¿Es la vacuna neumocócica polisacarídica de 23 serotipos necesaria en los niños de riesgo?

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JORNADAS DE VACUNAS AEP
Murcia, 13 y 14 de marzo de 2015

Potencial conflicto de intereses

Participación en actividades formativas organizadas o subvencionadas por industrias farmacéuticas del área de vacunas.

He recibido honorarios por docencia y financiación para asistir a cursos y congresos.

¿Por qué esta pregunta?

- Las vacunas conjugadas son mejores
- Duda que aporte algún beneficio adicional
- ¿Puede empeorar la respuesta a la VNC13?
- ¿Debemos continuar usándola?

Las vacunas conjugadas son mejores

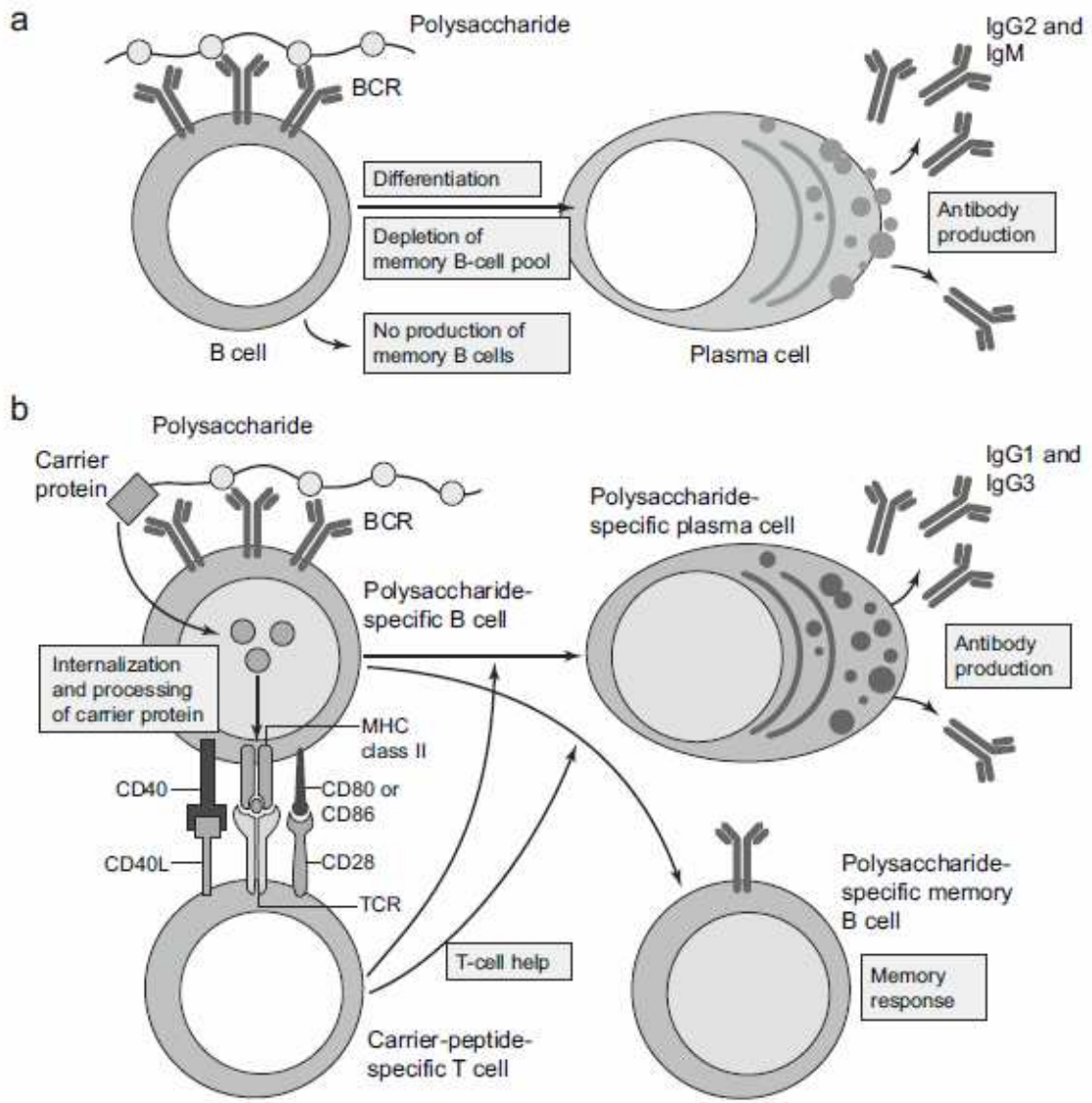
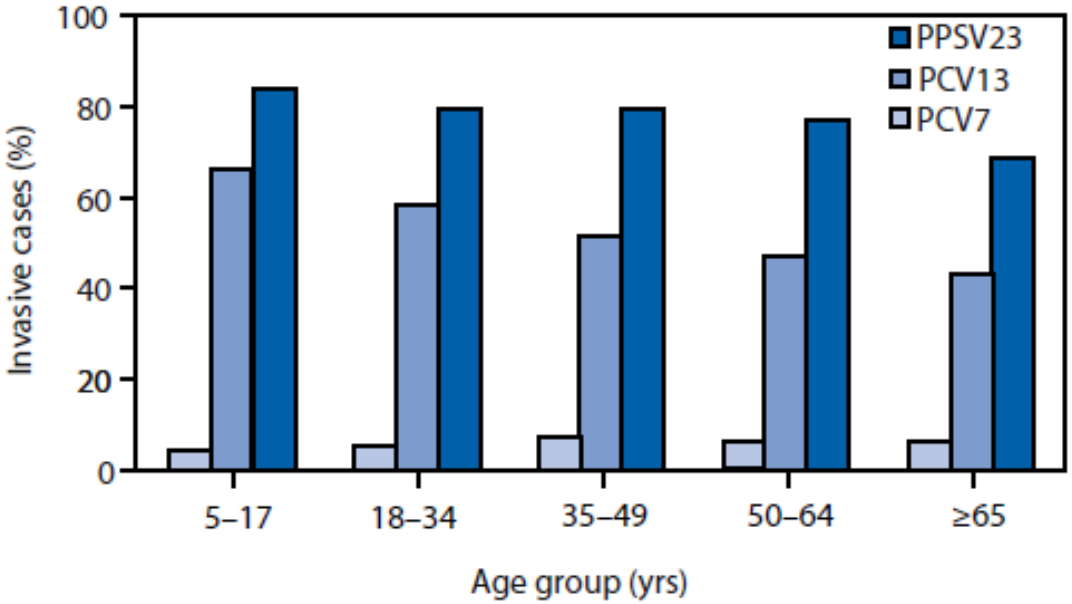


Fig. 1 Immune response to polysaccharide and conjugate vaccines. a Polysaccharides from the encapsulated bacteria that cause disease in early childhood stimulate B cells by cross linking the B cell receptor (*BCR*) and drive the production of immunoglobulins. This process results in a lack of production of new memory B cells and a depletion of the memory B cell pool, such that subsequent immune responses are decreased. b The carrier protein from protein–polysaccharide conjugate vaccines is processed by the polysaccharide specific B cell, and peptides are presented to carrier peptide specific T cells, resulting in T cell help for the production of both plasma cells and memory B cells. *CD40L*, CD40 ligand; *TCR*, T cell receptor. Reprinted with permission from Macmillan Publishers Ltd.: Pollard et al. Nat Rev Immunol 2009;9(3):213–20 [37], copyright 2009

A. Torres & P. Bonanni & W. Hryniewicz & M. Moutschen & R. R. Reinert & T. Welte. Pneumococcal vaccination: what have we learnt so far and what can we expect in the future? Eur J Clin Microbiol Infect Dis (2015) 34:19–31

¿Pueden aportar algún benefició adicional a la VNC13?

