

VACUNAS CONTRA NEUMOCOCO Y FACTORES DE RIESGO

PIO LOPEZ.M.D

JEFE DEL DEPARTAMENTO DE PEDIATRIA

DIRECTOR PROGRAMA DE ESPECIALIZACION EN INFECTOLOGIA PEDIATRICA. UNIVERSIDAD DEL VALLE.

INVESTIGADOR ASOCIADO DE COLCIENCIAS

CEIP. CENTRO DE ESTUDIOS EN INFECTOLOGIA PEDIATRICA.

CALI

PIO LOPEZ

Investigador Principal en Colombia del Proyecto Compas. (GSK).

Ponente en eventos cientificos patrocinados por:

GlaxoSmith Kline.

Bristol Meyer Squibb

Wyeth

Sanofi Aventis.

Merck Colombia.

Shering

Novartis




VACUNACION
“ Con la excepción del agua potable, ninguna otra modalidad, ni siquiera los antibióticos, ha tenido un efecto tan importante sobre la reducción de la mortalidad y el crecimiento de la población.”
Plotkin,S

Herejía?

Dios creó a los hombres semejantes,

Su codicia los hizo diferentes.

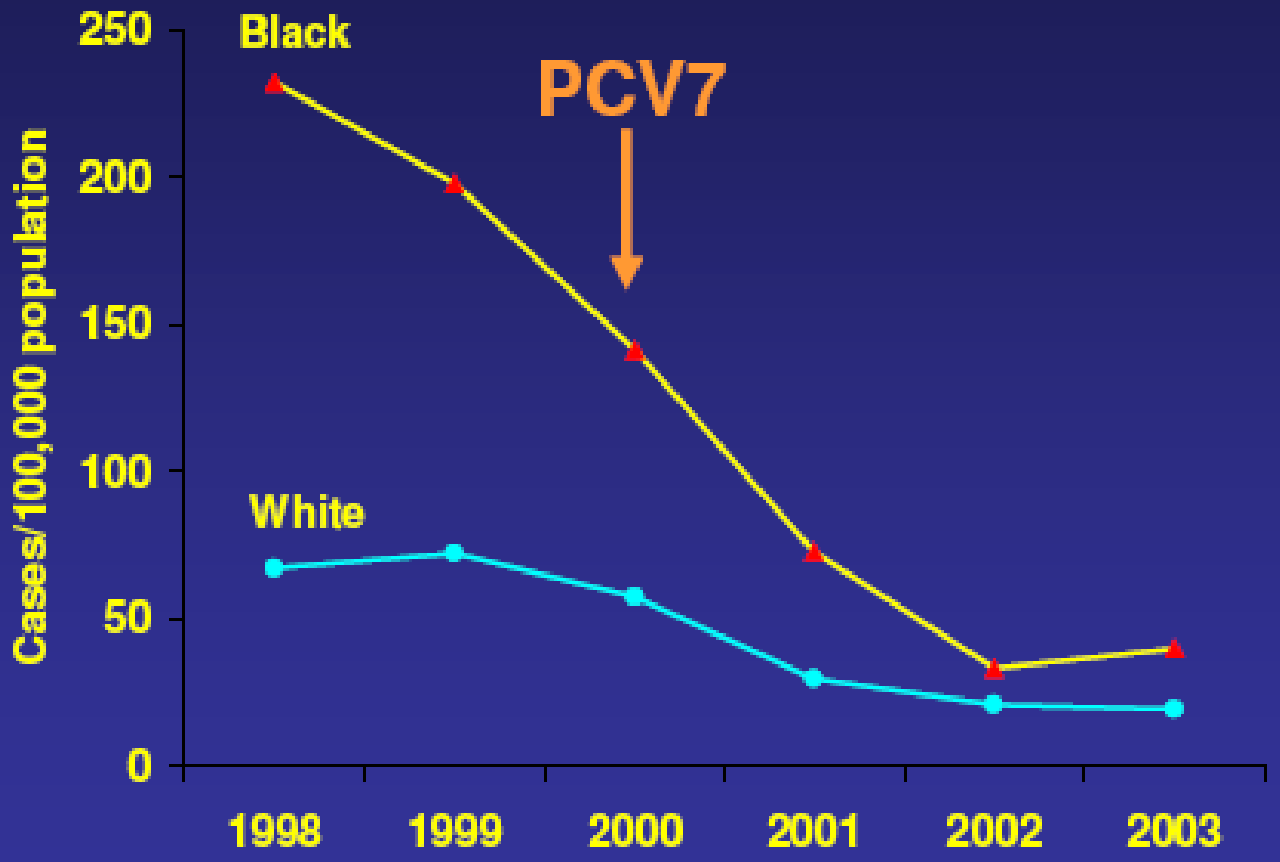
La vacuna los hará de nuevo iguales.

Fuente: “El Inmortal”



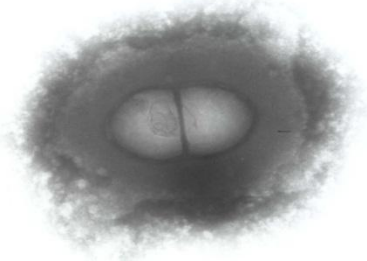
Racial Disparities

Invasive Pneumococcal Disease in Black and White Children <5, ABCs 1998–2003



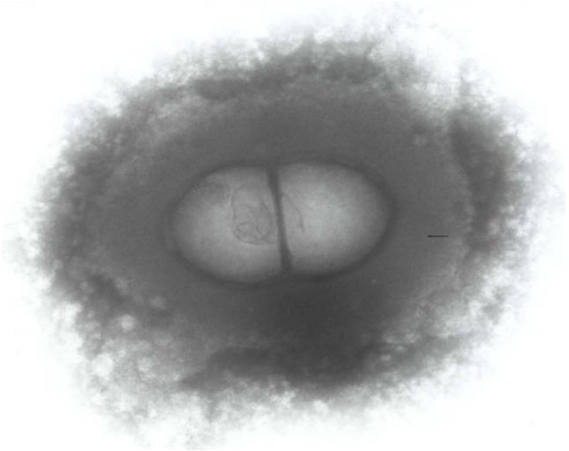
2003 preliminary data, Flannery et al JAMA 2004

STREPTOCOCCUS PNEUMONIAE



Cápsula: **Es el principal factor de virulencia; la estructura química de los polisacáridos que componen la cápsula configura su distinto comportamiento antigénico y permite su clasificación en 91 serotipos**

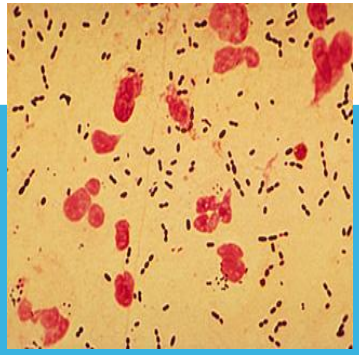
STREPTOCOCCUS PNEUMONIAE (neumococo)



- 91 serotipos capsulares en ~45 serogrupos
- Una minoría de serotipos (~15) causa la mayoría de infecciones invasoras







MUERTES POR INFECCIÓN NEUMOCÓCCICA

~ 1.6 millones de personas mueren cada año de Neumonía o Meningitis

700.000 a 1 millón de estas muertes niños < 5 años

61% de las muertes en Asia y Africa

Muertes por neumococo ocupan la primera causa de muertes prevenibles por vacuna < 5 años

11% de TODAS las muertes en niños son atribuibles al NEUMOCOCO

WHO. Pneumococcal conjugate vaccine for childhood immunization —WHO position paper. *Wkly Epidemiol Rec* 2007; **82:** 93–104.

MUERTES INMUNOPREVENIBLES EN NIÑOS <5 AÑOS EN LAS AMERICAS

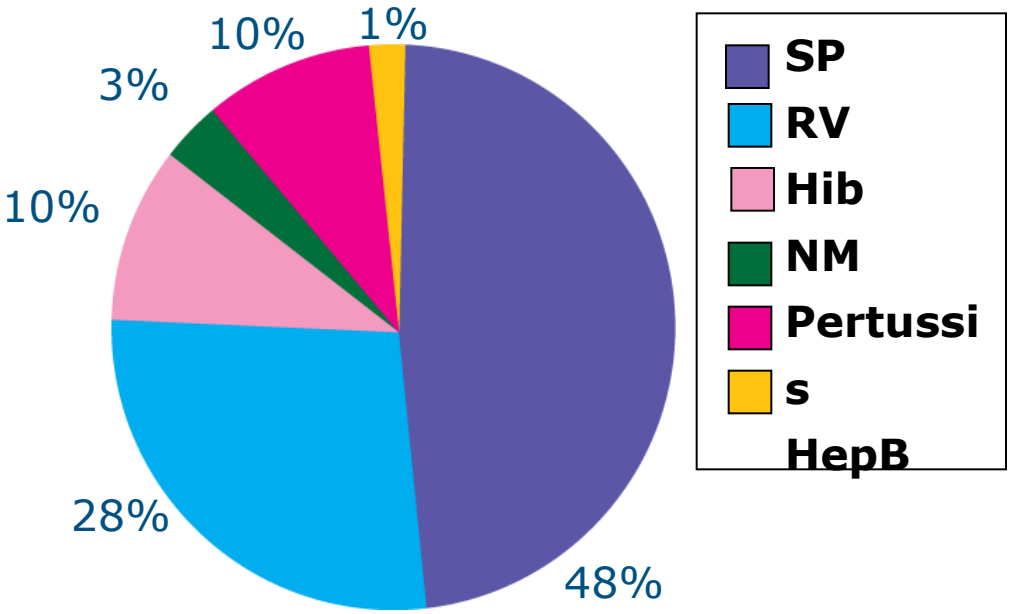
20,200 muertes son atribuidas a neumococo

- Neumonia ~16,960
- Meningitis ~3,220

Casi la mitad de muertes inmunoprevenibles son causadas por neumococo.

En Latinoamérica mueren 2.25 niños cada hora por enfermedad neumococica

Muertes Inmunoprevenibles en Latinoamérica



En Colombia mueren 3 a 4 niños < de 5 años cada día por enfermedad neumocócica

***PAHO Newsletter* June 2006: 5-6**

1. INEC, Egresos Hospitalarios 2006. 2. Di Fabio J, et al PIDJ 2001;20:959-67

TABLE 1. Underlying medical conditions that are indications for pneumococcal vaccination among children, by risk group --- Advisory Committee on Immunization Practices (ACIP), United States, 2010

Risk group	Condition
Immunocompetent children	Chronic heart disease*
	Chronic lung disease†
	Diabetes mellitus
	Cerebrospinal fluid leaks
	Cochlear implant
Children with functional or anatomic asplenia	Sickle cell disease and other hemoglobinopathies Congenital or acquired asplenia, or splenic dysfunction
Children with immunocompromising conditions	HIV infection
	Chronic renal failure and nephrotic syndrome
	Diseases associated with treatment with immunosuppressive drugs or radiation therapy, including malignant neoplasms, leukemias, lymphomas, and Hodgkin disease; or solid organ transplantation
	Congenital immunodeficiency§

* Particularly cyanotic congenital heart disease and cardiac failure.

