)	1 in 250	1 in 700 to 1 in 1200
Patients presenting with encephalitis (%)	60–75	58–62	58–85	50
Patients presenting with meningitis (%)	5–10	15–40	5–40	50
Case fatality rate (%)	20–30	4–16	3–30	15–30
Presence of neuropsychiatric sequelae at hospital discharge (%)	50–60	50–65	30–50	50

* Clinical data presented here for different viruses may not be directly comparable because of differences in study methods.

Encefalitis por Flavivirus

Diagnostico , vacunas

- Aislamiento viral de sangre poco exitoso ,viremia corta ,transitoria y títulos bajos
- Aislamiento en LCR (ocasional) antes de aparición de anticuerpos de producción intratecal tipo IgM,generalmente mal pronostico y postmorten tejido cerebral.
- ARN viral puede ser detectado por PCR (WNV)
- Estándar de diagnostico de encefalitis por flavivirus es IgM de captura por (ELISA) en muestra de LCR o suero (si es negativa la muestra al ingreso al hospital se debe repetir) falsos positivos en áreas donde hay varios flavivirus circulando, se minimiza con búsqueda simultanea de anticuerpos para varios flavivirus.
- Anticuerpos neutralizantes mas específicos (solo en laboratorios especializados)
- Persistencia en suero de anticuerpos por varios meses post infección
- Vacunas : encefalitis Japonesa (inactivada formalina ; licenciada en UE ,controversia en que viajeros a Asia la recibe ,general mente aceptada viajeros de mas de un mes, administración tres dosis 0-7-30 días) o virus vivos atenuados ,los altos costos de producción no la hace disponible para la población rural de Asia (alto riesgo EJ)

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N Engl J Med 2004;351:370-8.