FIGURE 3. Proportion of cases of invasive pneumococcal disease caused by serotypes in different vaccine formulations, by age group — United States, Active Bacterial Core surveillance areas, 2008



Abbreviations: PCV7 = 7-valent pneumococcal polysaccharide-protein conjugate vaccine, PCV13 = 13-valent pneumococcal polysaccharide-protein conjugate vaccine, and PPSV23 = 23-valent pneumococcal polysaccharide vaccine.

VNC13=PCV13
VNP23=PPSV23

MMWR **December 10, 2010 / Vol. 59 / No. RR-11**

¿Puede empeorar la respuesta a la VNC13?

Manual de vacunas en línea de la AEP
31. Neumococo

- Por ser **antígenos T-independientes**, las vacunas que contienen polisacáridos puros **no inducen memoria inmunológica ni respuestas secundarias de anticuerpos** y son poco inmunógenas por debajo de los 2 años de edad.

- Por otra parte, la **administración repetida** de estas vacunas conduce a una disminución de la respuesta de anticuerpos (**tolerancia**), aunque este **hecho ha sido cuestionado recientemente**.

Combined schedules of pneumococcal conjugate and polysaccharide vaccines: is hyporesponsiveness an issue?

Revisión en la que se analiza la hipótesis de la hiporrespuesta inmunitaria a antígenos neumocócicos tras esquemas combinados de vacunación con preparados conjugados y polisacarídicos no conjugados, sobre todo cuando se administran dosis múltiples de estos últimos.

- **No existe clara evidencia de este fenómeno, y en niños existen muy pocos estudios.**

O'Brien KL, Hochman M, Goldblatt D. Lancet Infect Dis 2007; 7: 597–606

Hyporesponsiveness and its clinical implications after vaccination with polysaccharide or glycoconjugate vaccines (Review)

Hyporesponsiveness (tolerance) follows vaccination with meningococcal polysaccharide and many pneumococcal polysaccharide serotypes

Use of conjugate vaccines has not been associated with hyporesponsiveness to date (possible exception of pneumococcal serotype 3)

- **Introduction of polysaccharide vaccines anywhere into a conjugate vaccination schedule may result in reduced immune responses on subsequent exposure**

Poolman J, Borrow R. Expert Rev Vaccines. 2011 Mar;10(3):307-322

Dosing regimen of the 23-valent pneumococcal vaccination: A systematic review

OBJETIVO

We aimed to **determine the optimal dose and timing of PPV23 booster in high-risk groups**

CONCLUSIÓN

The majority of evidence consistently indicated an **increase in antibody response following PPV23 revaccination in both adult and pediatric populations**.

Evidence on multiple revaccinations was limited and mixed. Revaccination with PPV23 was well tolerated.

The majority of evidence reviewed supports PPV23 revaccination in both adult and pediatric populations. However, data on multiple booster PPV23 vaccinations in these populations is needed.

C.A. Caya et al. / Vaccine 33 (2015) 1302–1312

Dosing regimen of the 23-valent pneumococcal vaccination: A systematic review

- Muy pocos estudios pediátricos
- En adultos, la revacunación con VNP23 da una respuesta tan buena (en general mejor) como la primovacunación (con VNP23).
- El intervalo óptimo de más de 5 años entre 2 dosis de VNP23 (también en niños)
- La revacunación con 2, 3 o 4 dosis produce un nivel de Ac similar
- No se ha evaluado la efectividad, solo la respuesta de Ac (todos los estudios usan marcadores subrogados de protección)
- Sin estudios de efectividad es difícil concluir si realizar múltiples revacunaciones puede aportar beneficios

C.A. Caya et al. / Vaccine 33 (2015) 1302–1312

- Las vacunas conjugadas son mejores
- Duda que aporte algún beneficio adicional
- ¿Puede empeorar la respuesta a la VNC13?
- **¿Debemos continuar usándola?**

A review of the evidence to inform pneumococcal vaccine recommendations for risk groups aged 2 years and older