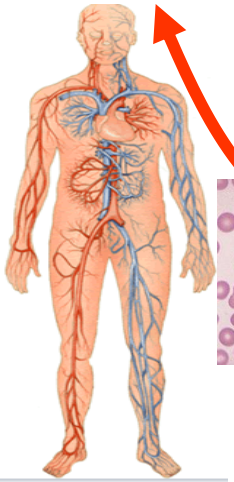
FISIOPATOLOGIA

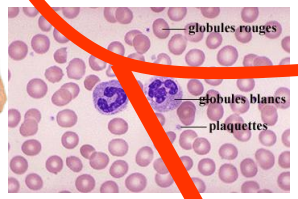


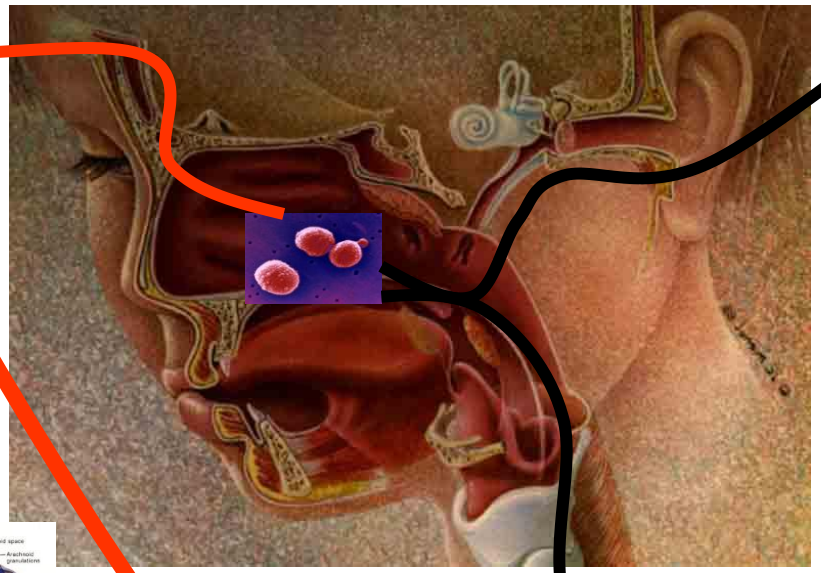
FISIOPATOLOGÍA DE LA ENFERMEDAD NEUMOCÓCCICA



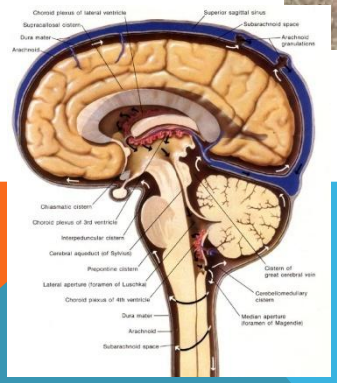
- **No existe infección neumocóccica sin colonización nasofaríngea previa**

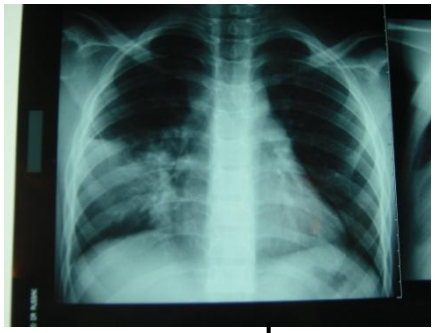






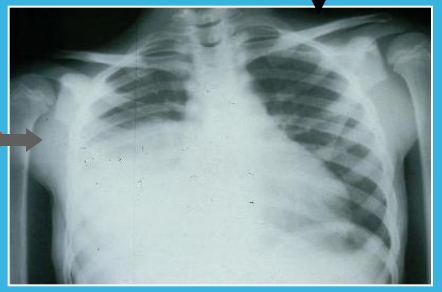






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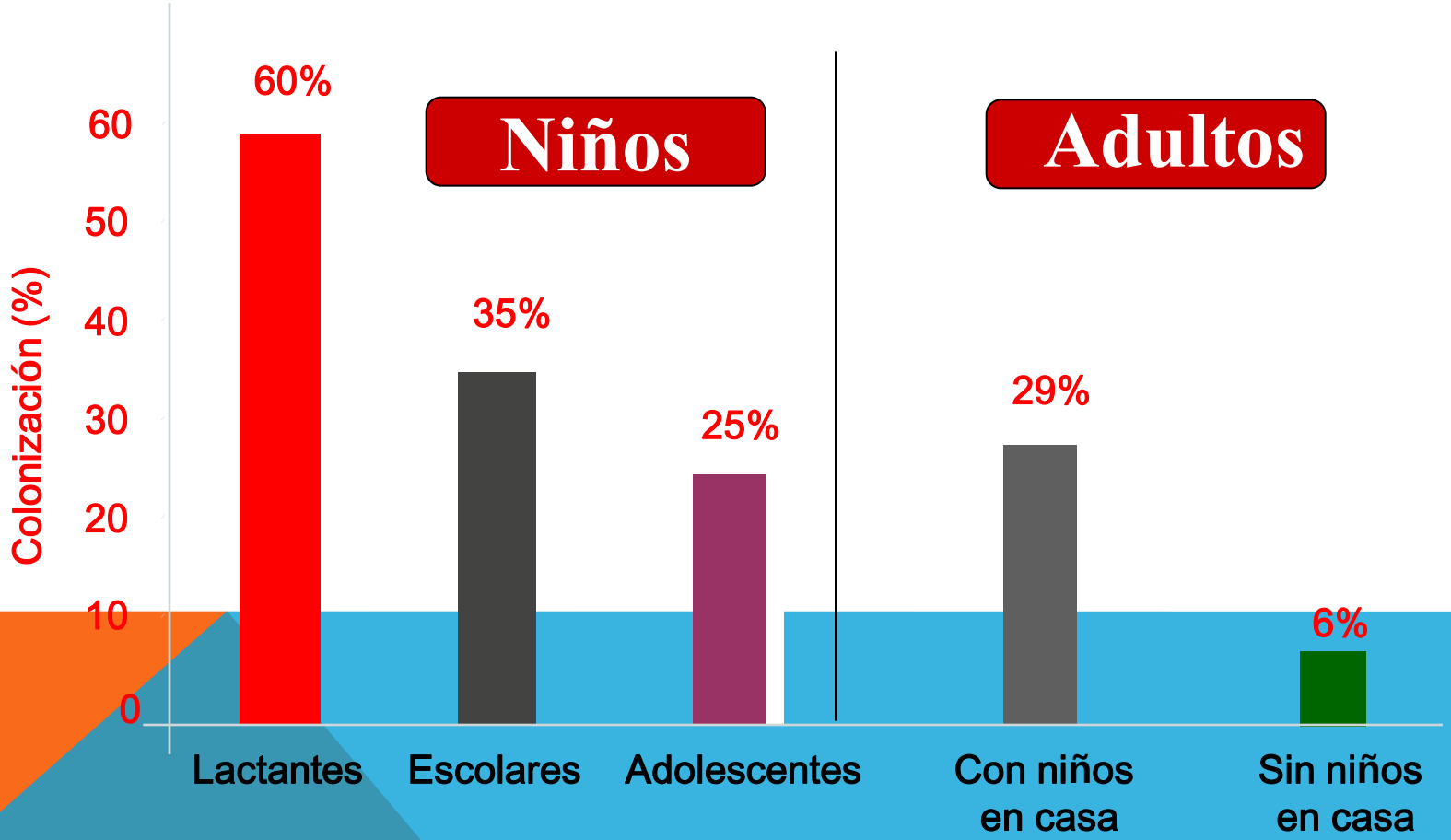
BHE



Invasión Directa

Infección Hematógena

PORTACIÓN NASOFARINGEA DEL *S. PNEUMONIAE* EN NIÑOS Y ADULTOS*



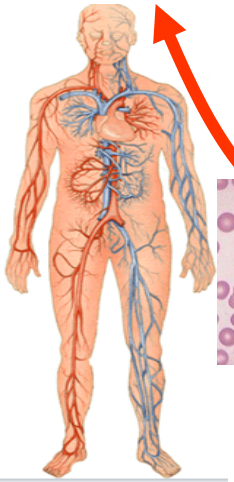
*promedios tomados de más de 30 estudios en el mundo

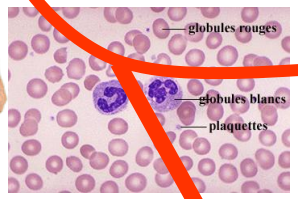
Lancet Infect Dis 2004; 4:144; J Antimicrob Chemother 2002; 50:S2, 59-73

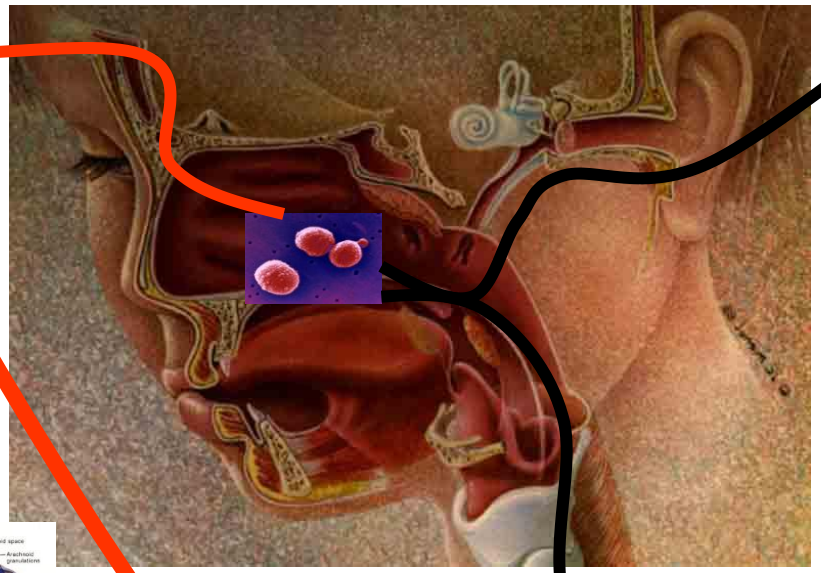
FISIOPATOLOGÍA DE LA ENFERMEDAD NEUMOCÓCCICA



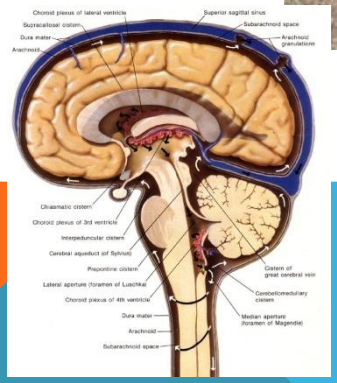
- **No existe infección neumocóccica sin colonización nasofaríngea previa**

