MENİNGOKOK AŞILARI

Prof. Dr. Ayper SOMER
İstanbul Tıp Fakültesi Çocuk Enfeksiyon Hastalıkları

02 Haziran 2017 İstanbul

Meningokok Enfeksiyonu

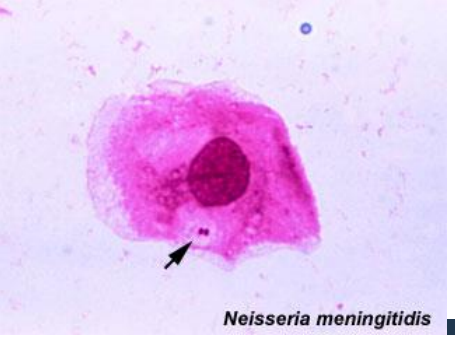
- Etken *Neisseria meningitidis*
- Aerobik gram-negatif diplokok
- Çocuklarda menenjit ve septiseminin en önemli ve en sık nedenlerinden
- Her yıl: 500,000 invazif meningokokal hastalık
  - 50,000-150,000 ölüm.
- Mortalite oranı: %10-14
- Yaşayanlarda ciddi sekeller: %5-30

MENİNGOKOK ENFEKSİYONU

- Tek kaynak: İnsan (asemptomatik taşıyıcılar)
- Bulaşma: Yakın temas (farengeal sekresyonlarla damlacık enfeksiyonu)
- Geç kış ve ilkbahar başlangıcında sık görülür.

- Akut hastalık 3 şekilde görülür:
  - Menenjit
  - Menenjit ile birlikte meningokoksemi
  - Menenjit olmadan meningokoksemi

- Menenjit intrakraniyal basınç artışı ile birlikte olabilir


Neisseria meningitidis

Neisseria meningitidis

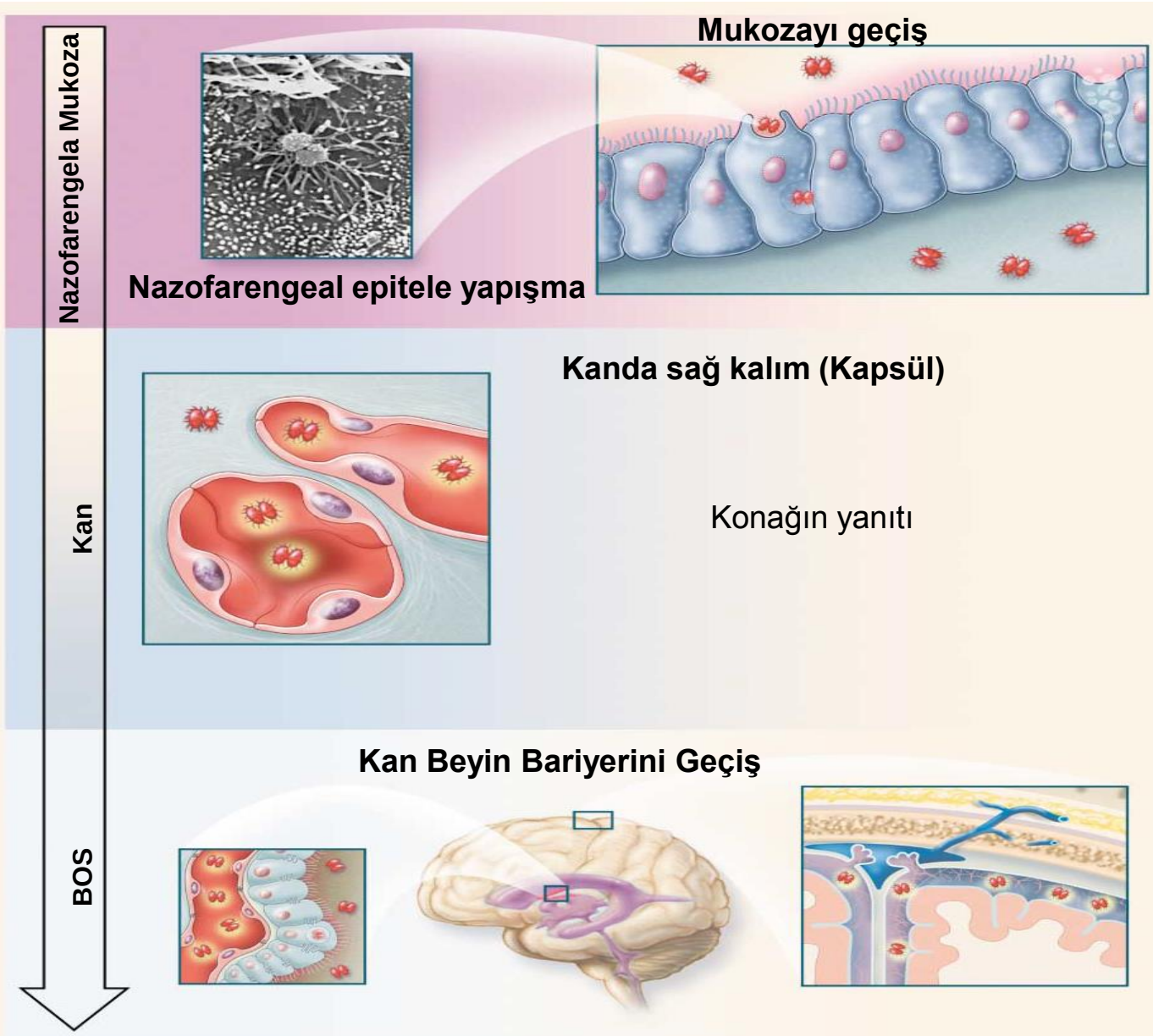
- A
- B
- C
- D
- X
- Y
- Z
- E
- W135
- H
- I
- K
- L

13 SEROGRUP

- A
- B
- C
- Y
- W135
- X

İNSANLARDA EN SIK HASTALIK YAPAN 6 SEROGRUP

Patogenez



Kolonizasyon

Meningokoksemi

ve / veya

Menenjit

Rosenstein NE et al. NEngl J Med 2001;344(18):1378-88

MENİNGOKOK ENFEKSİYONLARI İÇİN RİSK GRUPLARI

Meningokokal Hastalık İçin Risk Faktörleri

Serumda Bakteri
Antikorların
Eksikliği[1]

- İnfantlar
- Diğer
grupl

syal
törler[3,4]