El objetivo son las recomendaciones de vacunación de Noruega

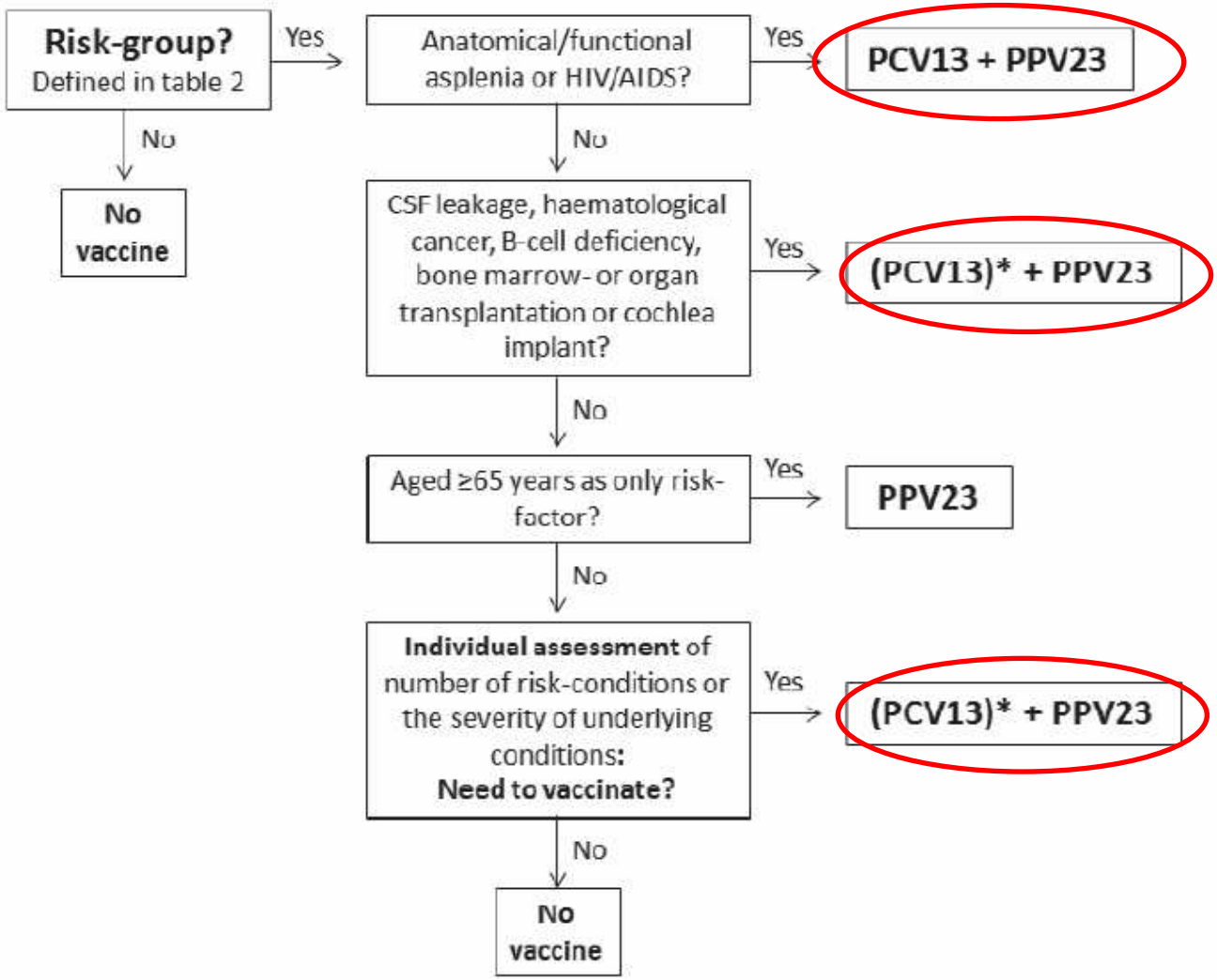
Table 1. *Differences between the pneumococcal polysaccharide and conjugate vaccines*

	Polysaccharide vaccine (PPV23) Pneumovax 23®	Conjugate vaccine (PCV13) Prevnar 13®
Immunogenic in children aged <2 years	No	Yes
Stimulation of T-cell immunity	No	Yes*
Induction of immunological memory	No	Yes*
Induction of mucosal immunity	No	Yes*
Effect on nasopharyngeal carriage	No	Yes*
Included serotypes	1, **2**, 3, 4, 5, 6B, 7F, **8**, **9N**, 9 V, **10A**, **11A**, **12F**, 14, **15B**, **17F**, 18C, 19A, 19F, **20**, **22F**, 23F, **33F**	1, 3, 4, 5, **6A**, 6B, 7F, 9 V, 14, 18C, 19A, 19F, 23F
Percentage of IPD cases with vaccine serotype in Norway in 2013	72%	39%
Antigen concentration (purified capsular polysaccharide)	25 μg of each of the 23 serotypes	2·2 μg of each serotype, except for serotype 6B: 4·4 μg
Adjuvants	None	Aluminium phosphate

IPD, Invasive pneumococcal disease.
Serotypes in bold indicate serotypes that are only included in the respective vaccine.
* Shown in children. Not yet known if this also accounts for adults.

A. STEENS et al. Epidemiol. Infect. (2014), 142, 2471–2482.

A. Steens and others



* Assessment of the need to vaccinate with PCV13 in addition to PPV23 should, a.o., be based on the number of risk-conditions, the severity of the conditions, the degree of risk for severe pneumococcal disease, the vaccine effectiveness in the appropriate risk-groups, and time aspects in relation to potential transplantation or start of immunosuppressive therapy.

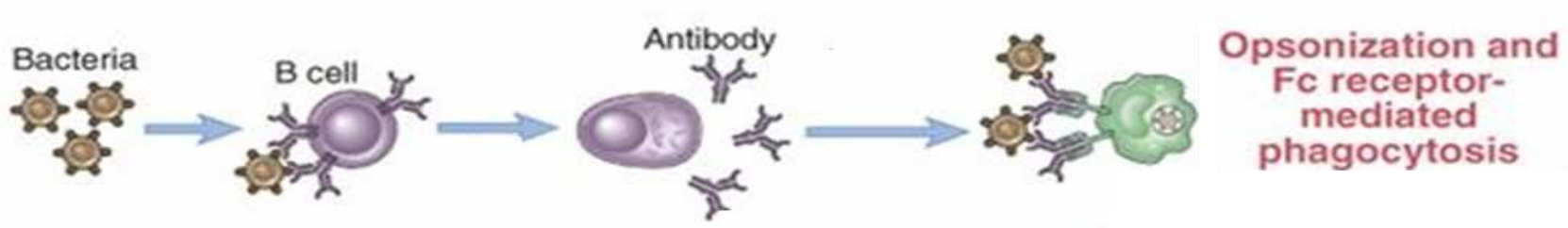
. Flow diagram for the decision on vaccination of risk groups aged ⩾2 years in Norway from May 2013

"To generate vaccine-mediated protection is a complex challenge. Currently available vaccines have largely been developed empirically, with little or no understanding on how they activate the immune system"

Claire-Anne Siegrist. Vaccine immunology in Plotkin SA, Orenstein WA, Offit PA, editors. Vaccines. 6a ed. Philadelphia: Elsevier; 2012, p.17-36

Respuesta inmune al neumococo

El principal mecanismo de defensa contra el neumococo es la opsonización de la bacteria por los anticuerpos, en presencia de los componentes tempranos del complemento, seguida de la fagocitosis y muerte del patógeno por los polimorfonucleares y macrófagos.



- En la sangre, la gruesa capsula impide que los antígenos subcapsulares sean reconocidos por las opsoninas del huésped. Son necesarios los anticuerpos que se unen a la cápsula para que la bacteria sea susceptible a la fagocitosis.
- Importancia del bazo.