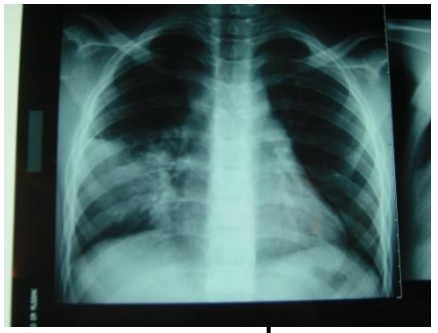


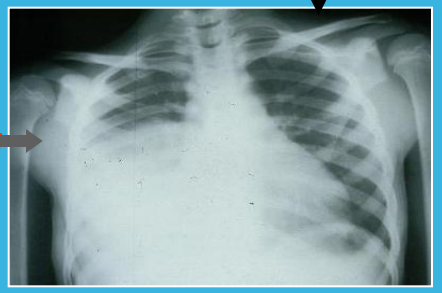












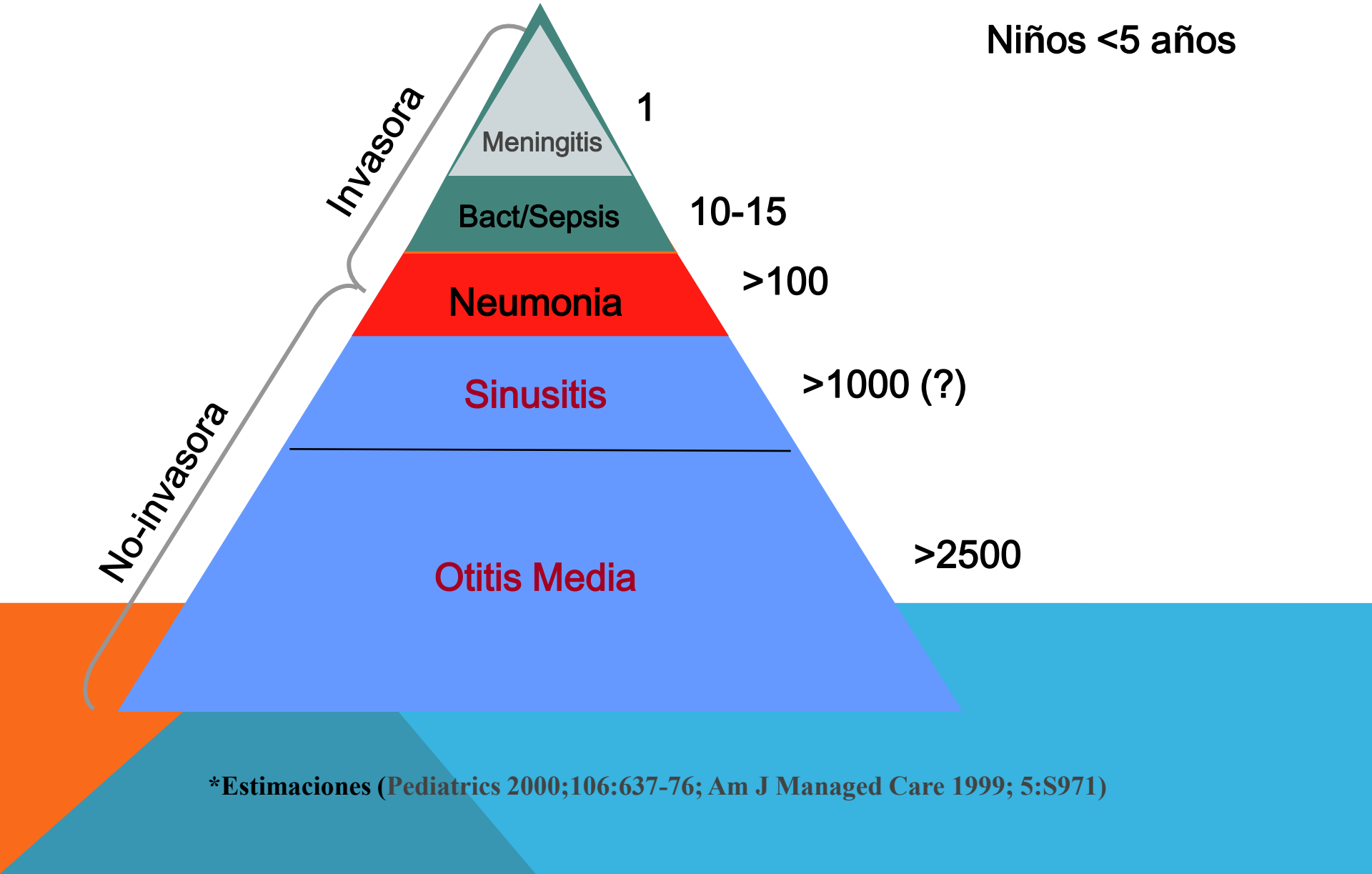
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Invasión Directa

Infección Hematógena

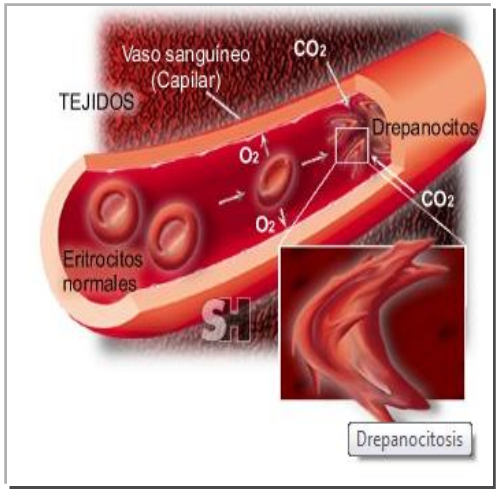
CARGA DE ENFERMEDAD NEUMOCÓCICA*

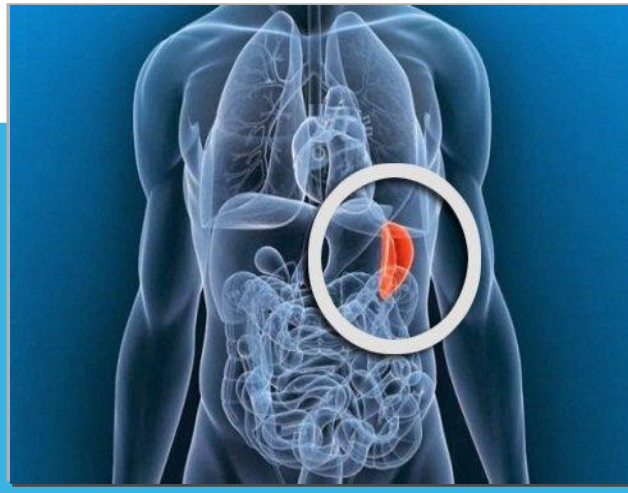


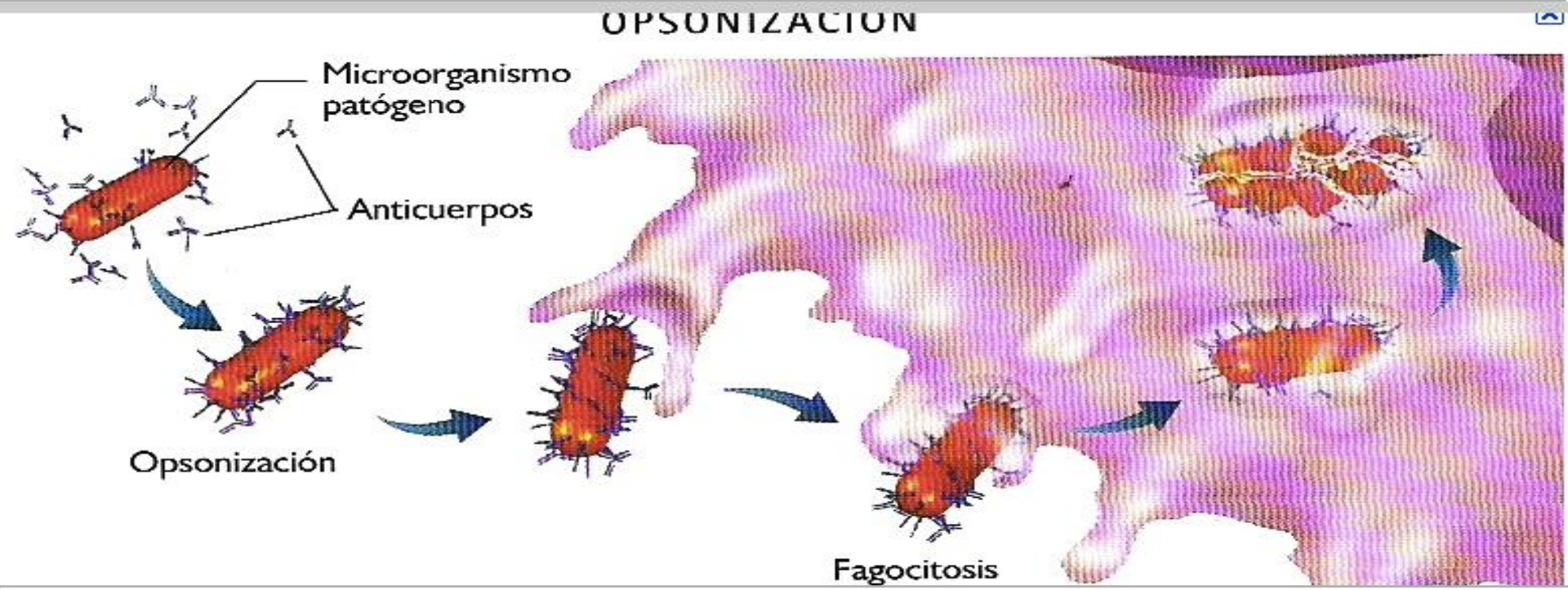
*Estimaciones (Pediatrics 2000;106:637-76; Am J Managed Care 1999; 5:S971)

HEMOGLOBINOPATIAS

En el bazo se produce una disminución de su capacidad funcional, inicialmente porque la gran cantidad de hematíes dañados sobrepasa su capacidad de filtrado (asplenia funcional), a lo que se suma posteriormente la fibrosis progresiva secundaria a infartos recurrentes por la vaso-oclusión autoesplenectomía). Eso conlleva un aumento de la susceptibilidad a infecciones por gérmenes encapsulados