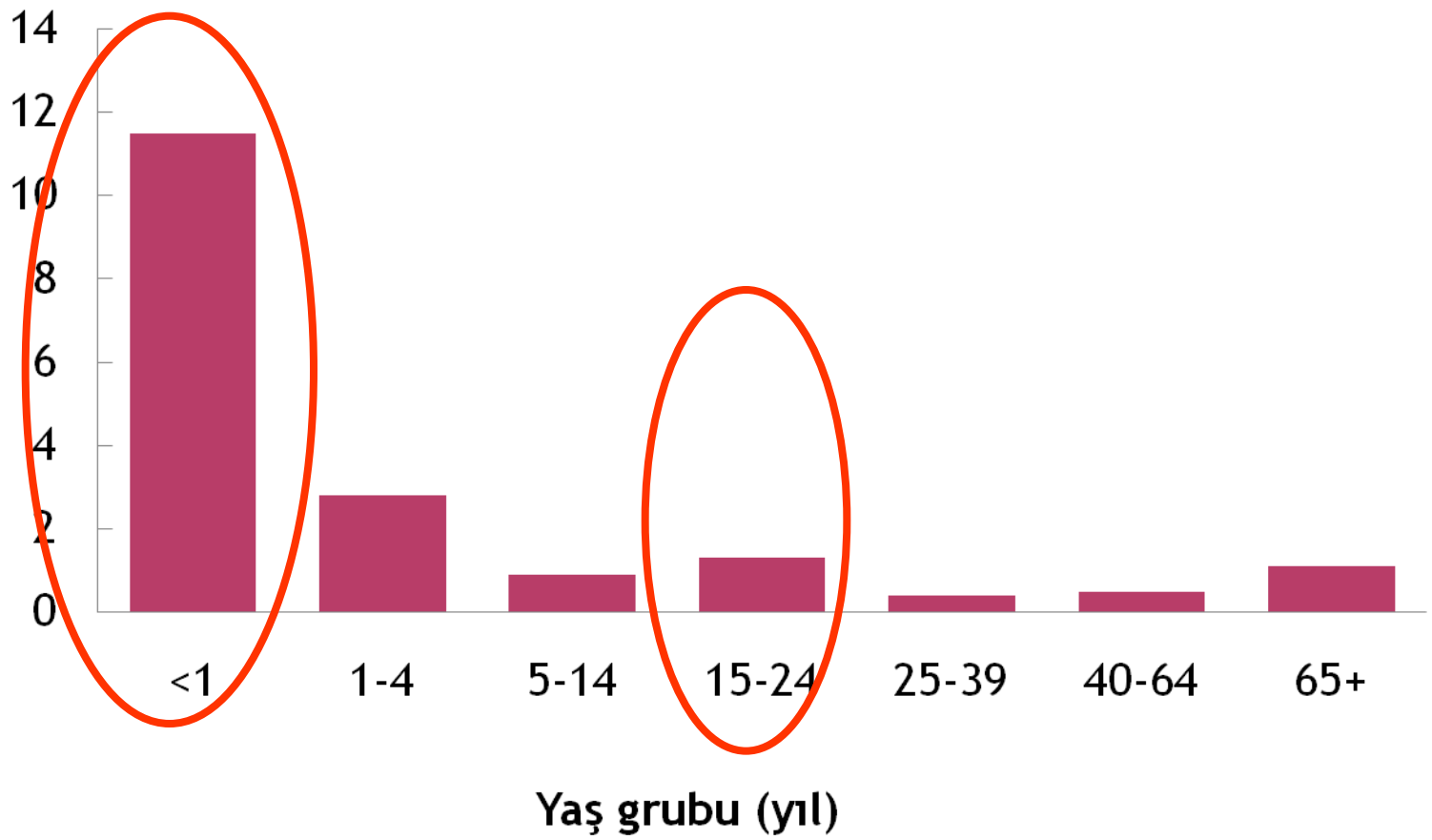
- Hasta ile yakın
mas
- k Çalışanları
- bireyleri
- alabalık
  - Öğrenciler
  - Askerler
  - Hacılar
- Öpüşme
- Bar/Disko

Hastalığın Çoğu daha önce sağlıklı olan ve risk faktörü olmayan bireylerde görülür

Meningokokal hastalıkları çog tanımlanmış bir risk faktörü bulunmayan sağlıklı kişilerde olur.

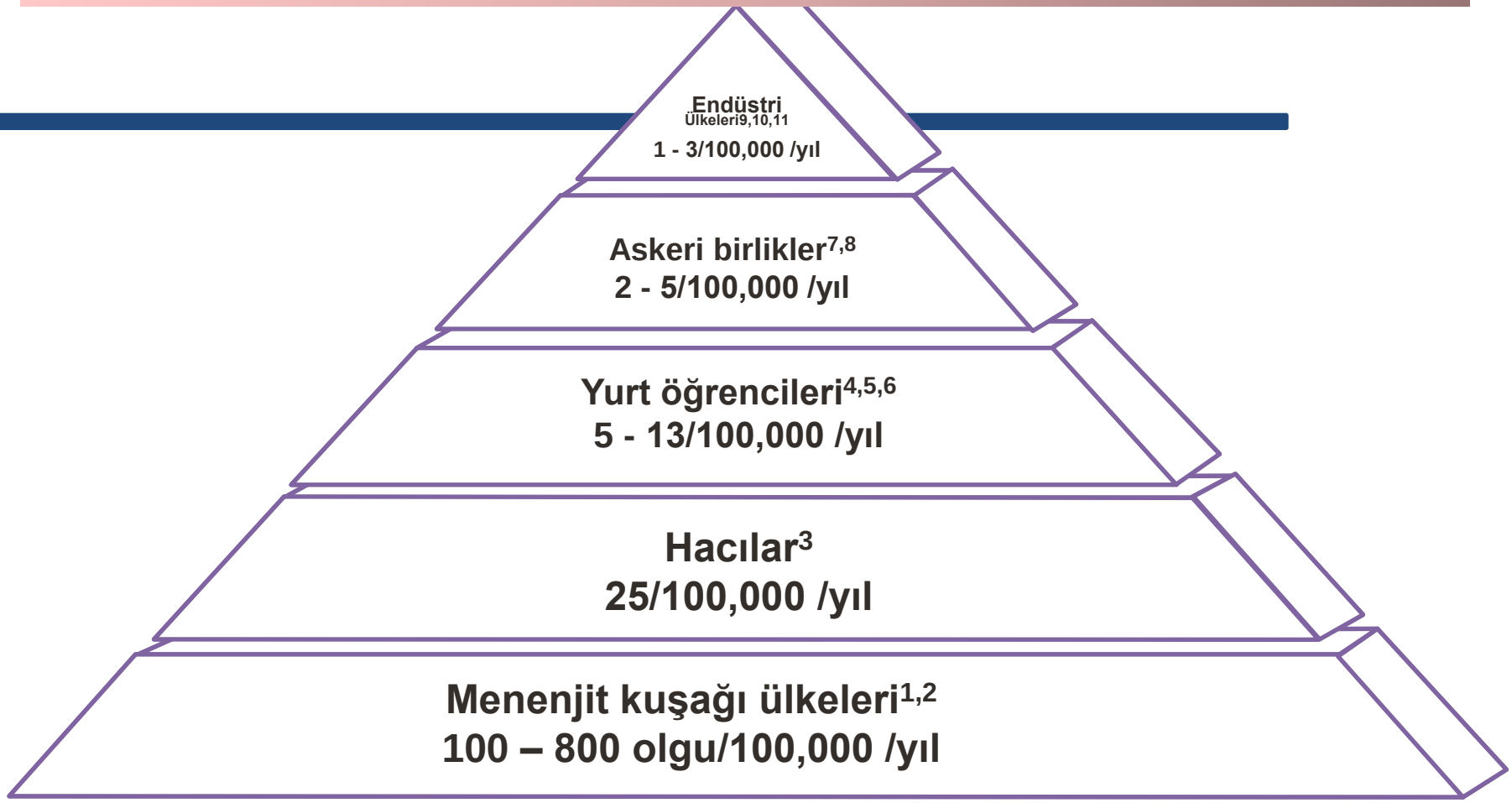
1. Rosenstein NE et al. *N Eng J Med*. 2001;344:1378-1388; 2. Figueroa JE et al. Clin Microbiol Rev. 1991;4:359- 395;
3. Bilukha OO et al. *MMWR Recomm Rep*. 2005;54:1-21; 4. Imrey PB et al. *J Clin Microbiol*. 1995;33:3133–3137.