Respuesta inmune al neumococo

- Reservorio natural en nasofaringe
- La inmunidad mucosa y sistémica, contribuyen en la defensa contra la portación nasofaríngea y en la prevención de infecciones posteriores
- IgG trasudada a las mucosas, junto con IgA secretora pueden interferir con la adhesión a la mucosa
- Tras la inflamación, los fagocitos migran a la mucosa y aumentan en el aclaramiento del patógeno

Respuesta inmune al neumococo (en no vacunados)

- Son frecuentes los Ac contra los PS a baja concentración
- La edad en la que se puede montar una respuesta de anticuerpos frente al PS capsular coincide con la que la enfermedad disminuye
- La colonización nasofaríngea (portación asintomática) induce una respuesta natural de Ac contra los PS y las proteínas de neumococo
- La inmunidad natural puede conferir protección por Ac o también mediada por células

Respuesta inmune humoral

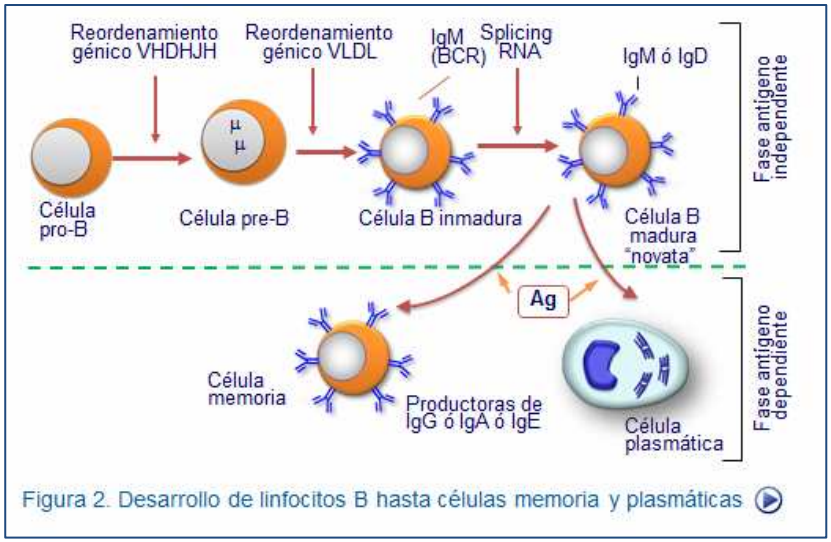


Figura 2. Desarrollo de linfocitos B hasta células memoria y plasmáticas

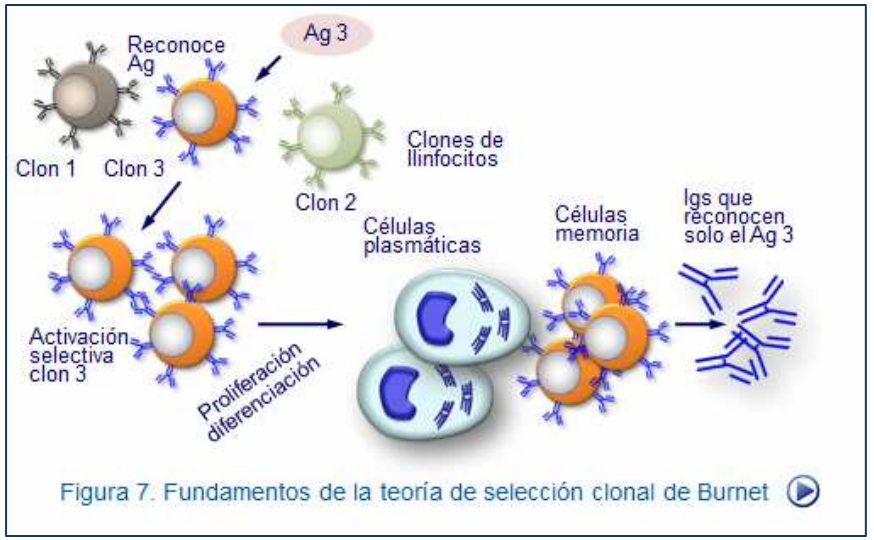


Figura 7. Fundamentos de la teoría de selección clonal de Burnet

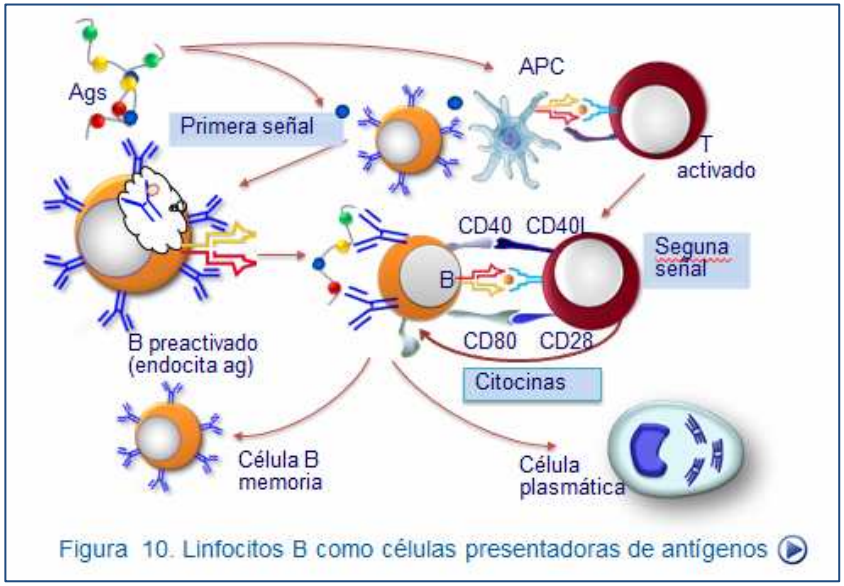


Figura 10. Linfocitos B como células presentadoras de antígenos

Los linfocitos B precisan de al menos dos señales para su activación. El reconocimiento de un determinado antígeno (**primera señal**) y la presencia de linfocitos T, que facilitarían una **segunda señal** necesaria para una óptima activación.

Las partes del antígeno reconocidas por los la inmunoglobulina de membrana de los linfocitos B, pueden ser distinta a las que reconcomen los receptores de los linfocitos T.

Inmunología en línea. José Peña Martínez. Universidad de Córdoba.
http://inmunologiaenlinea.es/