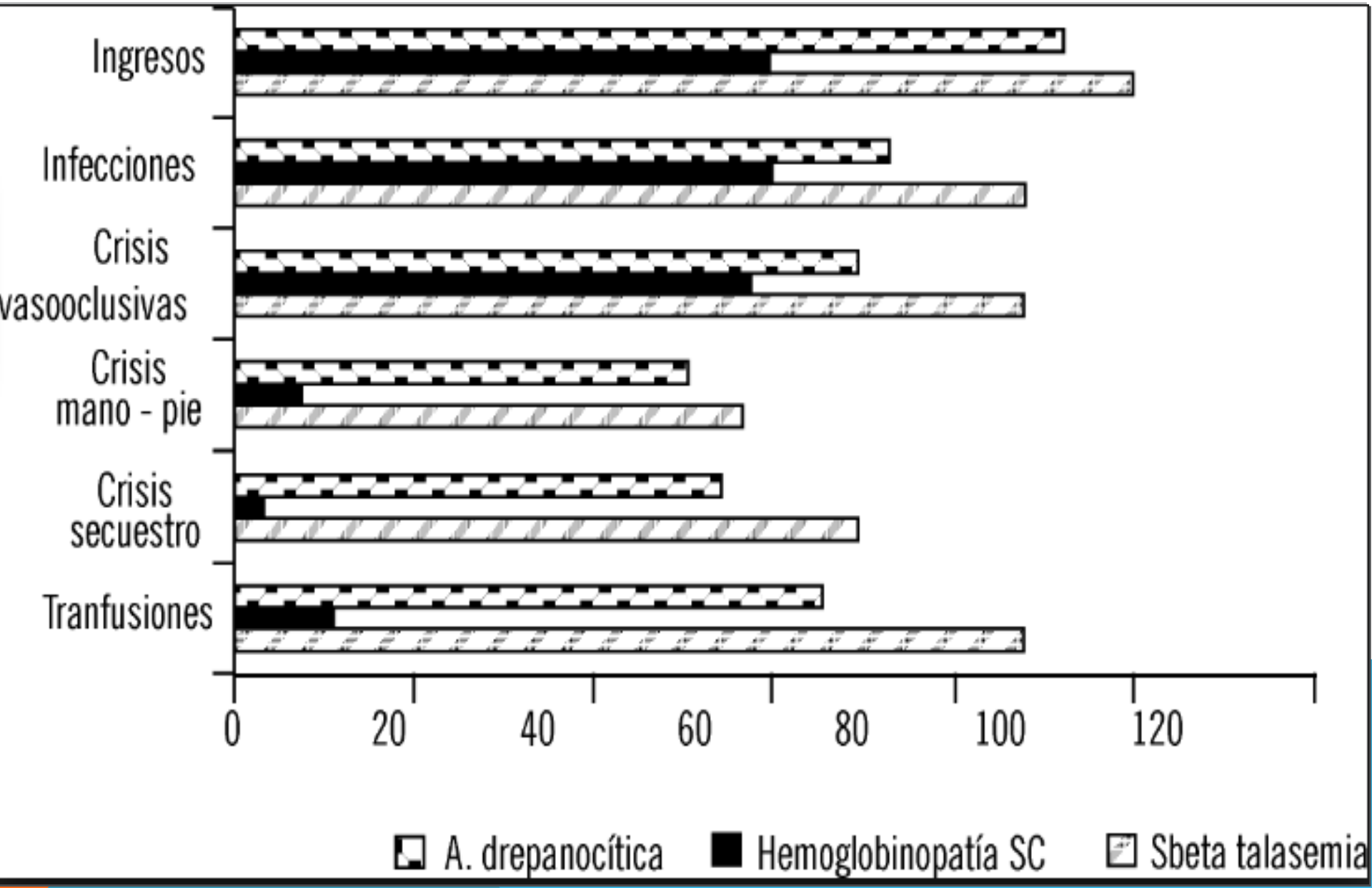




Opsonina

Las **opsoninas** son moléculas coadyuvantes de la fagocitosis. Entre ellas se encuentran las inmunoglobulinas IgG e IgA, componentes del sistema del complemento como C3b, C4b o iC3b y la lectina fijadora de manosa.

Las opsoninas reconocen los antígenos de las partículas a fagocitar, recubriéndolas. Los fagocitos (como los macrófagos o las células dendríticas) poseen receptores de opsoninas en su superficie, por lo que las opsoninas actúan como puente entre la partícula a fagocitar y el fagocito.



pediatric blood cancer 2015



Pediatr Infect Dis J 2013;32:1308–1312

Bacteremia in sickle hemoglobinopathies*

M.D. Harold S. Zarkowsky, M.S. Dianne Gallagher, M.D. Frances M. Gill, M.D. Winfred C. Wang, M.D. John M. Falletta, M.D. William M. Lande, Sc.D. Paul S. Levy, Ph.D. Joel I. Verter, M.D. Doris Wethers, Cooperative Study of Sickle Cell Disease

()

ORIGINAL STUDIES

Invasive Pneumococcal Disease Among Children With and Without Sickle Cell Disease in the United States, 1998 to 2009

Amanda B. Payne, MPH, Ruth Link-Gelles, MPH,† Ijeoma Azonobi, MD,* W. Craig Hooper, PhD,* Bernard W. Beall, PhD,† James H. Jorgensen, PhD,‡ Billie Juni, MS,§ and Matthew Moore, MD, MPH,† for the Active Bacterial Core Surveillance Team*

ORIGINAL ARTICLES and LETTERS
Infectious Disease

Prevalence of Pneumococcal Bacteremia in Children with Sickle Cell Disease

Ami Patel,[1] Amra Zuzo,[2] Hamayun Imran,[2] and Abdul Hafeez Siddiqui[2]

[1]University of South Alabama College of Medicine, Mobile, Alabama, USA; [2]Division of Hematology/Oncology, Department of Pediatrics, University of South Alabama Children's and Women's Hospital, Mobile, Alabama, USA

University on 09/27/13

TABLE 4 Causes of Febrile Illness ($n = 456$)

Lobar pneumonia	82 (18%)
Acute chest	47 (10%)
Occult bacteremia	19 (4%)
Viral infection	13 (3%)
Urinary tract infection	12 (3%)
No cause identified	283 (62%)

La incidencia de EPI es de 6 episodios /100 pacientes año, con un pico en los primeros 3 años de vida




ITAL NAVAL DE CARTAGENA

[redacted]

The NEW ENGLAND JOURNAL of MEDICINE

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ORIGINAL ARTICLE ARCHIVE

Prophylaxis with Oral Penicillin in Children with Sickle Cell Anemia

Marilyn H. Gaston, M.D., Joel I. Verter, Ph.D., Gerald Woods, M.D., Charles Pegelow, M.D., John Kelleher, M.D., Gerald Presbury, M.D., Harold Zarkowsky, M.D., Elliott Vichinsky, M.D., Rathi Iyer, M.D., Jeffrey S. Lobel, M.D., Steven Diamond, M.D., C. Tate Holbrook, M.D., Frances M. Gill, M.D., Kim Ritchey, M.D., John M. Falletta, M.D., and For the Prophylactic Penicillin Study Group

N Engl J Med 1986; 314:1593-1599 | June 19, 1986 | DOI: 10.1056/NEJM198606193142501

VACUNAS CONTRA NEUMOCOCO



META DE LA VACUNA IDEAL…

Proteja niños contra formas clínicas de enfermedad neumocócica

- Bacteriemia/Sepsis/Meningitis
- Neumonía
- Otitis Media Aguda/Sinusitis

Pueda incorporarse al calendario de inmunización infantil

Cubra serotipos circulantes en todas las áreas geográficas

Cubra serotipos involucrados en pacientes de diferentes edades

Cubra serotipos más virulentos y resistentes

Ejerza un gran efecto “rebaño”

No induzca enfermedad de “reemplazo”

Sea segura y barata

VACUNA POLISACÁRIDA DE 23 SEROTIPOS

- **23 serotipos responsables de > 90% de enfermedad invasora en niños y adultos**
- **Recomendada en niños y adultos de alto riesgo para enfermedad neumocócica severa**
- **No inmunogénica en niños menores de 2 años**
-
- **No reduce portación nasofaríngea**
- **Fenómeno de hipo-respuesta inmunológica**

	Vaccination Response		
	Poor (n = 45)	Good (n = 21)	P (χ^2)
Hb genotype			
SB	3	2	0.8336
SC	12	4	
SS	30	15	
Vaccines received			
PS23	18	6	0.3687
PCV-7 + PS23	27	15	
Age (y)			
< 16	27	15	0.3687
≥ 16	18	6	
Time since PS23 (mo)			
≤ 36	11	12	**0.0094**
> 36	34	9	
Age (y)*	13.0 + 5.3	10.6 + 5.6	0.0911
Hb*	9.1 + 1.8	8.4 + 1.7	0.2164
LDH*	487.7 + 205.5	521.1 + 140.2	0.5655
No. PS23*	1.7 + 0.9	1.7 + 0.6	0.9080
No. PCV-7*	2.0 + 1.9	2.8 + 2.0	0.1573
Time since last vaccine (mo)*	47.3 + 18.3	27.5 + 24.1	**0.0005**

*Mean + SD.
Hb indicates hemoglobin; LDH, lactate dehydrogenase.
Values in bold are statistically significant.

Estos resultados indican que la inmunidad contra neumococo puede ser de un tiempo menor del deseado cuando se utilizan las vacuna polisacarida de 23 serotipos y la conjugada de 7 serotipos. Muchos medicos suspenden profilaxis a los 5 años Se sugiere controlar con titulos antineumococicos a estos pacientes y revisar el tiempo de profilaxis

Pharmacotherapy Vol 35 Number 7, 2015

BRIEF REPORT

Adverse Reactions to Pneumococcal Vaccine in Pediatric and Adolescent Patients with Sickle Cell Disease

Jin Han,[1] Opeyemi Kemiki,[2] Lewis L. Hsu,[2] and Angela E. Rivers,[2*]
[1]Department of Pharmacy Practice, College of Pharmacy, University of Illinois at Chicago, Chicago, Illinois;
[2]Department of Pediatrics, Section of Hematology-Oncology, University of Illinois at Chicago, Chicago, Illinois