Yaşa göre dağılım- ABD



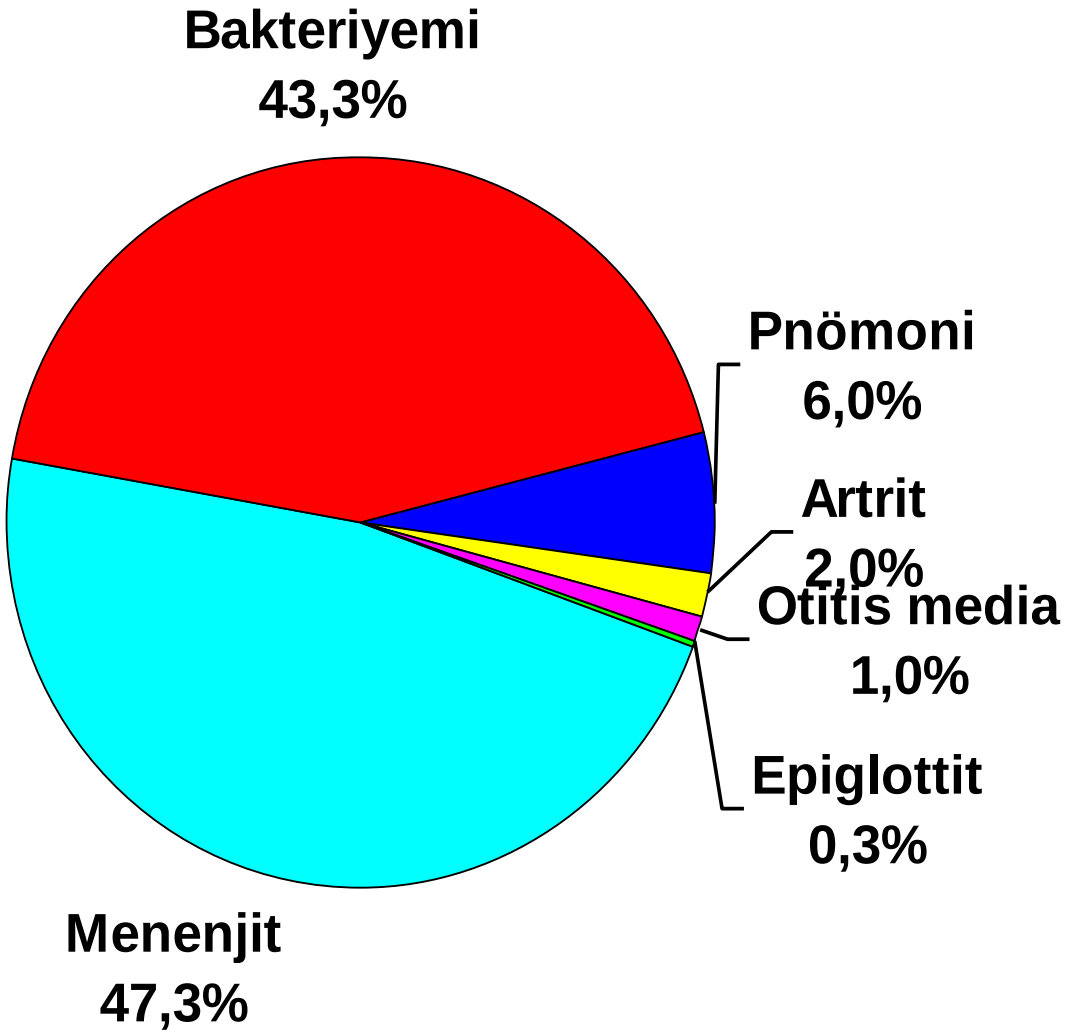
*** 100.000'de olgu sayısı

İnvazif Meningokokkal Hastalık (İMH) İnsidansı (Her 100.000 kişide)



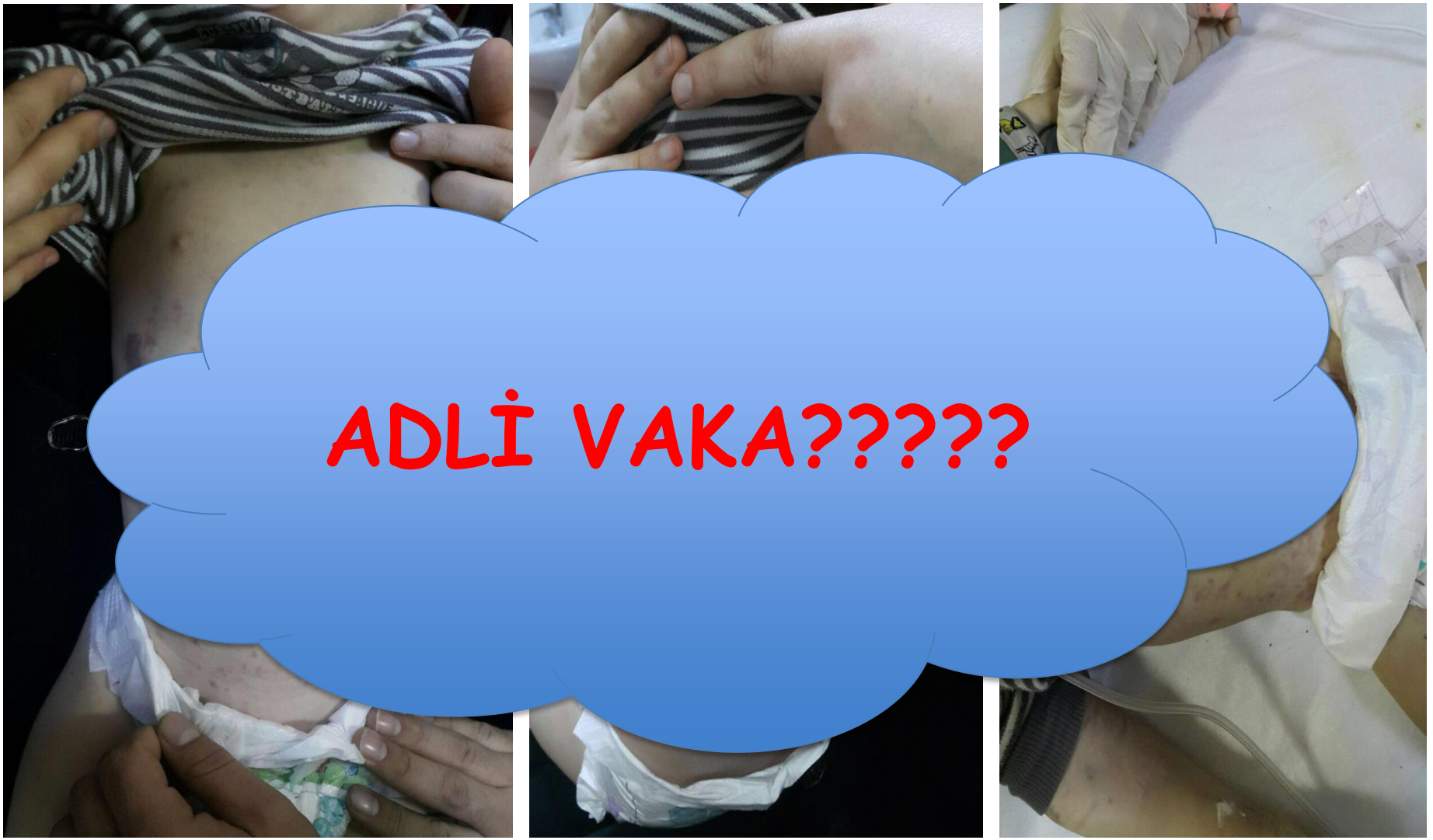
1. Campagne G, et al. *Bull World Health Organ*. 1999;77:499; Campagne G, et al. *Bull Soc Pathol Exot.* 1999;92:118
2. WHO. *Wkly Epidemiol Rec*. 2003;78:294
3. Wilder-Smith A, et al. *Clin Infect Dis*. 2003;36:679
4. Harrison LH, et al. *JAMA*. 2001;286:694
5. CDC. *MMWR Recomm Rep*. 2000;49(RR-7):13
6. Neal KR, et al. *Epidemiol Infect.* 1999;122:351
7. Brundage, JF, et al. *Clin Infect Dis*. 2002;35:1376
8. Spiegel A, et al. *Santé*. 1996;6:383
9. CDC. *MMWR Morbid Mortal Wkly Rep* 2003;50:1
10. Squires SG, et al. *Can Commun Dis Rep*. 2000; 26:177
11. EU-IBIS, Meningococci Network. Available at http://www.euibis.org/meningo/n_meningitidis_network.htm.