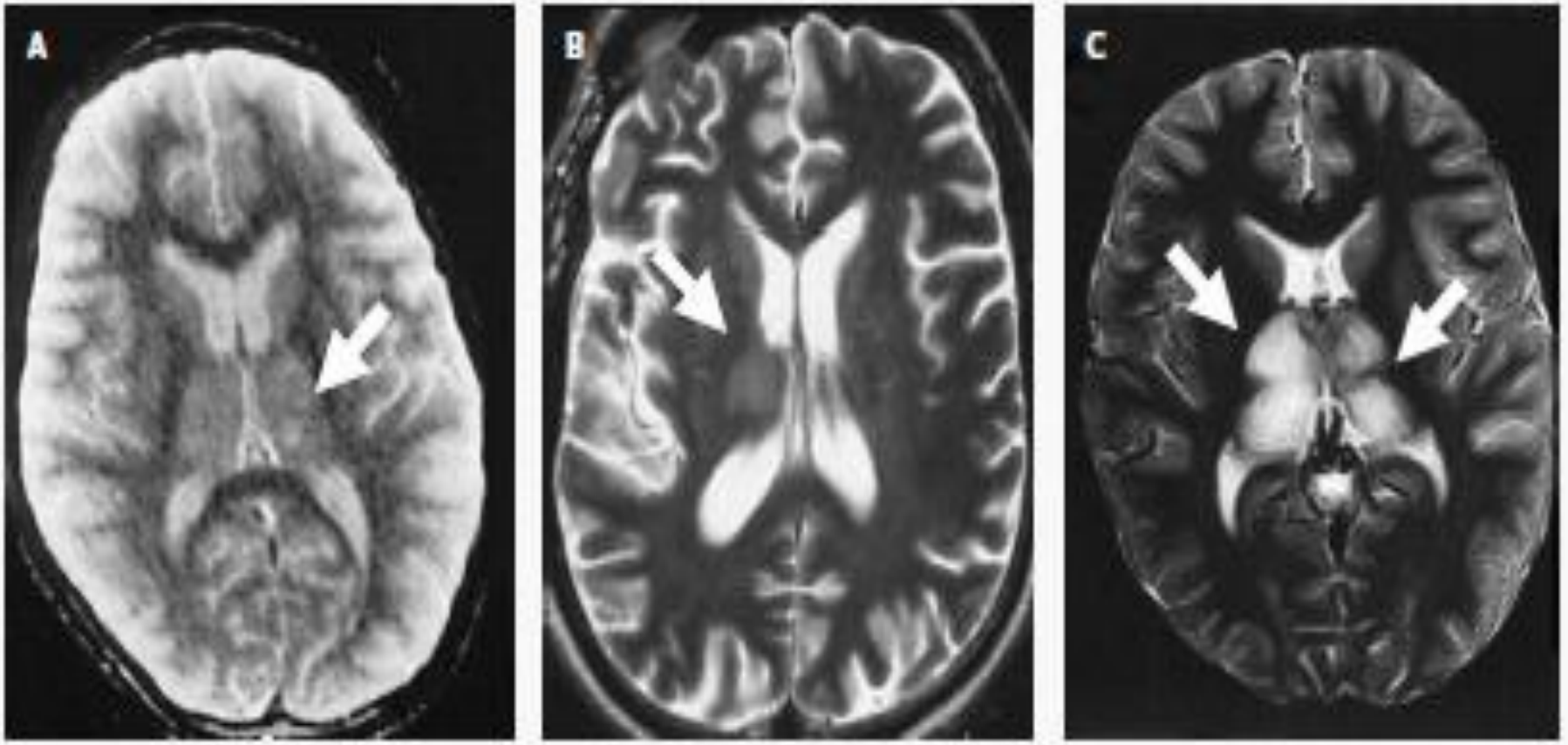

Figure 3. T_2-Weighted Magnetic Resonance Images Showing High Signal Intensity and Swelling in the Thalamus (Arrows) of Patients with Japanese Encephalitis (Panel A), West Nile Encephalitis (Panel B), and Murray Valley Encephalitis (Panel C).

Panel B is adapted from Solomon et al.,[66] and Panel C is adapted from Kienzle and Boyes.[68]

TABLE 91-4 Other Important and Emerging Causes of Viral Encephalitis

VIRAL ETIOLOGY	EPIDEMIOLOGY	CLINICAL FEATURES	DIAGNOSIS	TREATMENT
Adenovirus	Children and immunocompromised patients	Associated pneumonia	PCR or culture of brain biopsy specimen or CSF	Supportive
Chikungunya virus	Epidemic setting; India and Southeast Asia; mosquito vector	Febrile syndrome with rash and arthralgias	CSF and serum IgM and PCR	Supportive
Hendra virus	Australia; fruit bat reservoir; humans infected by secretions of bats	Fever, drowsiness, seizures, and coma associated with a flulike prodrome	Contact Special Pathogens Branch at CDC	Supportive
HIV	Worldwide epidemic; recent high-risk behavior	Fever, headache-associated acute retroviral syndrome; commonly associated with HIV dementia	HIV serology testing and HIV quantitative PCR of CSF; MRI may reveal T2 or FLAIR hyperintense lesions in periventricular regions and centrum semiovale	Combination antiretroviral therapy
Influenza	Fall and winter seasonal predilection; worldwide distribution; rare complication in children	Associated febrile syndrome, myalgias, respiratory prodrome; may be associated with bilateral thalamic necrosis	Viral culture, antigen detection, and PCR in respiratory secretions	Oseltamivir (C-III); poor outcomes
Japanese encephalitis	Mosquito vector, swine and bird reservoirs; most common cause of epidemic viral encephalitis throughout Southeast Asia and Australia	Seizures and parkinsonian features common; acute flaccid paralysis; case-fatality rate of 20%-30%	Serum IgM or acute/convalescent IgG; CSF IgM or antigen; MRI can show T2 and FLAIR hyperintense lesions at basal ganglia, thalami, and midbrain	Supportive; formalin-inactivated mouse brain–derived vaccine available for prevention
JC virus	Cell-mediated immunodeficiencies (AIDS) and immunomodulating therapy (natalizumab, rituximab, efalizumab)	Cognitive dysfunction, limb weakness, gait disturbance, visual loss, focal neurologic findings	CSF PCR (sensitivity 50%-70% for PML); MRI shows ≥1 nonenhancing, confluent subcortical white matter hyperintensity on T2 and FLAIR sequences	Combination antiretroviral therapy in AIDS patients or reversal of immunosuppression
Louping ill virus	Tick-borne disease; found in Ireland, Scotland, and England; associated with livestock	Usually mild febrile illness with associated confusion and stupor in some; deaths are rare	Serum IgM ELISA or a 4-fold increase in IgG antibody in paired acute and convalescent sera	Supportive