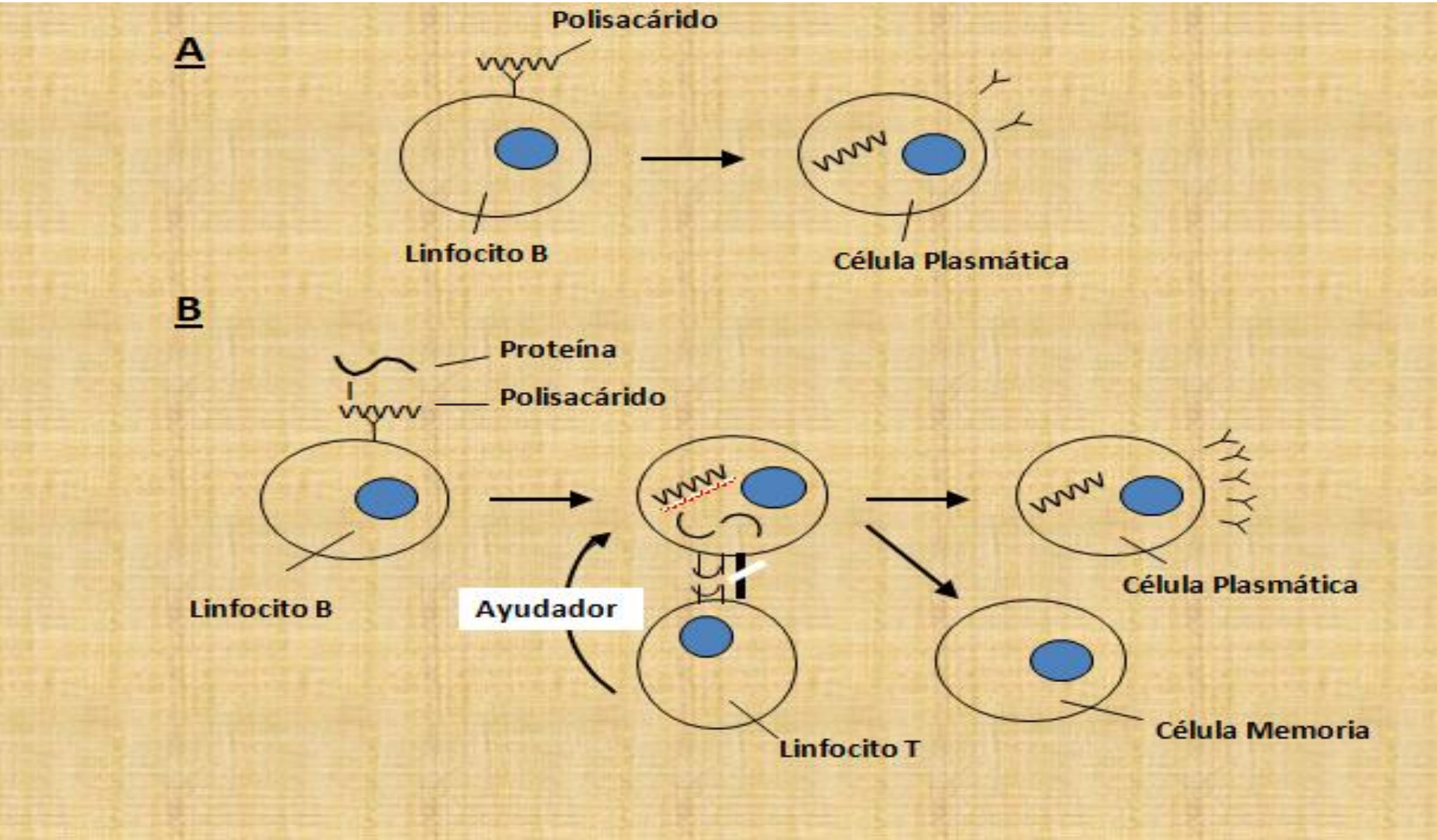
Table 2. Adverse Events Related to PPSV23 and Other Vaccines in the Vaccine Adverse Event Reporting System Database[a]

Vaccine	Patients with Sickle Cell Disease	Patients with Asthma	HIV-Positive Patients	Patients with All Other Eligible Conditions for PPSV23 Vaccination	p Value
PPSV23	76 (62)	1231 (16)	106 (16)	23,070 (7)	< 0.0001
Other vaccines	47 (38)	6538 (84)	538 (84)	307,875 (93)	
Total	123	7769	644	330,945	

CONCLUSION El riesgo de desarrollar eventos adversos relacionados con PPVSV23 es mayor en pacientes con SCF que en pacientes con Asma o VIH, especialmente en niños y adolescentes Los profesionales de salud deben monitorizae de cerca los posibles eventos adversos posterior a la aplicacion de la vacuna polisacarida, respetar el intervalo de tiempo entre PCV13 y PPVS23 y evitar la vacuna simultanea de la vacuna polisacarida con otras vacunas.

Pharmacotherapy Vol 35 Number 7, 2015

VACUNAS CONJUGADAS



VACUNAS NEUMOCÓCICAS CONJUGADAS

PCV7	4, 6B, 9V, 14, 18C, 19F, 23F		
	CRM197		
PHiD-CV	4, 6B, 9V, 14, 18C, 19F, 23F	1, 5, 7F	
	NTHi proteina D	T D	NTHi proteina D
PCV13	4, 6B, 9V, 14, 18C, 19F, 23F	1, 5, 7F	3, 6A, 19A
	CRM197		

EXPERIENCIA EN LA INTRODUCCIÓN DE LA VACUNA NEUMOCÓCICA CONJUGADA - COLOMBIA



PROGRAMA AMPLIADO DE INMUNIZACIONES

Acuerdo 335 del 6 de julio de 2006 del Consejo Nacional de Seguridad Social en Salud (CNSSS)

Fortalecimiento del Programa Ampliado de Inmunizaciones, Vacunación de la población de alto riesgo contra neumococo.

Población menor de 2 años de alto riesgo.

- Infección por HIV
- Cardiopatía congénita
- Asplenia
- Inmunodeficiencia primaria
- Diabetes Mellitus
- Asma bronquial en tratamiento con corticoesteroides
- Inmunocompromiso por Cáncer o por Insuficiencia Renal Crónica o síndrome nefrótico o por Quimioterapia inmunosupresora

Pediatric Hematology and Oncology, 30:432–436, 2013
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DOI: 10.3109/08880018.2013.786157

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ORIGINAL ARTICLES and LETTERS
Infectious Disease

Prevalence of Pneumococcal Bacteremia in Children with Sickle Cell Disease

Ami Patel,[1] Amra Zuzo,[2] Hamayun Imran,[2] and Abdul Hafeez Siddiqui[2]

[1] University of South Alabama College of Medicine, Mobile, Alabama, USA; [2] Division of Hematology/Oncology, Department of Pediatrics, University of South Alabama Children's and Women's Hospital, Mobile, Alabama, USA

TABLE 2. Incidence Rates of IPD Among Children With SCD Compared With Children Without SCD by Age Group and Time Period, 1998 to 2009

	Pre-PCV7 (1998 to 1999)			Early-PCV7 (2000 to 2004)			Late-PCV7 (2005 to 2009)		
	Cases per 100,000 (95% CI)		Rate Ratio* (95% CI)	Cases per 100,000 (95% CI)		Rate Ratio* (95% CI)	Cases per 100,000 (95% CI)		Rate Ratio* (95% CI)
	SCD+	SCD−		SCD+	SCD−		SCD+	SCD−	
0–4 yr	2266 (1519–3381)	825 (799–853)	3 (2–4)	587 (393–875)	58 (54–61)	10 (7–15)	537 (368–782)	33 (30–35)	16 (11–24)
5–17 yr	299 (142–627)	7 (6–9)	42 (19–90)	287 (193–429)	5 (4–5)	63 (41–97)	224 (146–343)	3 (3–4)	72 (45–113)

*Comparison of rate of IPD in children with SCD compared with rate of IPD in children without SCD.
CI indicates confidence interval.

VACUNA DECAVALENTE

PHiD-CV

4, 6B, 9V, 14, 18C, 19F, 23F

1, 5, 7F

NTHi proteina D

T

D

NTHi proteina D

PROTEÍNA D

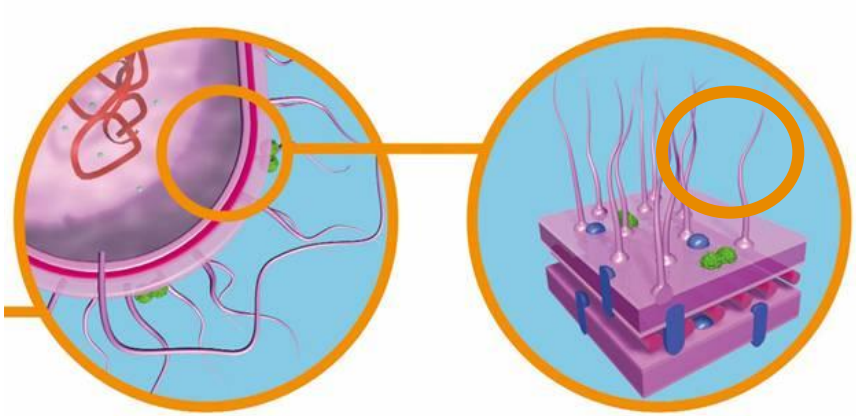
42 kDa.

Lipoproteína (LPD).

Expuesta a la membrana celular.

Enzima.

- Fosfodiesterasa de glicerofosfodiéster.



- Expresada en todas las cepas estudiadas de H. influenzae no tipificable.[1]

- Genéticamente estable entre cepas (~ 700 cepas de Hi).[2]
  ADN (97,5%) y secuencia proteica (98,3%).

La Proteína D de NTHi está expuesta a la superficie celular

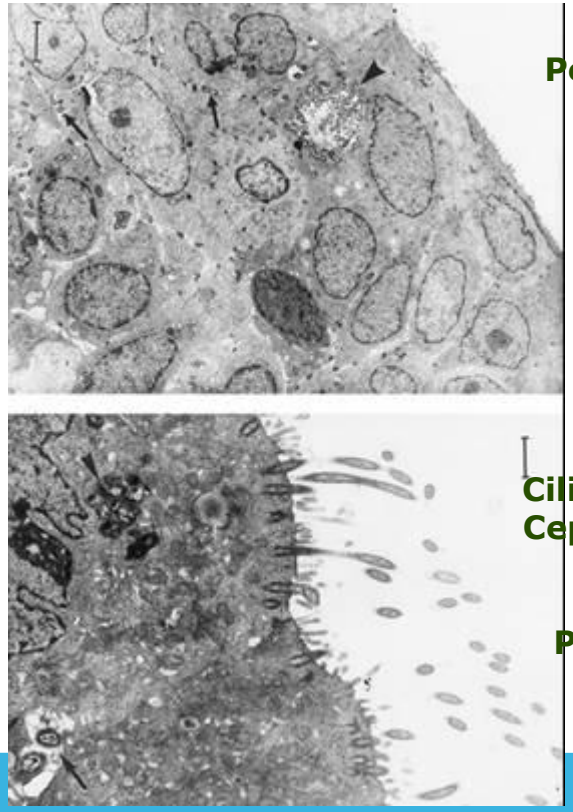
Janson H et al. Infect Immun 1994

1. Akkoyunlu M et al. Inf Immun. 1991; 2. Forsgren A, et al., Clin Infect Dis 2008; 3. V. Bouchet 2007 ISRAOM-Tampa,US;

PROTEÍNA D
ROL EN LA PATOGÉNESIS DE NTHI

La Proteína D facilita la infección con NTHi

- Contribuye al daño y a la inhibición del movimiento ciliar de las células epiteliales del huesped.[1]
- Disminuye la depuración bacteriana de los pulmones y del oído medio.[2,3]



Pérdida ciliar NTHi tipo silvestre

Cilios intactos Cepa mutante a la que le falta Proteína D

Microscopía electronica de cultivo de adenoides humana 48 horas después de la inoculación con NTHi

La Proteína D es un factor de virulencia

1. Janson et al. J Infect Dis 1999; 2. Poolman Vaccine 2001; 3. Bakaletz LO et al. Inf Immun. 1999

COMPAS

OPEN ACCESS Freely available online

PLOS | MEDICINE

Efficacy of Pneumococcal Nontypable *Haemophilus influenzae* Protein D Conjugate Vaccine (PHiD-CV) in Young Latin American Children: A Double-Blind Randomized Controlled Trial

Miguel W. Tregnaghi[1], Xavier Sáez-Llorens[2]*, Pio López[3], Hector Abate[4], Enrique Smith[5], Adriana Pósleman[6], Arlene Calvo[7], Digna Wong[8], Carlos Cortes-Barbosa[3], Ana Ceballos[1], Marcelo Tregnaghi[1], Alexandra Sierra[3], Mirna Rodriguez[8], Marisol Troitiño[7], Carlos Carabajal[5], Andrea Falaschi[4], Ana Leandro[9], Maria Mercedes Castrejón[10], Alejandro Lepetic[11], Patricia Lommel[12], William P. Hausdorff[12], Dorota Borys[12], Javier Ruiz Guiñazú[12], Eduardo Ortega-Barría[10], Juan P. Yarzábal[12], Lode Schuerman[12], on behalf of the COMPAS Group[¶]