Meningokok Hastalık Spektrumu

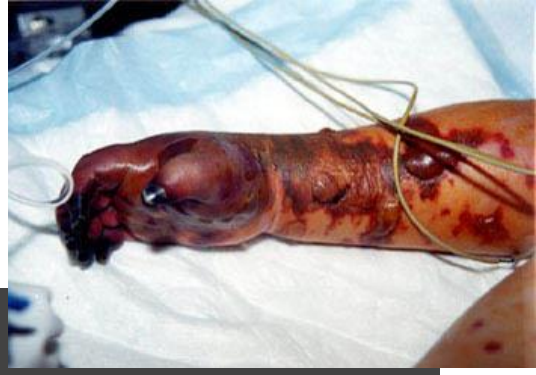


*1992-1996 data

MENİNGOKOK ENFEKSİYONU



Klinik Bulgular



Thompson MJ. Lancet. 2006;367(9508):397-403.

Tanı

ATEŞ + PETEŞİ

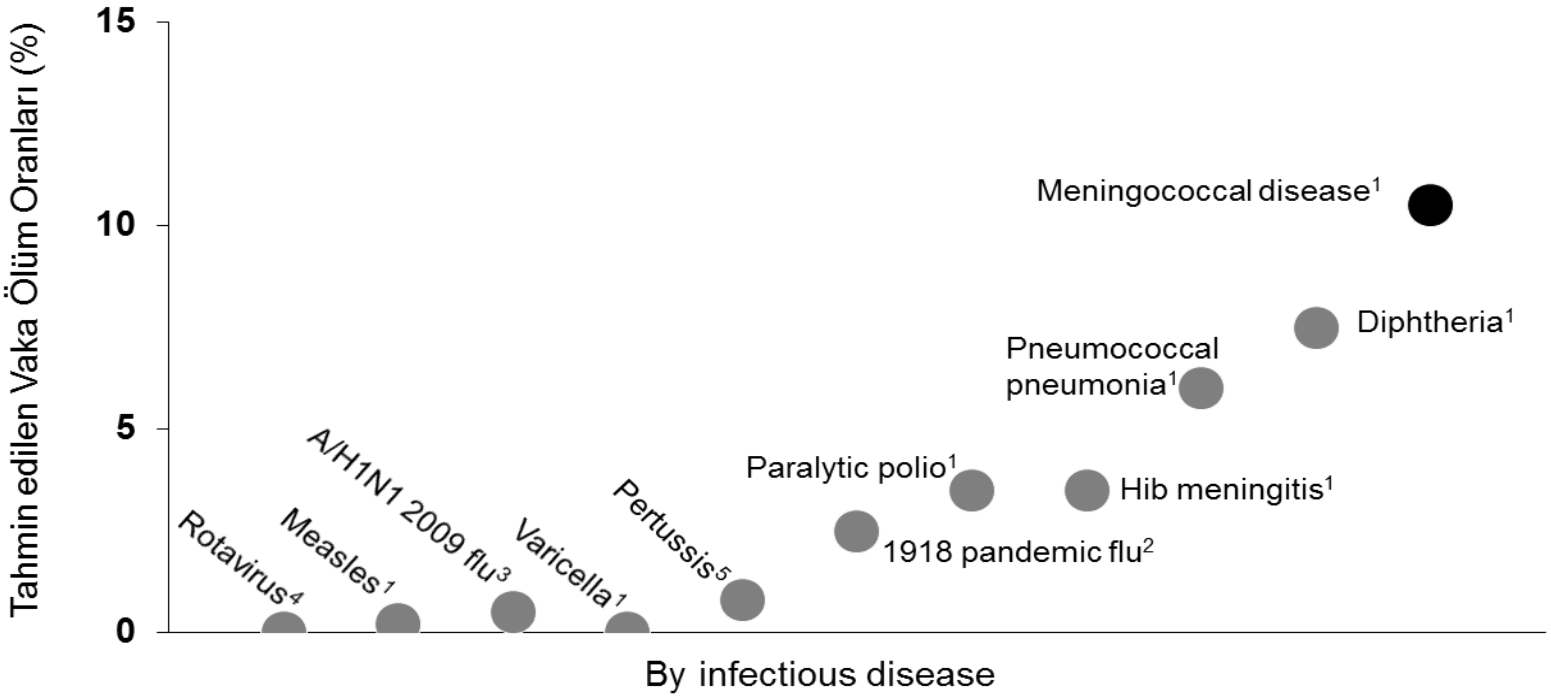
AKSİ İSPATLANANA DEK

= MENİNGOKOKSEMİ

MENİNGOKOK ENFEKSİYONU

- 1920'lerde tüm hastalıkta %70
- Günümüzde tüm hastalıkta %9-12
- Meningokoksik septik şokta %40
- Purpura fulminans ve çoklu organ yetersizliğinde %70-100

Vaka Sekel/Ölüm Oranları



Notes: Meningococcal disease and Hib meningitis: despite appropriate antimicrobial therapy; paralytic polio: in children; 1918 pandemic flu: in young adults; varicella: in children and adolescents; A/H1N1 2009 flu: worldwide; measles: US, 1985–1992; rotavirus: US general population; pertussis: infants <6 months of age, US, 2001–2003.