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Respuesta inmune humoral

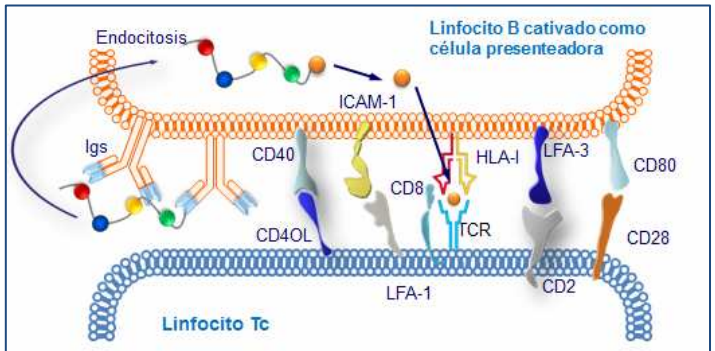

Figura 9. Sinapsis de linfocitos T y B y función de APC de linfocitos B

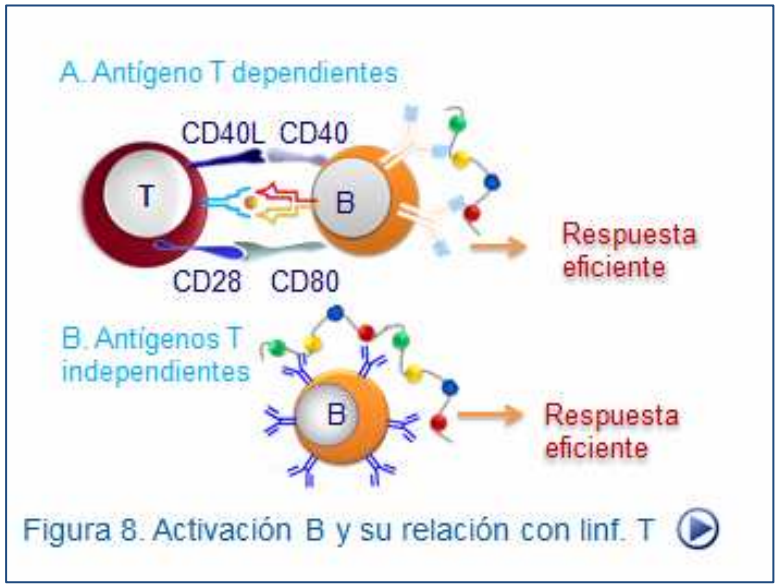

Figura 8. Activación B y su relación con linf. T

Hay antígenos que en ausencia de células T pueden producir una respuesta de linfocitos B, conocida como **activación B, independiente de linfocitos T.**

Los **antígenos T independientes** que se caracterizan por poseer **epitopos iguales muy repetidos** como ocurre con ciertos con estructuras, principalmente hidratos de carbono, presentes en bacterias que **son reconocidos simultáneamente por muchos receptores BCR, dando lugar a la activación de células B sin necesidad de la interacción con las T.**

La respuesta T independiente es incompleta, hay un predominio de producción de Ig M y no se producen linfocitos B de memoria.

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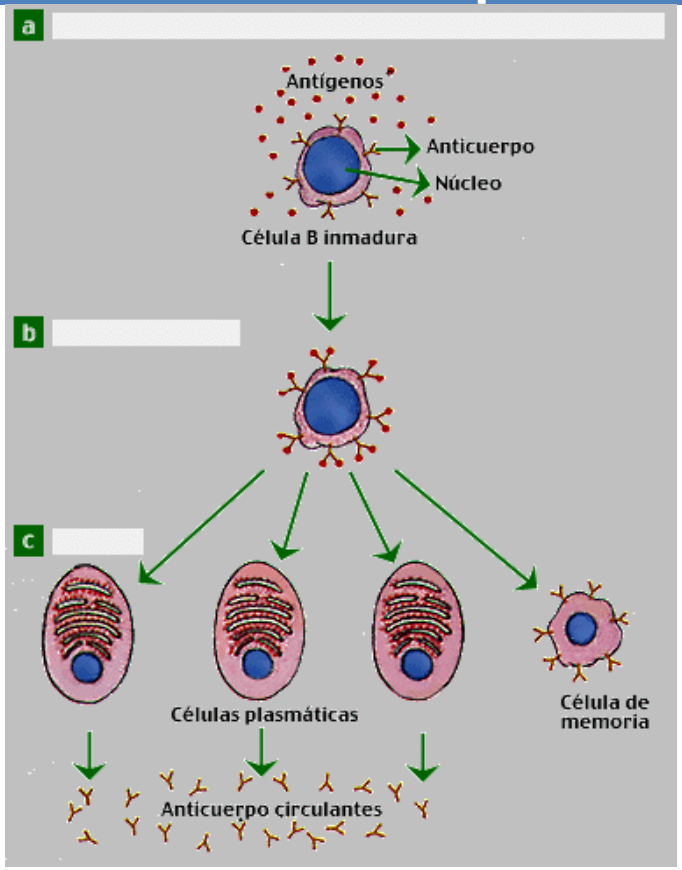
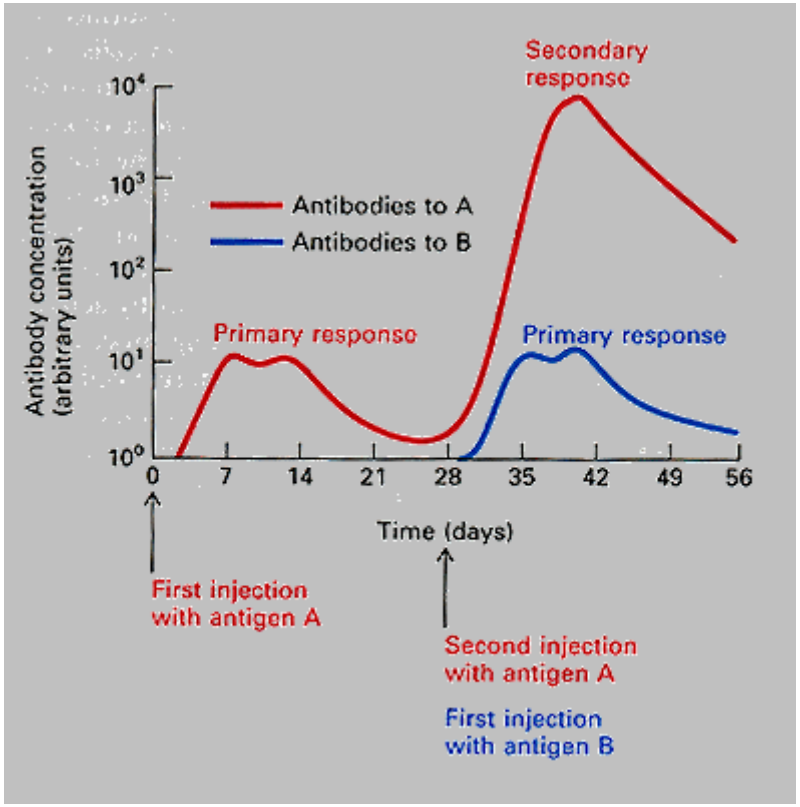
Respuesta inmune humoral





Los linfocitos B una vez activados se diferencian a células plasmáticas, que son las verdaderamente productoras de Acs solubles, pueden permanecer años produciendo anticuerpos desde los lugares donde normalmente se asientan (pulpa roja del bazo, ganglios linfáticos y médula ósea)

Durante la activación también se producen células B memoria que se mantendrán en el organismo durante mucho tiempo. Estas células al ser activadas por el Ag producirán una respuesta secundaria.