1 Centro de Desarrollo del Proyectos Avanzados en Pediatría, Córdoba, Argentina, **2** Department of Infectious Diseases, Hospital del Niño, Panama City, Panama, **3** Centro de Estudios en Infectología Pediátrica, Cali, Colombia, **4** Department of Infectious Diseases, Hospital Notti, Mendoza, Argentina, **5** Centro de Desarrollo del Proyectos Avanzados en Pediatría, Santiago del Estero, Argentina, **6** Centro de Desarrollo del Proyectos Avanzados en Pediatría, San Juan, Argentina, **7** Health Research International, Panama City, Panama, **8** Instituto de Investigaciones Científicas y Servicios de Alta Tecnología, Panama City, Panama, **9** Department of Pediatrics, Hospital del Niño, Panama City, Panama, **10** GlaxoSmithKline Vaccines, Panama City, Panama, **11** GlaxoSmithKline Vaccines, Buenos Aires, Argentina, **12** GlaxoSmithKline Vaccines, Wavre, Belgium

Miguel W.Tregnaghi et al Plos Medicine 2014; 11 (6): e10011657

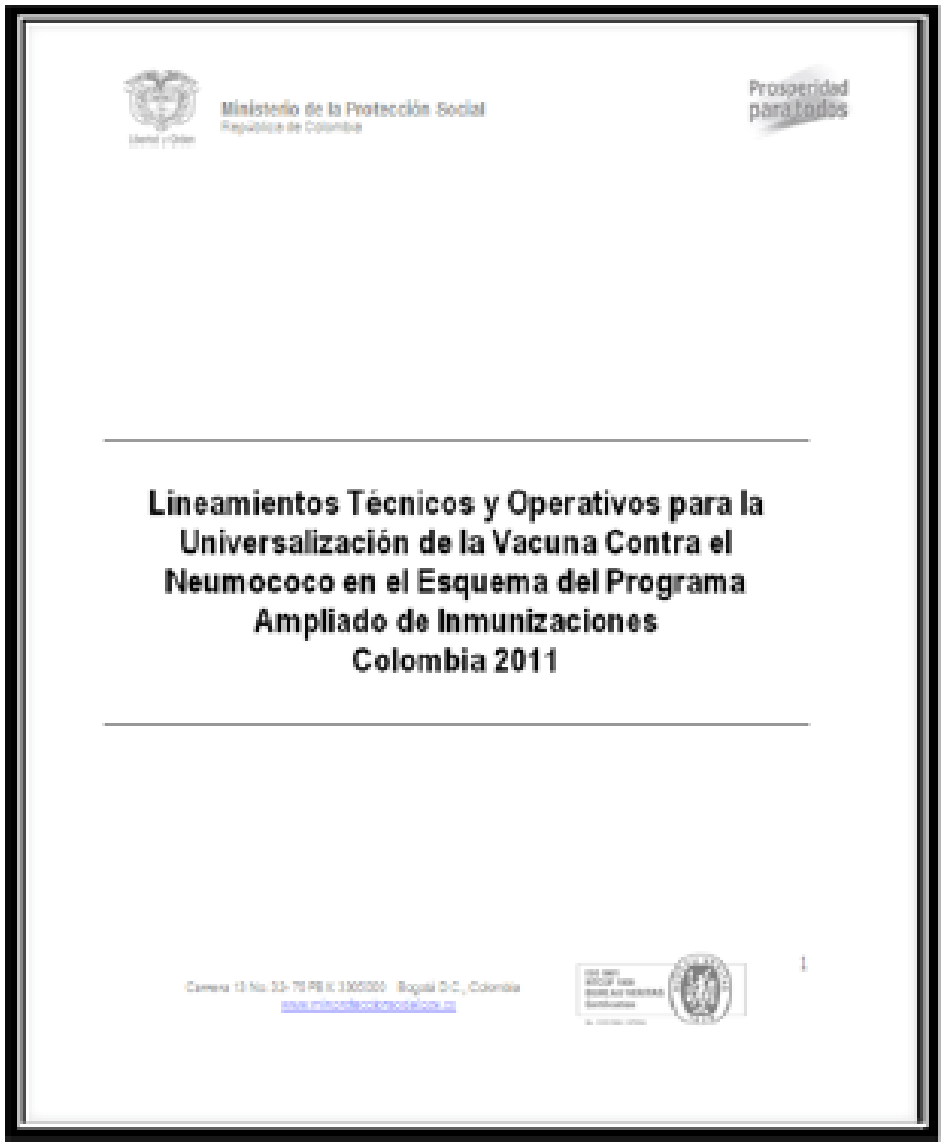
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Resultados: eficacia vacunal contra ENI

- **EV contra ENI fue 100% para ambos análisis por intención de tratar y por protocolo.**

Tipo de ENI	Análisis por protocolo			Análisis intención de tratar		
	Número de casos		EV (95% IC)	Número de casos		EV (95% IC)
	PHiD-CV N=10,211	Control N=10,140		PHiD-CV N=11,798	Control N=11,799	
VT	0	16	**100%** (74; 100)	0	18	**100%** (77; 100)
Todos los serotipos	6	17	**65%** (11; 86)	7	21	**67%** (22; 86)

EV, eficacia vacunal; IC, intervalo de confianza; N, número de niños en la cohorte por protocolo y de intención de tratar; VT, serotipo vacunal



Ministerio de la Protección Social
República de Colombia

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Lineamientos Técnicos y Operativos para la Universalización de la Vacuna Contra el Neumococo en el Esquema del Programa Ampliado de Inmunizaciones Colombia 2011

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1

UNIVERSALIZACIÓN DE LA VACUNA A LA COHORTE NACIDA A PARTIR DEL 1 DE NOVIEMBRE DE 2010

VACUNA DE TRECE SEROTIPOS

PEDIATRICS®

OFFICIAL JOURNAL OF THE AMERICAN ACADEMY OF PEDIATRICS

Policy Statement Recommendations for the Prevention of Streptococcus pneumoniae Infections in Infants and Children: Use of 13-Valent Pneumococcal Conjugate Vaccine (PCV13) and Pneumococcal Polysaccharide Vaccine (PPSV23)

COMMITTEE ON INFECTIOUS DISEASES

Pediatrics published online May 24, 2010;
DOI: 10.1542/peds.2010-1280

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://www.pediatrics.org

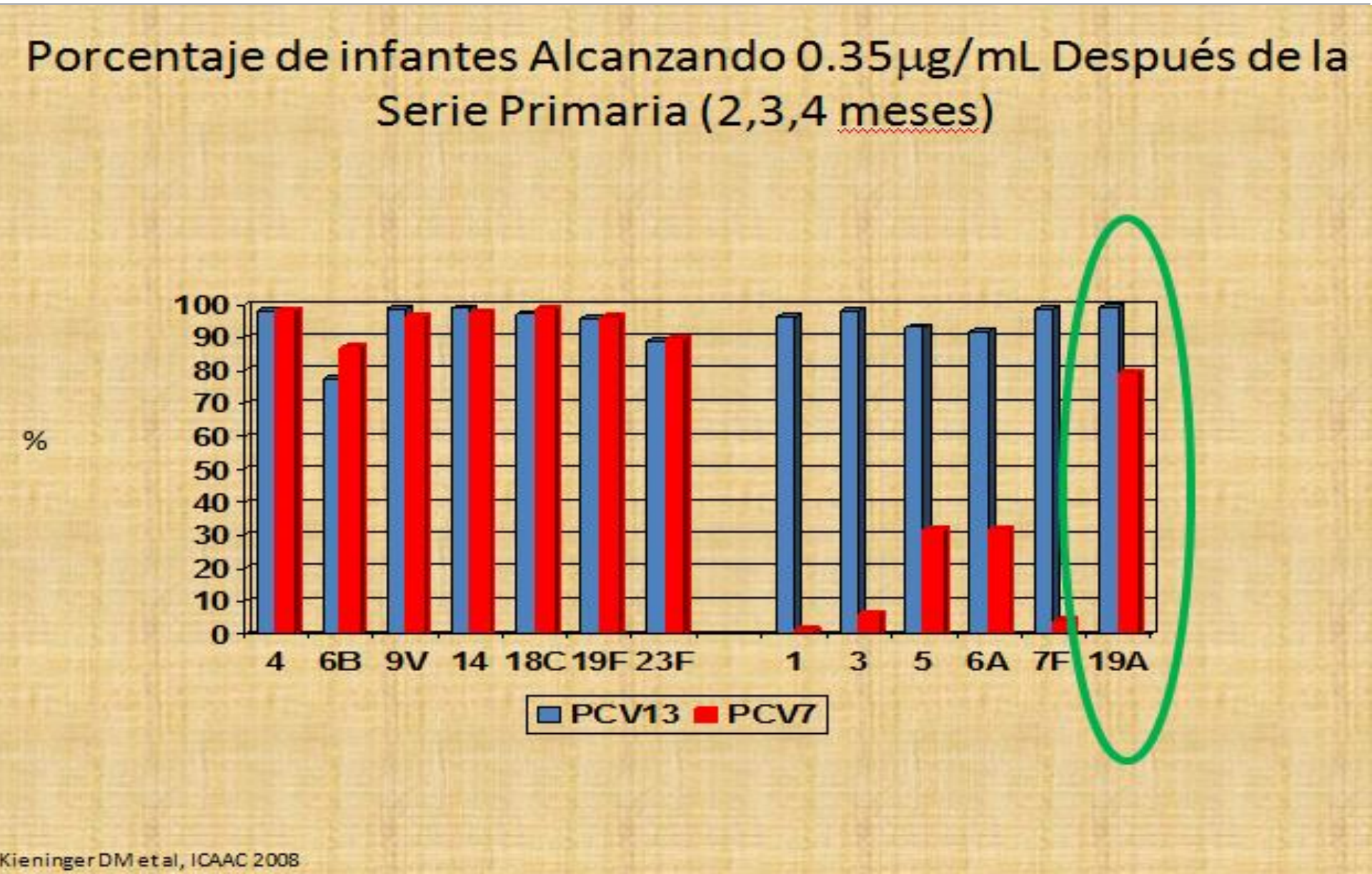
VACUNA DE 13 SEROTIPOS
DATOS INICIALES*

- G-2117 (N=2117 NIÑOS ALEMANES)
- G-2119 (N=613 NIÑOS FRANCESES)
- G-2118 (N=278 NIÑOS INGLESES)
- G-2116 (N=269 NIÑOS POLACOS)

"SIMILAR SEGURIDAD E INMUNOGENICIDAD A LA HEPTAVALENTE + >0.35MCG/ML CONTRA 6 SEROTIPOS ADICIONALES (>90% VACUNADOS)"