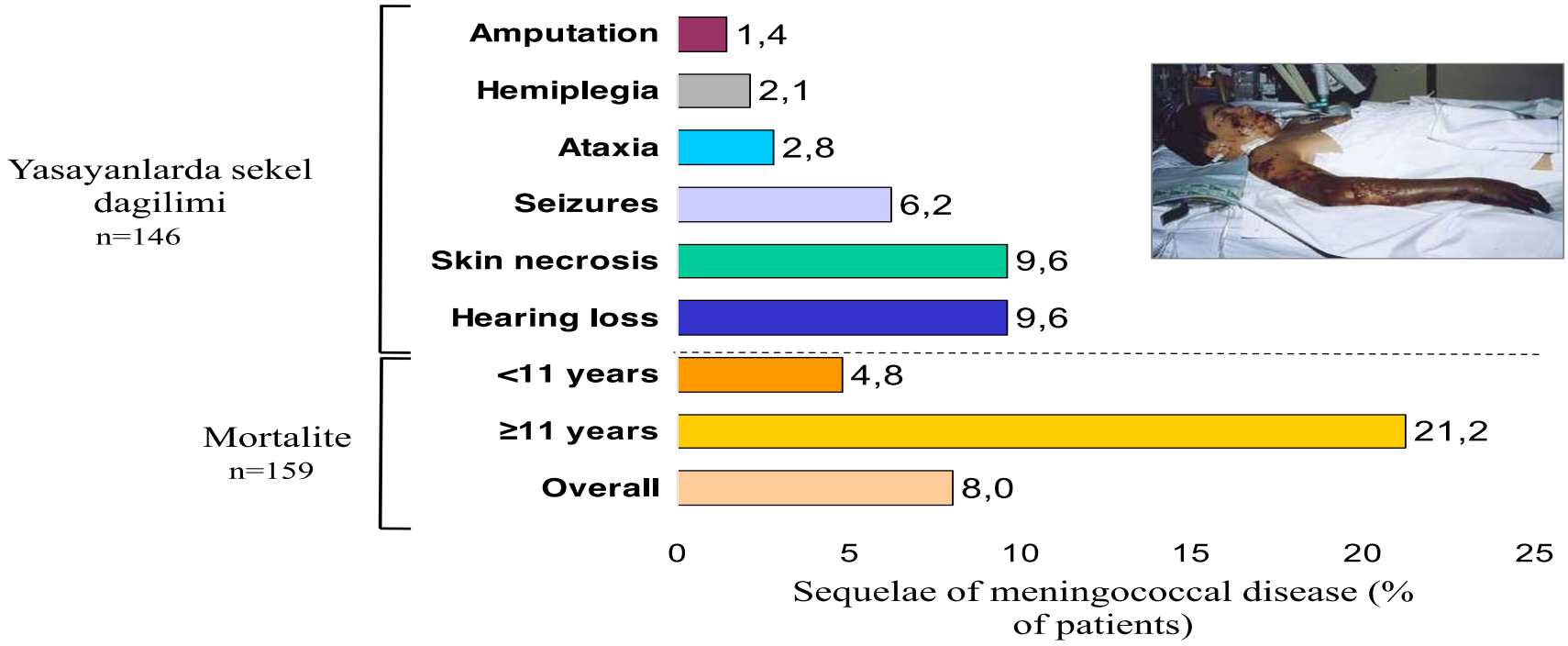
Hib=*Haemophilus influenzae* type b.

1. Centers for Disease Control and Prevention (CDC). *Epidemiology and Prevention of Vaccine-Preventable Diseases*. 12th ed. Atkinson W, et al, eds. Washington, DC: Public Health Foundation; 2012. http://www.cdc.gov/vaccines/pubs/pinkbook/index.html#chapters; 2. Taubenberger JK, et al. *Emerg Infect Dis*. 2006;12:15-22; 3. Pandemic H1N1 2009 Overview. CIDRAP website. http://www.cidrap.umn.edu/cidrap/content/influenza/swineflu/biofacts/h1n1_panview.html; 4. Gerba CP, et al. *Wat Res*. 1996:30;2929-2940; 5. Centers for Disease Control and Prevention (CDC). *MMWR Morb Mortal Wkly Rep*. 2005;54:1283-1286.

MENİNGOKOK ENFEKSİYONLARI VE SEKEL

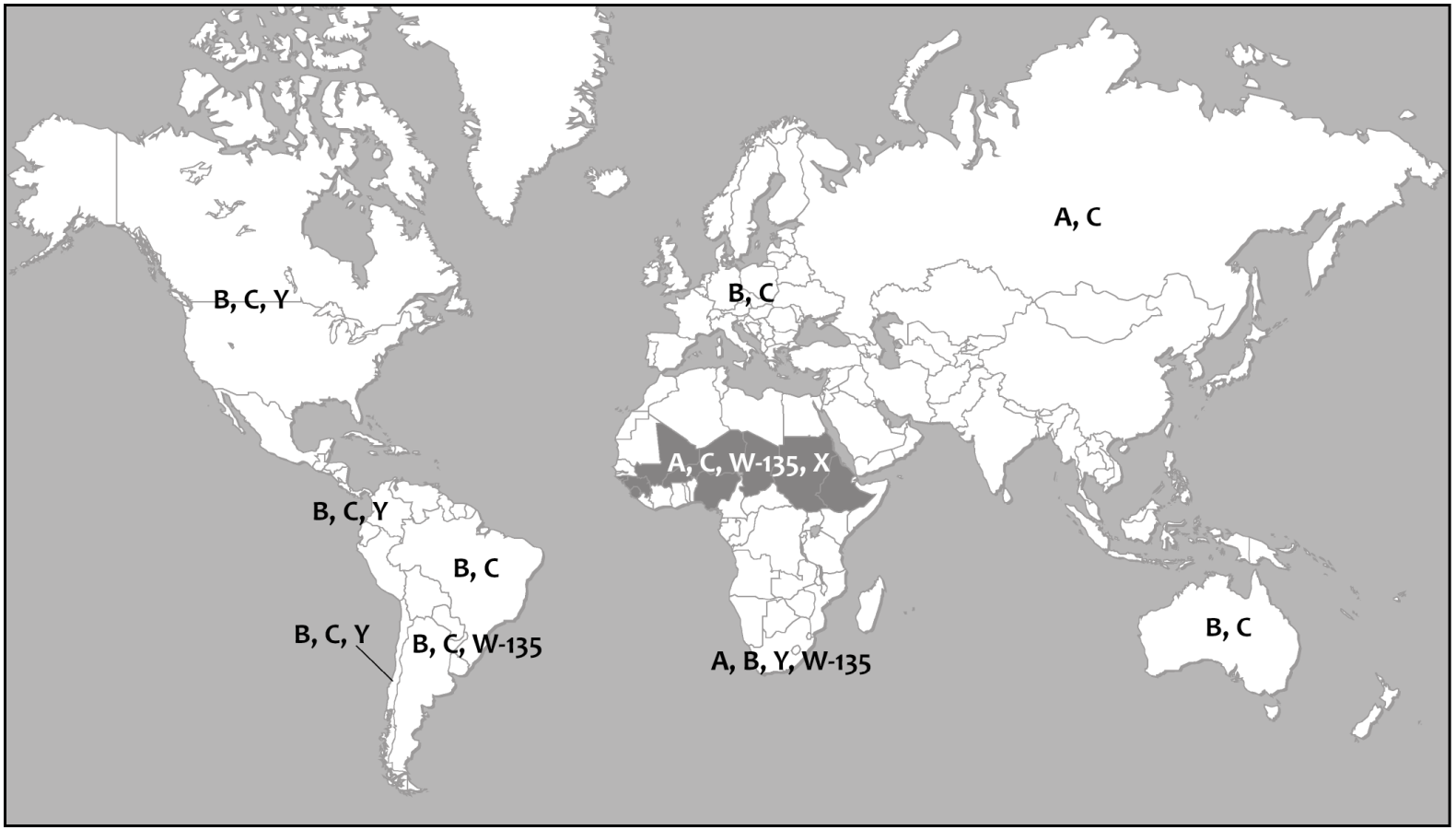
Yasayan invazif meningokok hastalikli cocuklarda sekeller ve mortalite