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LCMV (see Chapter 166)	Rodent-borne virus infects humans with exposure to infected urine, feces, saliva, or blood; severe disease in immunocompromised patients	Fever, headache, leukopenia, and thrombocytopenia; encephalitis characterized by personality changes, increased ICP, paraplegia, and cranial nerve and sensory dysfunction	CSF and serum IgM ELISA	Supportive
Me Tri virus	Mosquito-borne; Southeast Asia; transmitted among livestock	Fever, rash, seizures, lethargy, and meningismus	CSF PCR and IgM ELISA, serology	Supportive
Monkeypox	Prairie dog exposure	Vesiculopustular rash on head, extremities, palms, and soles; adenopathy; encephalitis is rare, with confusion, somnolence, and diminished reflexes	Skin biopsy, CSF, and serum IgM, serology; MRI showing T2 and FLAIR hyperintense lesions of the pons, thalamus, and subparietal cortex	Supportive care; consider cidofovir or vaccinia immune globulin (C-III)
Mumps virus	Unvaccinated	Previous parotitis followed by headaches, vomiting, seizures, altered consciousness, and sensorineural hearing loss	4-fold IgG increase in paired acute and convalescent sera, culture of saliva, CSF culture and PCR	Supportive
Murray Valley encephalitis virus	Mosquito vector; bird reservoir; Australia and New Guinea	Rapid onset in infants with case-fatality rate of 15%-30%	IgG antibody testing with 4-fold increase in paired acute and convalescent sera	Supportive
Nipah virus	Exposure to infected pigs; pteropid bat reservoir; exposure to infected bats or bat roosting sites; close contact to infected humans; South Asia	Fever, headache, altered consciousness, dizziness, vomiting, myoclonus, dystonia, areflexia, hypotonia; pneumonitis	4-fold IgG increase in paired acute and convalescent sera; CSF culture; MRI may show T2 focal hyperintensity of subcortical and deep white matter of cerebral hemispheres; contact Special Pathogens Branch at CDC	Supportive; ribavirin (C-III)
Powassan virus	Tick vector; rodent reservoir; New England states, Canada, and Asia	Case-fatality rate of 10%-15% and focal neurologic findings in >50% of patients	Serum and CSF IgM; IgG antibody 4-fold increase in acute and convalescent paired sera	Supportive
Rift Valley fever virus	Sub-Saharan Africa, Egypt, Saudi Arabia, Yemen; mosquito vector and livestock reservoir; humans infected via exposure to infected animal secretions	1% of infected humans develop encephalitis with headache, meningismus, and altered consciousness	ELISA antigen detection or culture from serum and PCR; contact Special Pathogens Branch at CDC	Supportive
Rocio virus	Cause of epidemic encephalitis in Brazil; mosquito vector	Fever, headache, confusion, motor impairment, and cerebellar syndrome; sequelae include ataxia, dysphagia, incontinence, and memory problems	4-fold IgG increase in acute and convalescent sera	Supportive
Rubella virus	Unvaccinated adults	Rash followed by headache, dizziness, behavioral changes, and seizures	CSF IgM; 4-fold IgG increase in paired acute and convalescent sera	Supportive
Snowshoe hare virus	Mosquito-borne; North America; children predominantly affected by encephalitis	Fever, headache, confusion, and lethargy; low mortality and rare long-term neurologic sequelae	CSF and serum IgM ELISA or 4-fold increase in IgG acute and convalescent sera	Supportive
Tick-borne encephalitis virus	Tick vector; rodent reservoir; unpasteurized milk; Eastern Russia, central Europe, Far East	Acute encephalitis; acute flaccid paralysis	Serum IgM or 4-fold increase in IgG antibody in paired acute and convalescent sera	Supportive