*ICAAC/IDSA, WASHINGTON OCT 2008

VACUNA DE TRECE SEROTIPOS



Kieninger DM et al, ICAAC 2008

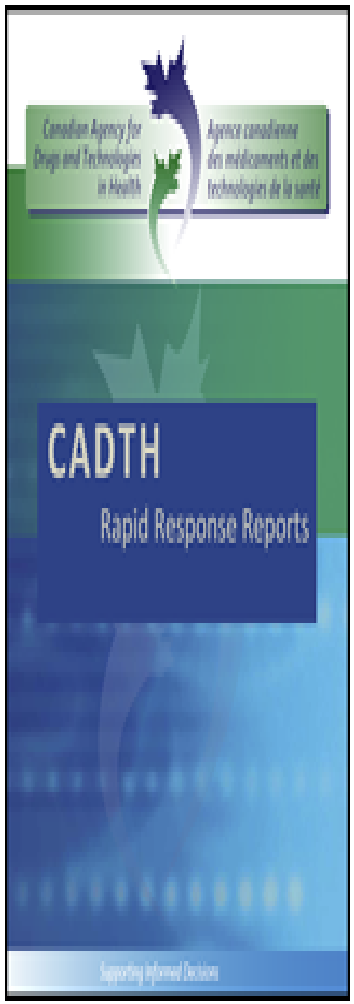
RECOMENDACIONES AAP

Vacunacion rutinaria a todos los niños entre 2 a 59 meses :2- 4-6 meses mas un refuerzo a los 15 meses

Una dosis única de PCV13 puede ser administrada a personas entre 6 a 18 años , con factores de riesgo para adquirir infección neumococica

Niños que habian iniciado su vacunación con PCV7 pueden Continuar con PCV13

Pediatrics 2010



Conjugate Pneumococcal Vaccine (13-Valent) for Immunocompromised Populations: A Review of the Clinical Evidence

Rapid Response Report: Summary with Critical Appraisal

Ottawa (ON): Canadian Agency for Drugs and Technologies in Health; 2014 Mar 27.

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TABLE 1. Underlying medical conditions that are indications for pneumococcal vaccination among children, by risk group --- Advisory Committee on Immunization Practices (ACIP), United States, 2010

Risk group	Condition
Immunocompetent children	Chronic heart disease*
	Chronic lung disease†
	Diabetes mellitus
	Cerebrospinal fluid leaks
	Cochlear implant
Children with functional or anatomic asplenia	Sickle cell disease and other hemoglobinopathies
	Congenital or acquired asplenia, or splenic dysfunction
Children with immunocompromising conditions	HIV infection
	Chronic renal failure and nephrotic syndrome
	Diseases associated with treatment with immunosuppressive drugs or radiation therapy, including malignant neoplasms, leukemias, lymphomas, and Hodgkin disease; or solid organ transplantation
	Congenital immunodeficiency§

* Particularly cyanotic congenital heart disease and cardiac failure.

ORIGINAL ARTICLE

Assessing the Immunogenic Response of a Single Center's Pneumococcal Vaccination Protocol in Sickle Cell Disease

Jonathan D. Santoro, MD, Leann Myers, PhD,† and Julie Kanter, MD‡*

Summary: Sickle cell disease (SCD) is the most common inherited hematologic disorder in the United States. Patients with SCD are at increased risk of invasive pneumococcal disease and are reliant on both early penicillin prophylaxis and antipneumococcal vaccination for prevention of infection. Although studies examining vaccine response have demonstrated a drop-off of titer response after 3 years, an optimal vaccination regimen has not been identified. Our study sought to assess the immunogenicity of our center's pneumococcal vaccination strategy, which included Prevnar (PCV-

Sickle cell disease (SCD) is the most common inherited hematologic disorder in the United States. Before the advent of newborn screening, over 50% of affected patients died before 5 years of age. Because of early diagnosis and improved preventative care, over 95% of children are surviving into adulthood.[1–3] Previous studies have established that individuals with SCD have a higher risk of certain infections, particularly by encapsulated bacteria such as *Streptococcus pneumoniae*.[4] Before the initiation of new-

(*J Pediatr Hematol Oncol* 2016;38:e102–e106)

Pediatr Blood Cancer

13-Valent Pneumococcal Conjugate Vaccine (PCV13) is Immunogenic and Safe in Children 6-17 Years of Age With Sickle Cell Disease Previously Vaccinated With 23-Valent Pneumococcal Polysaccharide Vaccine (PPSV23): Results of a Phase 3 Study

Mariane De Montalembert, MD, PhD,[1]* Miguel R. Abboud, MD,[2] Anne Fiquet, MD,[3] Adlette Inati, MD,[4] Jeffrey D. Lebensburger, DO,[5] Normeen Kaddah, MD,[6] Galila Mokhtar, MD,[7] Antonio Piga, MD,[8] Natasha Halasa, MD, MPH,[9] Baba Inusa, MD,[10] David C. Rees, FRCPCH,[11] Paul T. Heath, FRCPCH,[12] Paul Telfer, MD,[13] Catherine Driscoll, MD,[14] Sami Al Hajjar, MD,[15] Alberto Tozzi, MD,[16] Qin Jiang, MS,[17] Emilio A. Emini, PhD,[18] William C. Gruber, MD,[18] Alejandra Gurtman, MD,[18] and Daniel A. Scott, MD[18]

Background. A large population of older children with sickle cell disease (SCD) is currently vaccinated with only 23-valent pneumococcal polysaccharide vaccine (PPSV23). In immunocompetent adults, PPSV23 vaccination reduces immune responses to subsequent vaccination with a pneumococcal vaccine. The 13-valent pneumococcal conjugate vaccine (PCV13), which addresses this limitation, may offer an advantage to this population at high risk of pneumococcal disease. ***Procedure.*** Children with SCD 6–17 years of age previously vaccinated with PPSV23 at least 6 months before study enrollment received two doses of PCV13 6 months apart. Anti-pneumococcal polysaccharide immunoglobulin G (IgG) geometric mean concentrations (GMCs) and opsonophagocytic activity (OPA) geometric mean titers (GMTs) were measured before, 1 month after each administration, and 1 year after the second administration. ***Results.*** Following each PCV13 administration, IgG GMCs and OPA GMTs significantly increased, and antibody levels after doses 1 and 2 were generally comparable. Antibody levels declined over the year following dose 2. At 1 year after the second administration, OPA GMTs for all and IgG GMCs for most serotypes remained above pre-vaccination levels. Most adverse events were due to vaso-occlusive crises, a characteristic of the underlying condition of SCD. ***Conclusions.*** Children with SCD who were previously vaccinated with PPSV23 responded well to 1 PCV13 dose, and a second dose did not increase antibody response. PCV13 antibodies persisted above pre-vaccination levels for all serotypes 1 year after dose 2. Children with SCD may benefit from at least one dose of PCV13. Pediatr Blood Cancer © 2015 Wiley Periodicals, Inc.

Key words: 13-valent pneumococcal conjugate vaccine; 23-valent pneumococcal polysaccharide vaccine; hydroxycarbamide; immunogenicity; safety; sickle cell disease

INTRODUCTION

Children with sickle cell disease (SCD) are at increased risk of invasive pneumococcal disease (IPD), in part due to functional asplenia [1]. In North America, *Streptococcus pneumoniae* infection was the leading cause of death in SCD children in the 1980s [2]. Interventions aimed at reducing pneumococcal disease in this population have focused primarily on prophylactic penicillin coccal infection, particularly useful in children under 5 years of age who are at greatest risk [3,4]. However, the burden of IPD-associated morbidity and mortality among SCD children continues to be a challenge [5].

The 23-valent pneumococcal polysaccharide vaccine (PPSV23) was recommended for children ≥2 years of age with functional or anatomic asplenia, including SCD, as a preventative strategy [6]. PPSV23 was the only vaccine option until 2000, when the 7-valent