ABD – 10 cocuk hastanesi, 20001 – 2005



Kaplan SL, et al. *Pediatrics*. 2006;118:e979-e984.

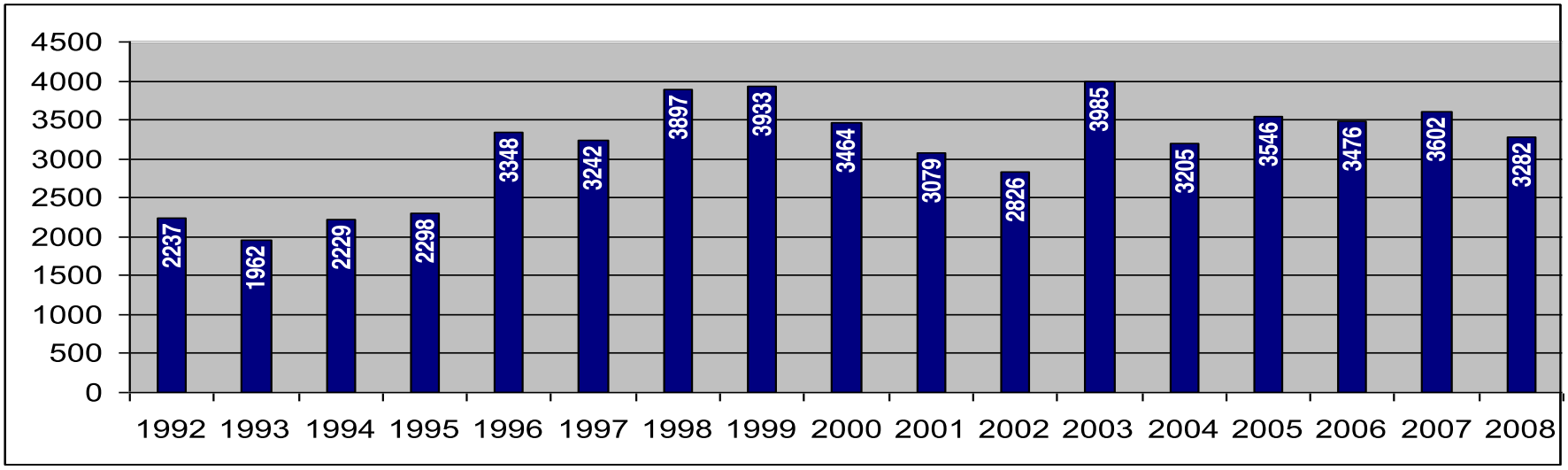
İnvazif meningokok hastalıkları dünyanın her yerinde meydana gelir



Jafri RZ et al (2013) Global epidemiology of invasive meningococcal disease. Popul Health Metr 11:17

ÜLKEMİZDE MENİNGOKOK MORTALİTESİ

Türkiye' de Meningokokal Hastalık Nedenli Ölümler



TÜİK verilerine göre yıllık meningokokal enfeksiyon kaynaklı ölümler, 1992-2008
Grafik referanslardan uyarlanmıştır

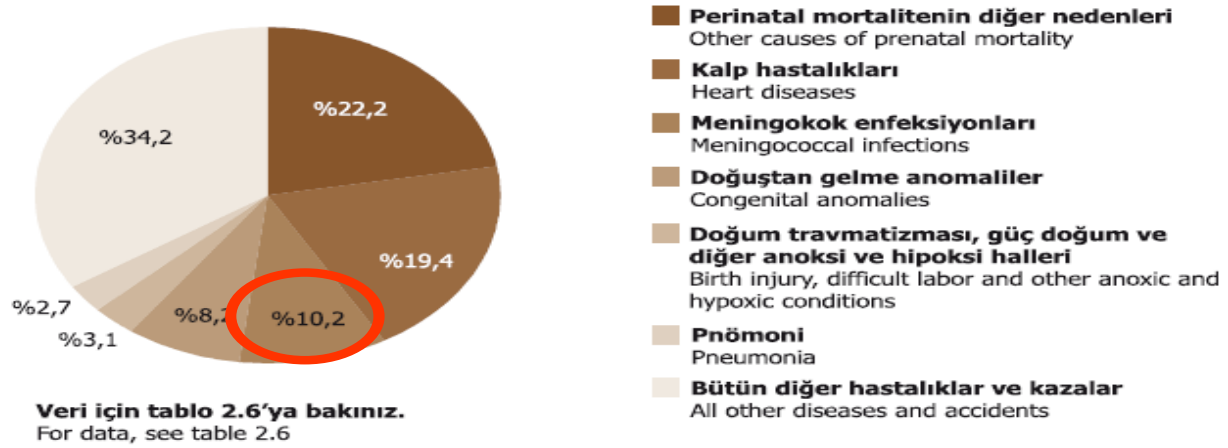
Akyıldız B, et al. Çocuk Sağlığı ve Hastalıkları Dergisi 2008 ; 51: 26-30. Uzel N, Hacımustafaoğlu M. ANKEM Derg 2006; 20(3):194-8.
T.C. Başbakanlık Türkiye İstatistik Kurumu. Seçilmiş 150 neden ve cinsiyete göre ölümler, İl ve ilçe merkezleri, 1999-2008.
http://www.tuik.gov.tr/PreIstatistikTablo.do?istab_id=97 (06.01.2011tarihinde ulaşılmıştır)

ÜLKEMİZDE MENİNGOKOK MORTALİTESİ

Türkiye'de 5 yaş altında Meningokokal Hastalık Nedeniyle Ölümler

Death Statistics, 2008 | **Ölüm İstatistikleri, 2008**

2.2 Beş yaş altındaki çocuk ölümlerinin ölüm nedenlerine göre oranı, 2008
Proportion of child mortality under five years of age by causes of death, 2008



Veri için tablo 2.6'ya bakınız.
For data, see table 2.6

5 yaş altı toplam ölüm: 13.047
5 yaş altı meningokokal hastalık nedeniyle ölüm: 1.336