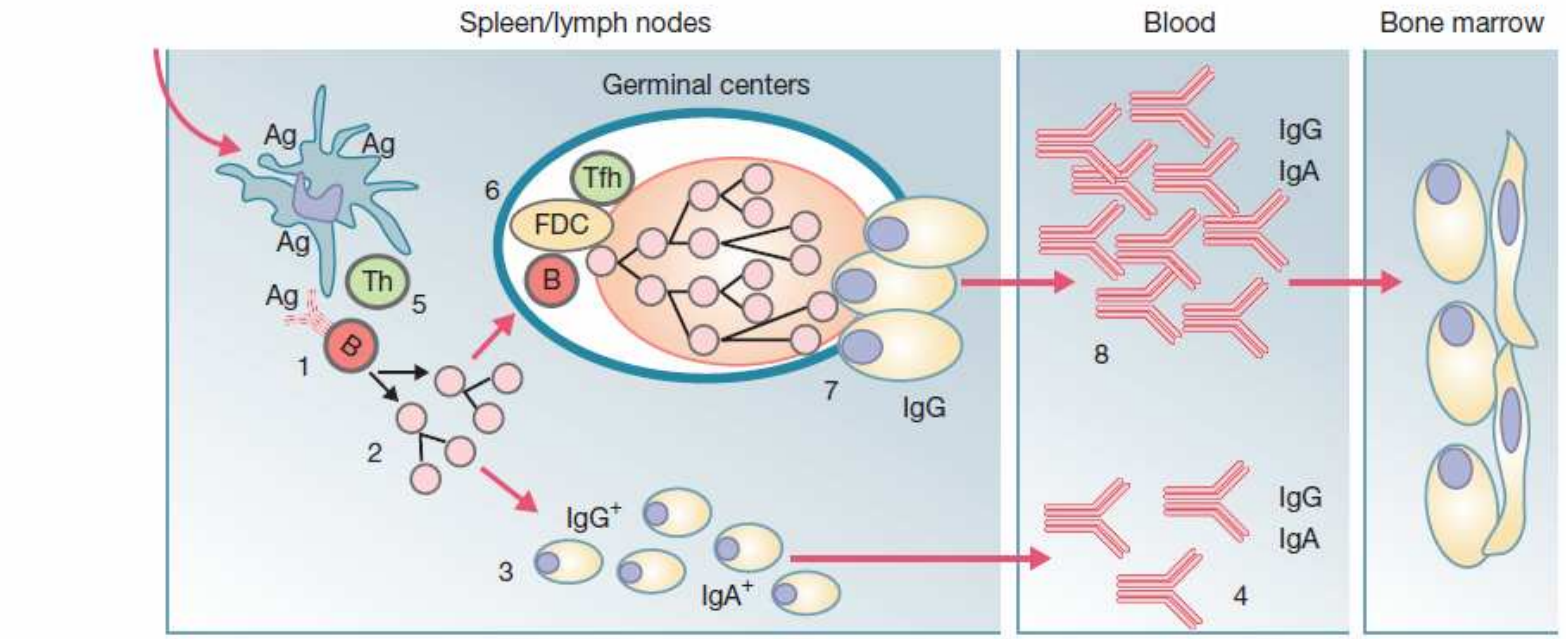


Figure 2–2 Extrafollicular and germinal center responses to protein antigens. In response to a protein antigen reaching lymph nodes or

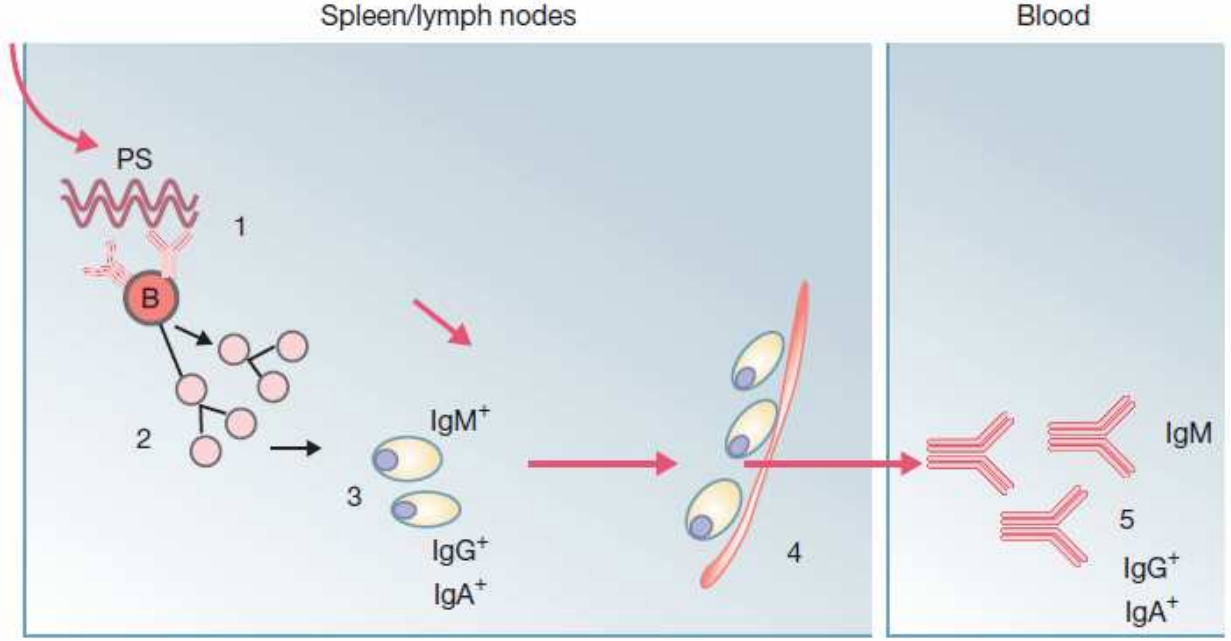
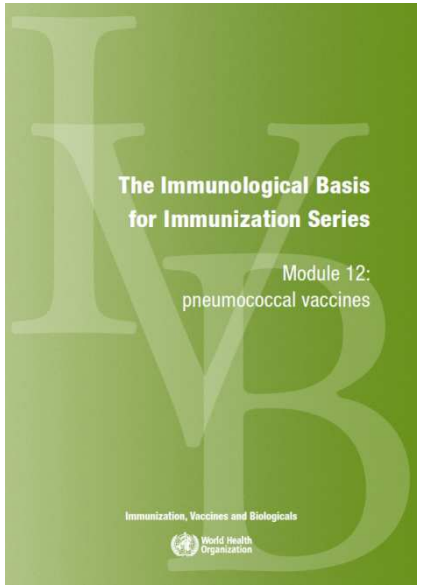


Figure 2–4 Extrafollicular B cell responses to polysaccharide antigens. B cells use their specific Ig surface receptors (1) to bind to the repetitive structures of polysaccharides reaching the marginal zone of spleen/nodes. In the absence of antigen-specific T cell help, B cells are activated, proliferate (2) and differentiate in plasma cells (3) without undergoing affinity maturation in germinal centers. These plasma cells migrate towards the red pulp of the spleen (4) where they survive for a few weeks / months, secreting low levels of low affinity IgM, IgG or IgA antibodies (5).



5.2.6 A booster dose of PCV or PPSV

Independently from the PCV formulation or the primary immunization schedule, a booster dose of either PCV or PPSV is able to induce higher or similar antibody concentrations compared with the primary immunization.