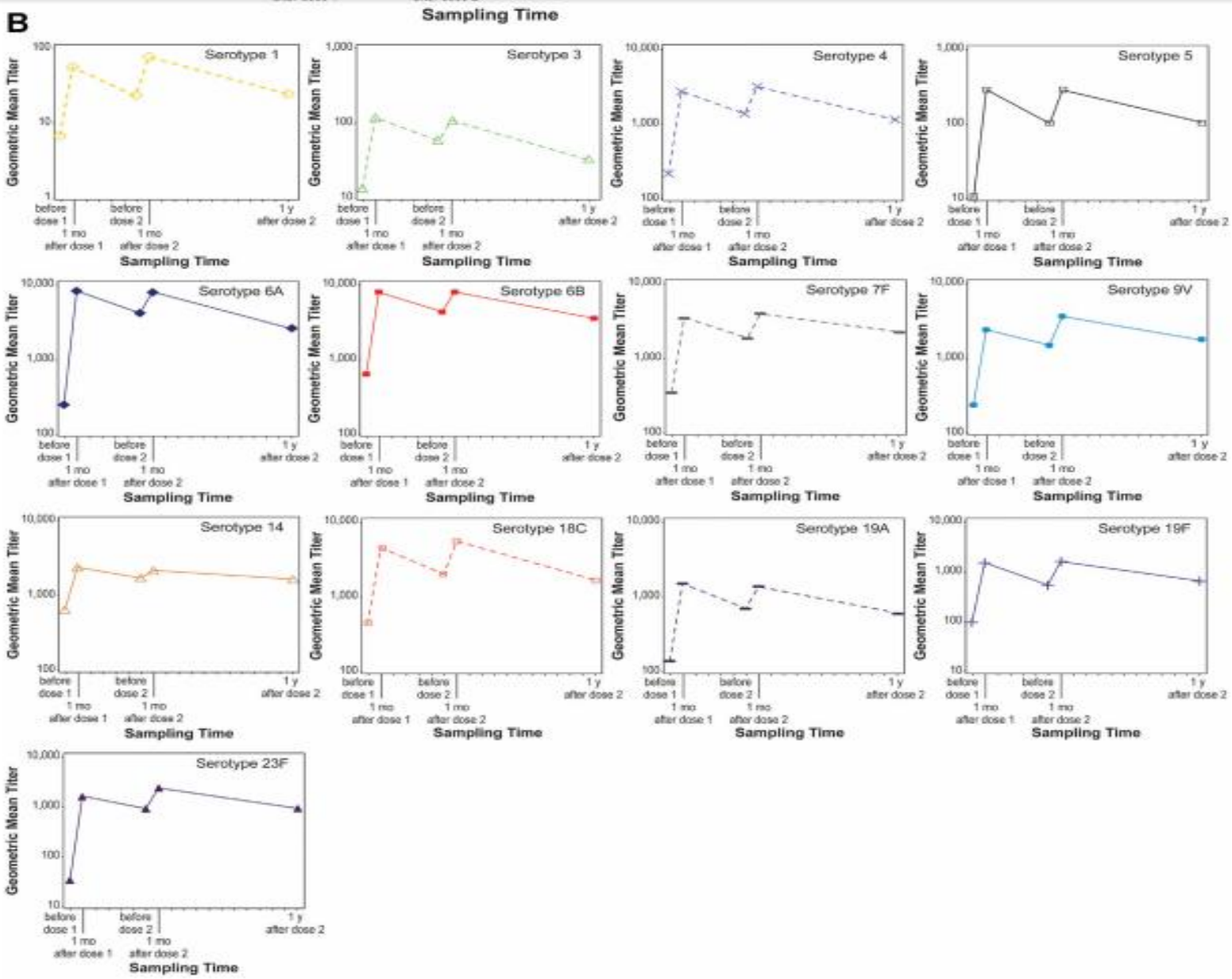
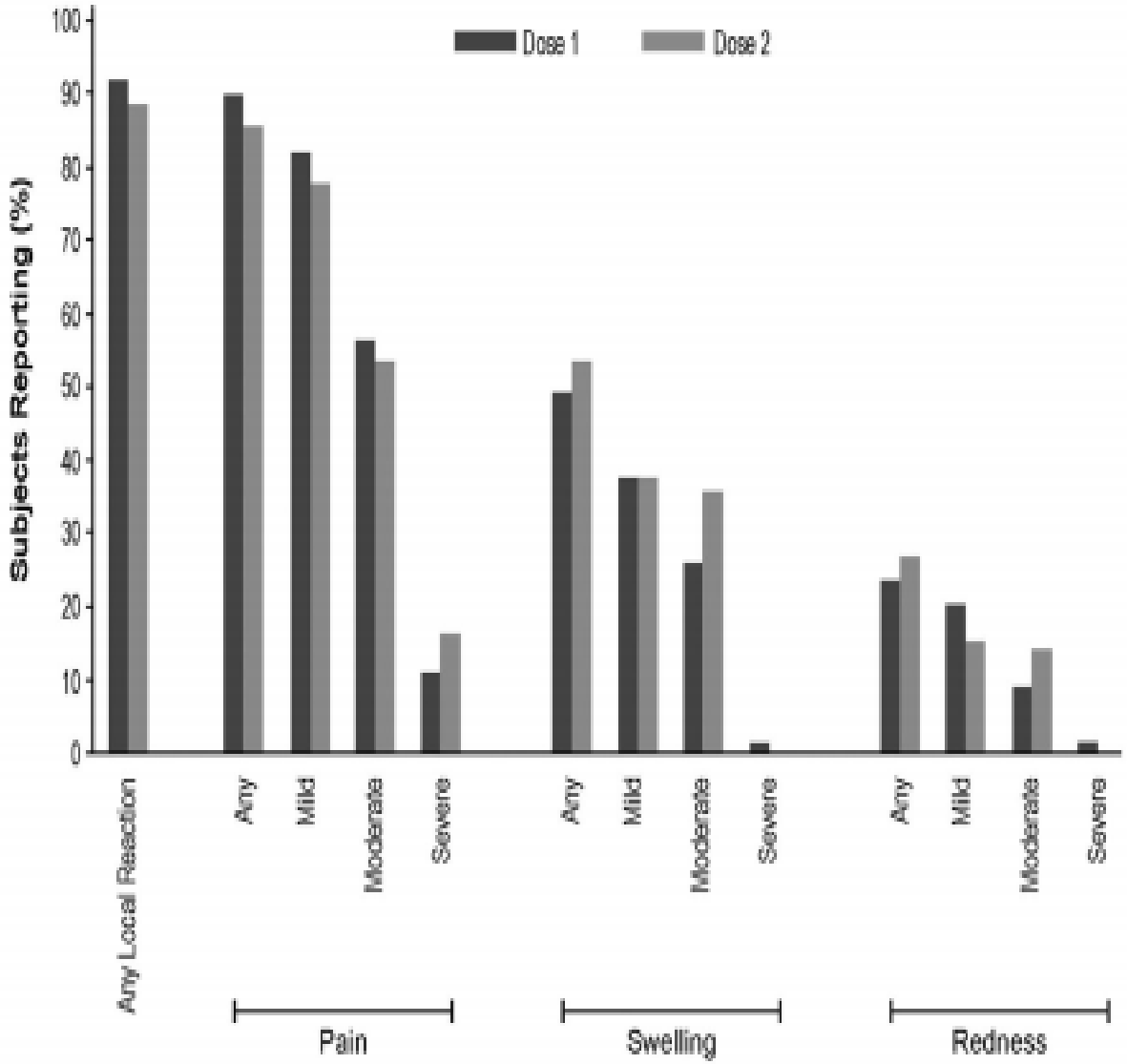


Figure 1. Pneumococcal IgG GMCs and OPA GMTs at each sampling time for PCV13 (evaluable immunogenicity population). IgG = immunoglobulin G; GMC = geometric mean concentration; OPA = opsonophagocytic activity; GMT = geometric mean titer; PCV13 = 13-valent pneumococcal conjugate vaccine.

A


Dose 1
Dose 2
Subjects Reporting (%)
100
90
80
70
60
50
40
30
20
10
0
Any Local Reaction
Any
Mild
Moderate
Severe
Any
Mild
Moderate
Severe
Any
Mild
Moderate
Severe
Pain
Swelling
Redness

B

Pneumococcal vaccines for sickle cell disease (Review)

Davies EG, Hirst C, Lottenberg R, Dower N



We recommend that conjugate pneumococcal vaccines are used in people with sickle cell disease.

Morbidity and Mortality Weekly Report (*MMWR*)

Persons using assistive technology might not be able to fully access information in this file. For assistance, please send e-mail to: mmwrq@cdc.gov. Type 508 Accommodation and the title of the report in the subject line of e-mail.

Use of 13-Valent Pneumococcal Conjugate Vaccine and 23-Valent Pneumococcal Polysaccharide Vaccine Among Children Aged 6-18 Years with Immunocompromising Conditions: Recommendations of the Advisory Committee on Immunization Practices (ACIP)

Weekly
June 28, 2013 / 62(25);521-524

RECOMENDACIONES PCV 13

Una dosis suplementaria de PCV13 se debe aplicar a niños sanos de 15 a 71 meses de edad, que no recibieron al menos 1 dosis de PCV 13 y padecen una afeccion medica subyacente (CELULAS FALCIFORMES) .

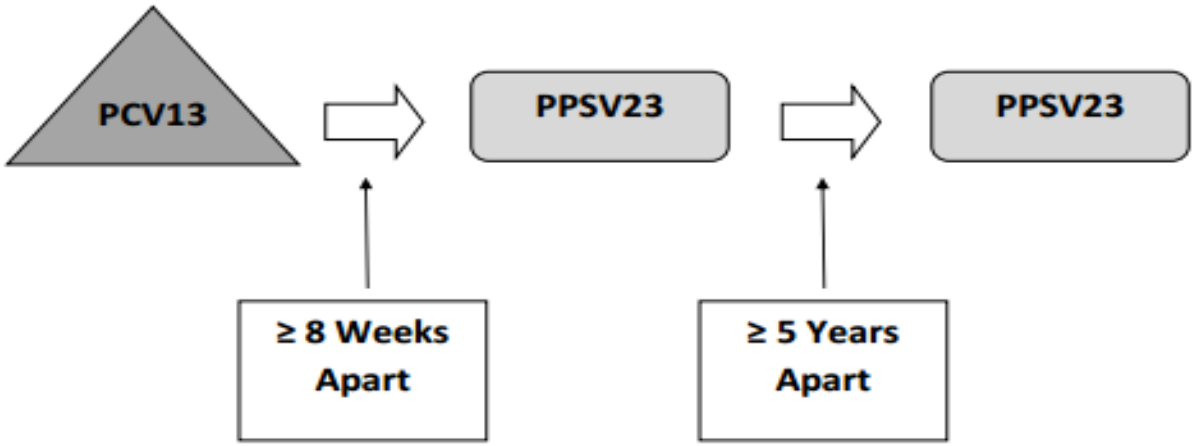
En niños mayores de 2 años de edad con afección medica subyacente una dosis de PPSV23 debe ser aplicada 8 semanas después de la ultima dosis de PCV 13.

Se recomienda la revacunación con dosis de PPSV23, 5 años después de la primera dosis para > de 2 años. No deben administrarse mas de 2 dosis de PPSV23.

RED BOOK 2015

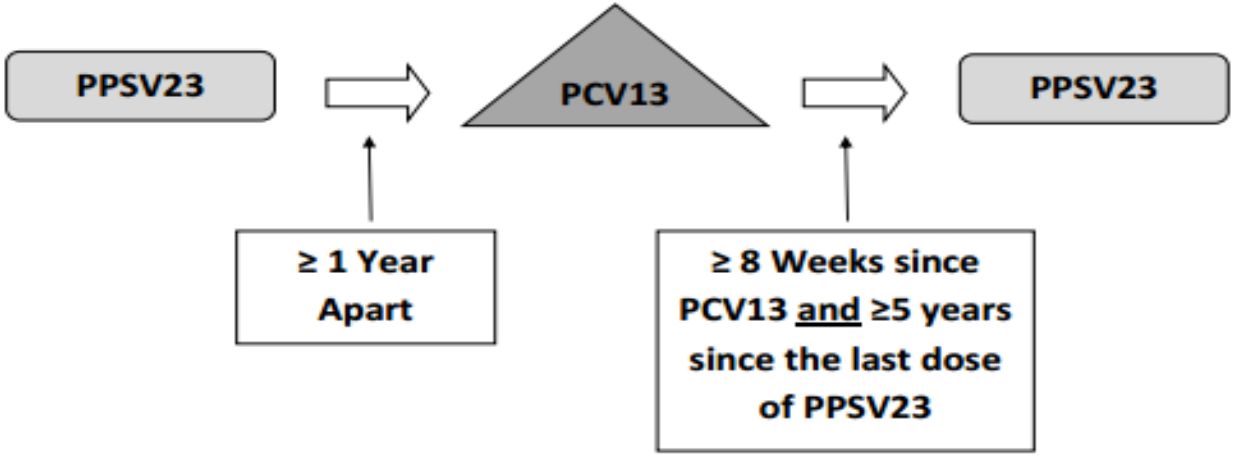
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ACIP RECOMMENDATIONS FOR SEQUENTIAL ADMINISTRATION AND RECOMMENDED INTERVALS FOR PNEUMOCOCCAL VACCINE-NAÏVE HIGH-RISK PERSONS 19–64 YEARS OF AGE: [5]



SECTION III H:

ACIP RECOMMENDATIONS FOR SEQUENTIAL ADMINISTRATION AND RECOMMENDED INTERVALS FOR HIGH-RISK PERSONS 19–64 YEARS OF AGE WITH PRIMARY PPSV23 IMMUNIZATION: [5]



Revised: 01–2016

Oregon Health Authority

CONCLUSIONES

La infección neumocócica invasora representa una de las principales causas de morbilidad, mortalidad y secuelas en todos los países del mundo.

Una gran cantidad de limitaciones diagnósticas contribuye a menospreciar la carga de enfermedad neumocócica invasora, particularmente en regiones subdesarrolladas.

El impacto económico que produce la enfermedad neumocócica invasora es substancial, tanto en el sistema sanitario, como en la sociedad como en el individuo afectado.

La prevención por vacunas es la mejor estrategia para reducir considerablemente la carga y severidad de la enfermedad neumocócica invasora mediante una relación costo-beneficio ampliamente favorable**.**

Universidad del Valle

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GRACIAS