T.C. Başbakanlık, Türkiye İstatistik Kurumu. Ölüm İstatistikleri, İl ve ilçe merkezleri, 2008. Türkiye İstatistik Kurumu Matbaası Ankara, 2009:5. http://www.tuik.gov.tr/IcerikGetir.do?istab_id=21 (20.06.2011 tarihinde ulaşılmıştır)

MENİNGOKOK TAŞIYICILIK SIKLIĞI

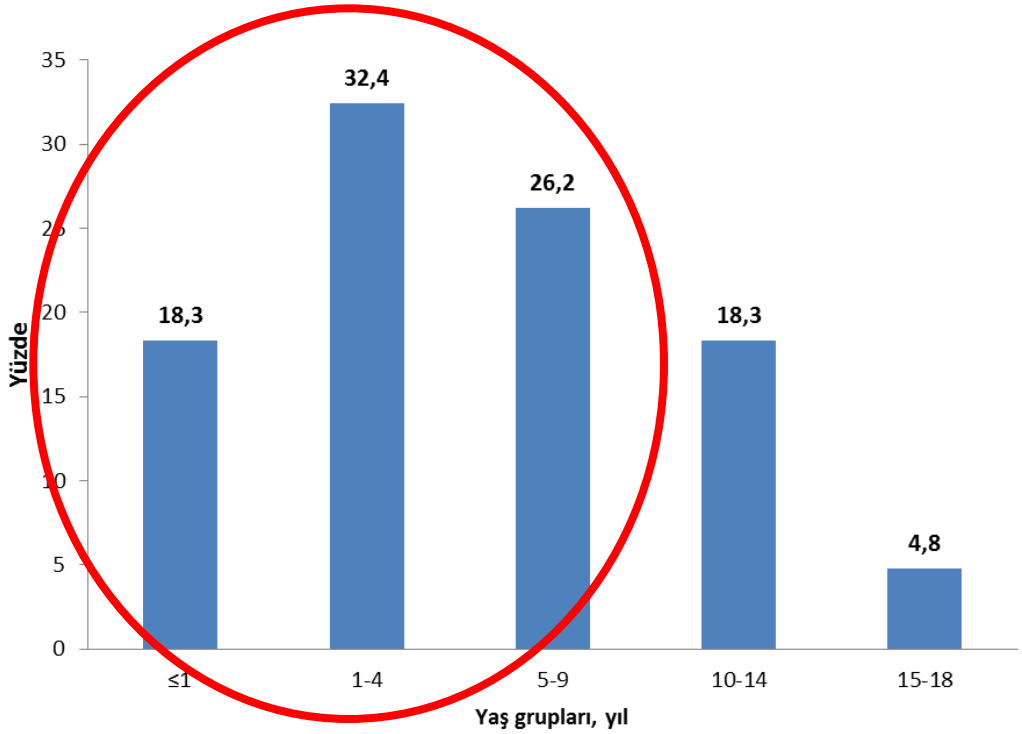
Türkiye' de Taşıyıcılık

yazar	merkez	yıllar	yaş grubu	Toplam Örnek	Meningokok pozitifliği (n)	Taşyıcılık %
Punar	İstanbul	1997	9-11	84	18	21.00
Bakır	İstanbul	12.01-25.04.2000	0-10	1382	17	1,23
Gazi	Manisa	2001-2002	9-14	1128	71	6,20
Karabela	İstanbul	Mart - Nisan 2005	6 -10	340	24	7,00
Ercis	Ankara	6 Mayıs 1996 - 13 Haziran 1996	7-19	1155	120	10,40

- Türkiye' de yapılan çalışmalarda, taşıyıcılık oranı % 1,23 ile % 21 arasında değişmektedir.

Punar M. Klimik Dergisi 2001:14(1):17-8. Bakır M European Journal of Epidemiology 2001;17: 1015–18. Gazi H. Ann Acad Med Singapore 2004;33:758-62. Karabela Ş. Zeynep Kamil Tıp Bülteni 2007;38(3):115-9. Ercis M. Mikrobiyol Bült 2005;39:411-20.

Vakaların yaş dağılımı
Türkiye



Şekil: Yaş gruplarına göre olgu dağılımı, çok merkezli sürveyans, 2005-2012, Türkiye, n:333

Referanstan uyarlanmıştır.

Ceyhan M, et al. Human Vaccines & Immunotherapeutics 2014; 10

EPİDEMİYOLOJİ

TÜRKİYE

Meningitis Caused By Neisseria Meningitidis

Study Period (Year)	2005-2012	
Causative Bacteria	**n**	**%**
Serogroup W-135	127	38.1
Serogroup B	87	26.1
Serogroup A	28	8.4
Serogroup C	0	0
Serogroup Y	3	0.9
Nongroupable	88	26.4
N. meningitidis (Total)	333	51.6
S. pneumonia	195	30.2
H. influenzae type b	117	18.1
Total number of Positive Samples	645	100
Total number of Evaluted Clinical Samples	1452	N/A

Ceyhan M, et al. Human Vaccines & Immunotherapeutics 2014; 10

EPİDEMİYOLOJİ TÜRKİYE 2013-2014

Table 1. Distribution of causative agents of bacterial meningitis and meningococcal serogroups during 2013–2014 in Turkey.

Study Period (Year)	2013		2014		2013–2014 (2 years)	
Causative Bacteria	n	%	n	%	n	%
Serogroup W-135	7	36.8	29	43.9	36	42.4
Serogroup B	5	26.4	23	34.9	28	32.9
Serogroup A	0	0	3	4.5	3	3.5
Serogroup C	0	0	0	0	0	0
Serogroup Y	0	0	2	3.0	2	2.4
Nongroupable	7	36.8	9	13.7	16	18.8
N. meningitidis (Total)	19	86.4	66	91.7	85	90.4
S. pneumonia	3	13.6	6	8.3	9	9.6
H. influenzae type b	0	0	0	0	0	0
Total number of Positive Samples	22	100	72	100	94	100

HUMAN VACCINES & IMMUNOTHERAPEUTICS
2016, VOL. 0, NO. 0, 1–6
http://dx.doi.org/10.1080/21645515.2016.1209278

DSÖ Önerileri

Öneri 1.

Ülkeler endemik oranlarına göre;

- Yüksek (>10 vaka /100 000 kişi/yıl) veya
- Orta (2 - 10 vaka /100 000 kişi/yıl)
  → rutin bağışıklama programı

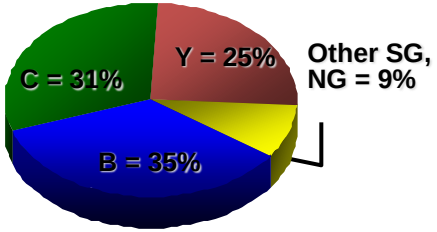
- Düşük (< 2 vaka /100 000 kişi/yıl)
  →tanımlanmış risk grupları
  (örn: çocuklar, yatılı okul veya askeri birliklerdeki gençler gibi)

Wkly Epidemiol Rec. 2011;78(47):521-39.

DSÖ önerileri

Öneri 2.