In many cases the PPSV boosting induces higher mean antibody concentrations than the PCV boosting

La VNP23 en personas previamente vacunadas con vacuna conjugada dan una respuesta *booster* intensa

WHO Library Cataloguing-in-Publication Data
The immunological basis for immunization series : module 12: pneumococcal vaccines / Helena Käyhty … [et al]. World Health Organization 2009

5.2.2 Mucosal antibody responses to PCVs

PCVs prevent mucosal infections (AOM and colonization), and some groups have made efforts to characterize the mucosal immune response after vaccination, in the hope of finding serological correlates of mucosal protection. Such studies have addressed IgG and secretory IgA antibody concentrations in salivary fluid.

Lymphocytes encountered by antigens in the respiratory tract migrate back to the mucosal tissues after maturation to antibody production in local lymph nodes.

The PCVs induce the production of local antibodies but thus far no direct link has been established between the salivary antibody concentration and vaccine-induced protection.

La protección en mucosas se debe a que en la respuesta T dependiente hay una maduración en los centros germinales (CG) que produce Ac de alta afinidad y en más cantidad. Salen células plasmáticas con estas características. Mientras que en la respuesta T-independiente no pasa.

WHO Library Cataloguing-in-Publication Data
The immunological basis for immunization series : module 12: pneumococcal vaccines / Helena Käyhty … [et al]. World Health Organization 2009

- En los vacunados el título de anticuerpos va disminuyendo (más en los grupos de riesgo que en los sanos)

- A los 4-5 años de edad las concentraciones de Ac han bajado menos frente a los serotipos 6B, 14, 19F y 23F que son frecuentes en portadores sanos

Interacciones entre la inmunidad producida por vacuna y los neumococos que pasan por la nasofaringe?

WHO Library Cataloguing-in-Publication Data
The immunological basis for immunization series : module 12: pneumococcal vaccines / Helena Käyhty … [et al]. World Health Organization 2009

Safety and immunogenicity of sequential pneumococcal immunization in preschool asthmatics. M.A. Rose et al. / Vaccine 27 (2009) 5259–5264

Patients and Methods: Seventy preschool asthmatics (2–5-year-old; mild to moderate asthma) underwent **sequential immunization**: one dose of **PCV-7 followed by a single dose PPV-23.** We randomly assigned half of the vaccinees to receive PPV-23 eight weeks after PCV-7 (group A), and the rest to a 10-month interval (group B)……

Sequential pneumococcal immunization was immunogenic in preschool asthmatics, inducing protection in the majority of our children. Subjects **boostered after eightweeks had significantly lower antibody levels than those boostered after 10 months**. Local and systemic adverse events were mild in character and self-limiting.

Conclusions: Although both sequential pneumococcal vaccine regimens were safe and immunogenic among preschool asthmatics, **immunogenicity was higher when the booster was given after 10 months**

Intervalo entre VNC7 y VNP23

Hay una buena respuesta *booster* en los dos grupos, pero los títulos de anticuerpos son mayores con un intervalo de 10 meses que de 8 semanas

Safety and Immunogenicity of the 23-Valent Pneumococcal Polysaccharide Vaccine at 12 months of age, following One, Two, or Threes Doses of the 7-valent Pneumococcal Conjugate Vaccine in Infancy. F.M. Russell et al. **Vaccine. 2010 April 19; 28(18): 3086–3094**

•Infants aged 6 weeks were stratified and randomized to receive 0, 1, 2, or 3 PCV-7 doses **with or without PPV-23** at 12 months.

•The PPV-23 induced excellent responses for all serotypes which were greatest in the single PCV-7 group. Strong booster effects for all 7 PCV-7 serotypes were elicited, **and for 4/7 serotypes these responses were highest in the single PCV-7 group.**

•There were fourfold rises in GMC for all non-PCV-7 serotypes. Were **good antibody responses to the 16 non-PCV-7 serotypes following PPV-23 at 12 months**.

•By 17 months the PPV-23 group still had significantly higher GMC (each p<0.001) for all serotypes, compared to the group that had not received PPV-23

- Mejor respuesta en los *primed* con solo 1 dosis de VNC7.
- En los que han recibido una dosis puede haber más B memoria y menos células plasmáticas?
- Algo de tolerancia inducida por las 2 o 3 dosis de VNC7?

Hyporesponsiveness to re-challenge dose following pneumococcal polysaccharide vaccine at 12 months of age, a randomized controlled trial. Russell F.M. Et al.

Vaccine 2010 28:19 (3341-3349)

Eight groups to receive zero, one, two, or three PCV doses at 14 weeks, six and 14 weeks, or six, ten, and 14 weeks. Within each group, half received **23vPPS at 12 months and all received mPPS at 17 months**. Sera were taken prior and one month post-mPPS

After adjusting for the pre-mPPS level, **exposure to 23vPPS was associated with a lower response to mPPS for all serotypes** (each $p < 0.001$)

Interpretation: Despite higher antibody concentrations at 17 months in children who had received 23vPPS at 12 months, the response to a re-challenge was poor for all 23 serotypes compared to children who had not received the 12 month 23vPPS

¿INTERVALO PEQUEÑO ENTRE LAS DOS DOSIS DE VACUNA POLISACARÍDICA?

Serotype-specific avidity is achieved following a single dose of the 7-valent pneumococcal conjugate vaccine, and is enhanced by 23-valent pneumococcal polysaccharide booster at 12 months. FM Russell et al. **Vaccine.** 2011 June 15; 29(27): 4499–4506

Aim—To evaluate whether the avidity of serotype-specific IgG to pneumococcal serotypes is enhanced by an increased number of doses of the 7-valent pneumococcal conjugate vaccine (PCV) in infancy or by a 12 month 23-valent pneumococcal polysaccharide vaccine (23vPPS) booster, and /or subsequent re-exposure to a small dose of pneumococcal polysaccharide antigens (mPPS) at 17 months.

Results—At one month post primary series, the 2 and 3 PCV dose groups demonstrated similar avidity, with the **single dose group tending to have lower avidity**.
However, by age 9 months, the single dose group had similar avidity to the 2 and 3 PCV groups for most serotypes.
The 23vPPS booster enhanced affinity maturation for most serotypes and this was most marked in those groups that received a single PCV dose. There was little further increase following the mPPS.

La respuesta inmunitaria requiere tiempo para que se produzca un incremento de la afinidad de los anticuerpos y la maduración de las células B memoria

Pneumococcal nasopharyngeal carriage following reduced doses of a 7-valent pneumococcal conjugate vaccine and a 23-valent pneumococcal polysaccharide vaccine booster.