Continued

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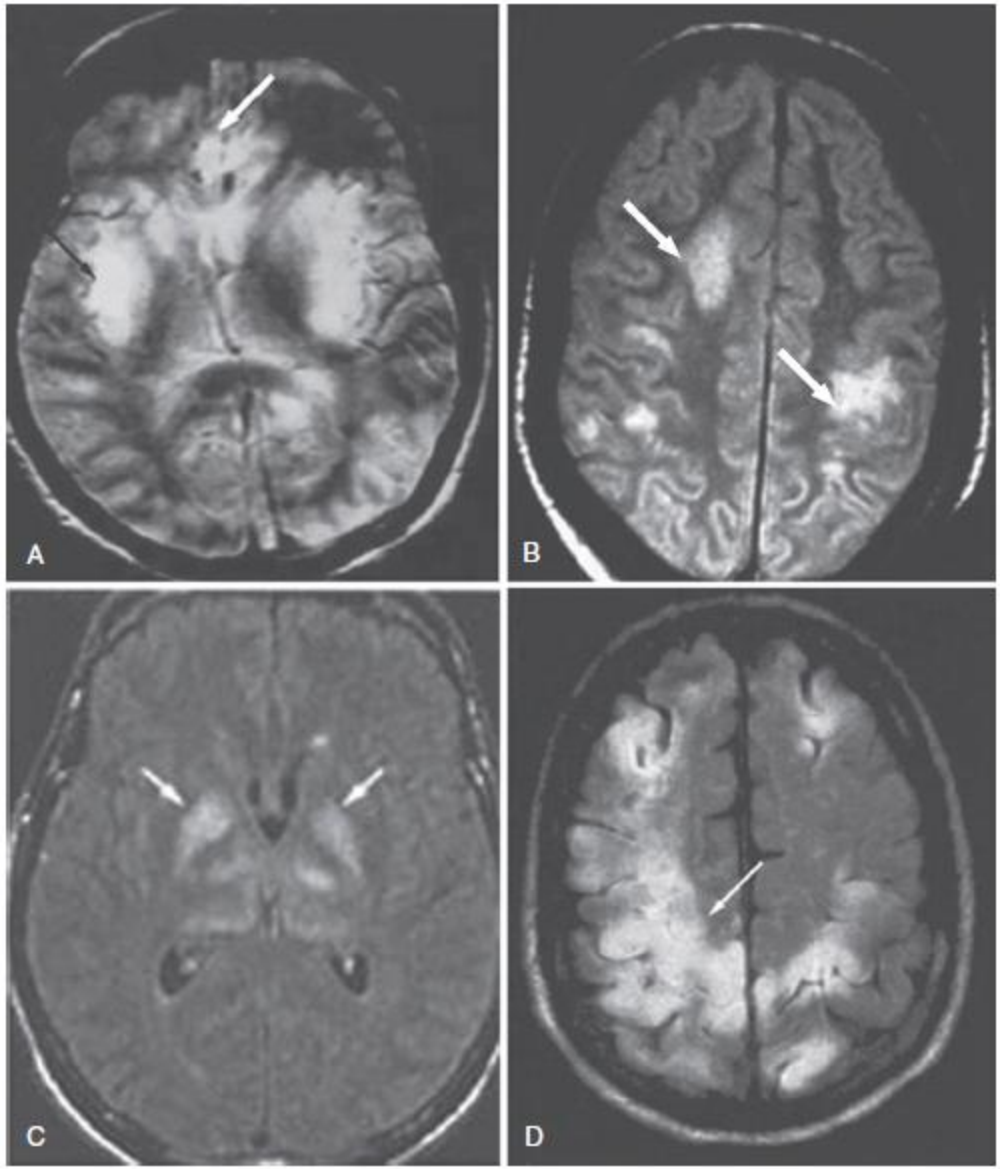

FIGURE 91-3 Typical magnetic resononance imaging (MRI) changes associated with viral encephalitis. A, Herpes simplex virus type 1 encephalitis with increased T2-weighted signal in bilateral temporal lobes. Increased signal does not extend beyond the insular cortex *(black arrow)* but does involve the cingulate gyrus *(white arrow)*. **B,** Varicella-zoster virus vasculopathy on proton-density MRI scan with multiple areas of infarction in both hemispheres *(arrows)*. **C,** West Nile virus encephalitis with increased signal on FLAIR MRI of the basal ganglia *(arrows)*. **D,** Enterovirus encephalitis with increased signal intensity on FLAIR MRI in both hemispheres, greater on the right, in the posterior cerebral hemisphere *(arrow)*. *(Modified from Gilden DH, Mahalingam R, Cohrs RJ, Tyler KL. Herpesvirus infections of the nervous system.* Nat Clin Pract Neurol. *2007;3:83; and Debiasi RL, Tyler KL. West Nile virus meningoencephalitis.* Nat Clin Pract Neurol. *2006;2:264.)*

Meningitis / encefalitis

- Epidemiologia (edad,contactos con animales,con humanos,lugar del mapa,viajes fuera del país,ingresó a lugares selváticos)
- Evaluación del tiempo de enfermedad aguda ,subaguda, cronica
- Evaluación del LCR
- Me métodos de diagnóstico sangre Serologia,Pcr,LCR (antg,anticuerpos ,det de ácidos nucleicos,directo cultivo)
- Evaluación de posibles tratamiento específicos (antimicrobianos,anti vírales)
- Vacunas(bacterianas conjugadas y no conjugadas nemococo meningococo,haemophylus b,fiebre amarilla ,varicela zoster ,influenza a-b ,virus rabia)