Russell F.M. Et al. **Clinical and Vaccine Immunology** 2010 17:12 (1970-1976)

•Parece haber un efecto directo, cuantas más dosis de VNC7 menos portación

•A los 17 meses las ratios de portadores se igualan en todos los grupos

•La VNP23 no influye en la portación, a pesar del booster que produce en los niveles de anticuerpos

A corto plazo, a más dosis de VNC7 (más y mejores anticuerpos) menos portadores
¿Son suficientes 5 meses para medir el efecto de la VNP?

The 23-valent pneumococcal polysaccharide vaccine does not provide additional serotype antibody protection in children who have been primed with two doses of heptavalent pneumococcal conjugate vaccine
Balmer P., Borrow R., Arkwright P.D. **Vaccine** 2007 **25:34 (6321-6325)**

•We assessed the serotype responses to two doses of PCV-7 and a dose of PPV-23 in children in the 2-16-year age range in order to determine whether PPV-23 induced effective immunity to non-PCV-7 serotypes.

•Vaccinated children had 7-30-fold higher antibody concentrations than unvaccinated children to all serotypes contained in the PCV-7 ($P < 0.001$). In contrast, serotypes covered by the PPV-23 but not PCV-7 were only one- to two-fold higher and there was no significant increase in the number of children who had protective concentrations of antibody **(≥0.35 mcg/ml**) against these serotypes.

•In this cohort of children, **PPV-23 vaccine did not broaden the protection in vitro** against potentially pathogenic strains of Streptococcus pneumoniae. We call into question the recommendation to use the PPV-23 in children.

The 23-valent pneumococcal polysaccharide vaccine does not provide additional serotype antibody protection in children who have been primed with two doses of heptavalent pneumococcal conjugate vaccine
Balmer P., Borrow R., Arkwright P.D. **Vaccine** 2007 **25:34 (6321-6325)**

In all cases had involved giving two doses of the PCV-7 and then one dose of PPV-23 **at monthly intervals.**

After pneumococcal vaccination, protection against **serotypes covered by the PCV-7** vaccine was significantly enhanced to **between 82 and 100%.** In contrast, there was no significant difference in the percentage of children protected against **serotypes covered by the PPV-23 but not PCV-7 vaccine**, where levels of protection remained at **between 44 and 82%.**

PCV-7 should replace PPV-23 for all high risk children, not just those less than 5 years old, requiring immunisation against community acquired *S. pneumoniae* and (2) **the use of PPV-23 as an additional booster following PCV-7 should be discontinued or at least be reevaluated.**

- Pauta inadecuada?
- 3 dosis de los serotipos de la VNC y solo 1 de los otros

Table 25.2 Vaccination schedule for those in a clinical risk group

Patient age at presentation	Vaccine given and when to immunise	
	13-valent PCV (PCV13)	23-valent PPV
At-risk children 2 months to under 12 months of age (including infants who have asplenia or splenic dysfunction or who are immunosuppressed)	Vaccination according to the routine immunisation schedule at 2, 4 and 12 months	One dose after the second birthday.
At-risk children 12 months to under 5 years of age who have asplenia or splenic dysfunction or who are immunosuppressed	Two doses, with an interval of 2 months between doses	One dose after the second birthday and at least 2 months after the final dose of PCV13
All other at-risk children 12 months to under 5 years of age	One dose	One dose after the second birthday and at least 2 months after the final dose of PCV13
At-risk children aged 5 years and at-risk adults	PCV is not recommended unless severely immunocompromised (see below for advice for severely immunocompromised)	One dose (see below for advice for severely immunocompromised)

Immunogenicity and safety of 23-valent pneumococcal polysaccharide vaccine as a booster dose in 12- to 18-month-old children primed with 3 doses of 7-valent pneumococcal conjugate vaccine. Usa Thisyakorn, et al. **Human Vaccines & Immunotherapeutics 10:7, 1859–1865; July 2014**; c 2014 Landes Bioscience

Children primed with 3 doses of PCV7 were randomized 1:1 to receive **a booster immunization with PPV23 or PCV7.** Pneumococcal antibody concentrations were measured by enzyme-linked immunosorbent assay and functional antibody levels by multiplex opsonophagocytosis assay on day 30.

Geometric mean serum antibody concentrations against serotypes common to PCV7 and PPV23 (4, 6B, 9V, 14, 18C, 19F, and 23F) **increased in both groups** but they were **higher for serotypes 4, 9V, 18C, and 19F in the PPV23 group**.

Opsonization indices increased in both groups for all measured serotypes (1, 6B, 14, 19A, and 23F) and were **higher for serotypes 6B, 14, and 23F in the PCV7 group and for serotypes 1 and 19A in the PPV23 group.**

This suggests that, although PPV23 alone is poorly immunogenic in children younger than 2 y of age, when used as a booster in PCV7-primed children, it can provide broader pneumococcal antibody responses than boosting with PCV7.

PPSV23 contains 12 of the serotypes included in PCV13, plus **11 additional serotypes**, which account for **23% of IPD** among immunocompromised children aged 6–18 years (CDC, Active Bacterial Core surveillance 2007–2009, unpublished data, 2013)

TABLE. Medical conditions or other indications for administration of PCV13,* and indications for PPSV23† administration and revaccination for children aged 6–18 years§

		PCV13	PPSV23	
Risk group	Underlying medical condition	Recommended	Recommended	Revaccination 5 yrs after first dose
Immunocompetent persons	Chronic heart disease¶		✓	
	Chronic lung disease**		✓	
	Diabetes mellitus		✓	
	Cerebrospinal fluid leaks	✓	✓	
	Cochlear implants	✓	✓	
	Alcoholism		✓	
	Chronic liver disease		✓	
	Cigarette smoking		✓	
Persons with functional or anatomic asplenia	Sickle cell disease/other hemaglobinopathies	✓	✓	✓
	Congenital or acquired asplenia	✓	✓	✓
Immunocompromised persons	Congenital or acquired immunodeficiencies††	✓	✓	✓
	Human immunodeficiency virus infection	✓	✓	✓
	Chronic renal failure	✓	✓	✓
	Nephrotic syndrome	✓	✓	✓
	Leukemia	✓	✓	✓
	Lymphoma	✓	✓	✓
	Hodgkin disease	✓	✓	✓
	Generalized malignancy	✓	✓	✓
	Iatrogenic immunosuppression§§	✓	✓	✓
	Solid organ transplant	✓	✓	✓
	Multiple myeloma	✓	✓	✓

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). MMWR / June 28, 2013 / Vol. 62 / No. 25 / 521-524

Conclusiones

- En niños de riesgo el CAV-AEP recomienda pautas secuenciales (VNC13+VNP23) que pueden proporcionar un beneficio adicional respecto a la vacuna conjugada sola
- Es razonable mantener estas pautas (no parece probable que puedan producir hiporespuesta) por:
  1. Siempre recomienda iniciar la vacunación con vacuna conjugada
  2. No recomienda más de 2 dosis de VNP23
- El intervalo mínimo puede no ser el óptimo: No tener prisa

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Muchas gracias

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