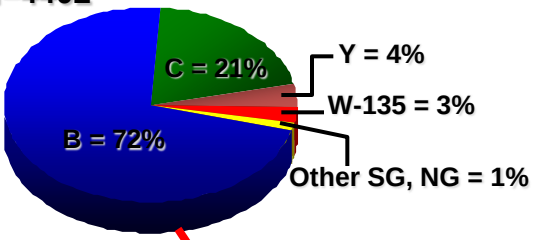
- Tüm ülkeler aşı seçimi yerel olarak sık görülen *N. meningitidis* serogrubuna (serogruplarına) göre seçilmelidir



ABD 2008 n=123

KMA 4, ACYW135
2005'ten beri

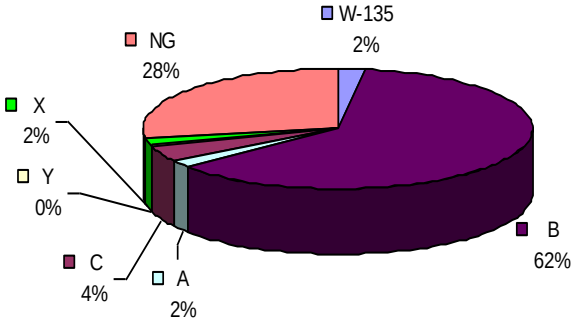
Avrupa 2006
n=4402



KMC,

1999'da başlandı

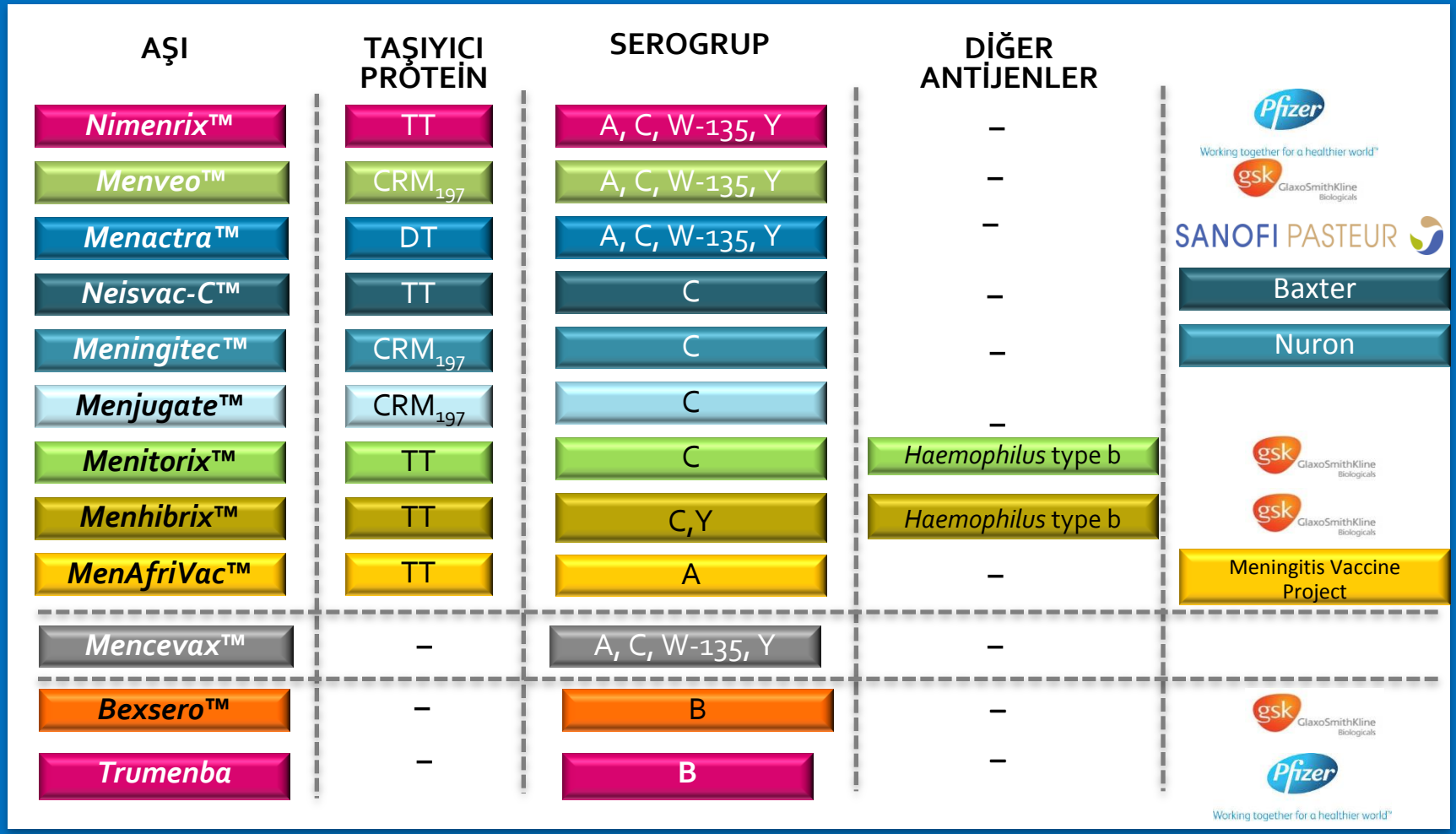
Bakır, 2006-2009, Çok merkezli, n:47



KMA 4, ACYW135 ?

4CMenB?

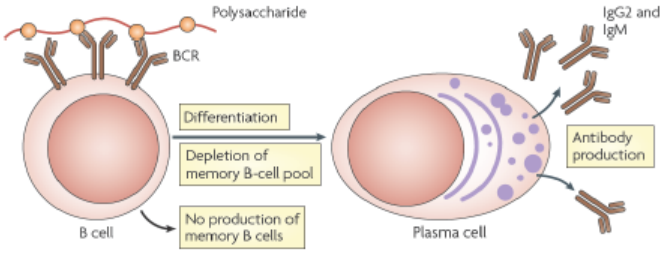
MENİNGOKOK AŞILARI



Konjuge ve polisakkarid meningokok aşılarının farklılıkları

Polisakkarid aşı

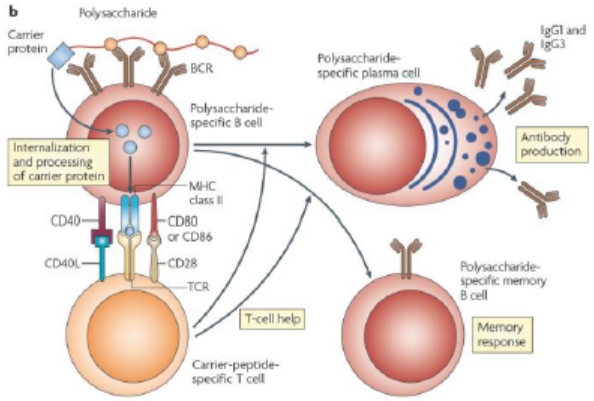
- Aşıya yanıt B hücresi olgunlaşmasına bağlıdır.
- Bu yüzden, polisakkarit aşı infantlarda immunojenik değildir ve immunolojik hafıza oluşturmazlar



*A .J. Pollard, Nature Reviews Immunology 2009

Konjuge aşı

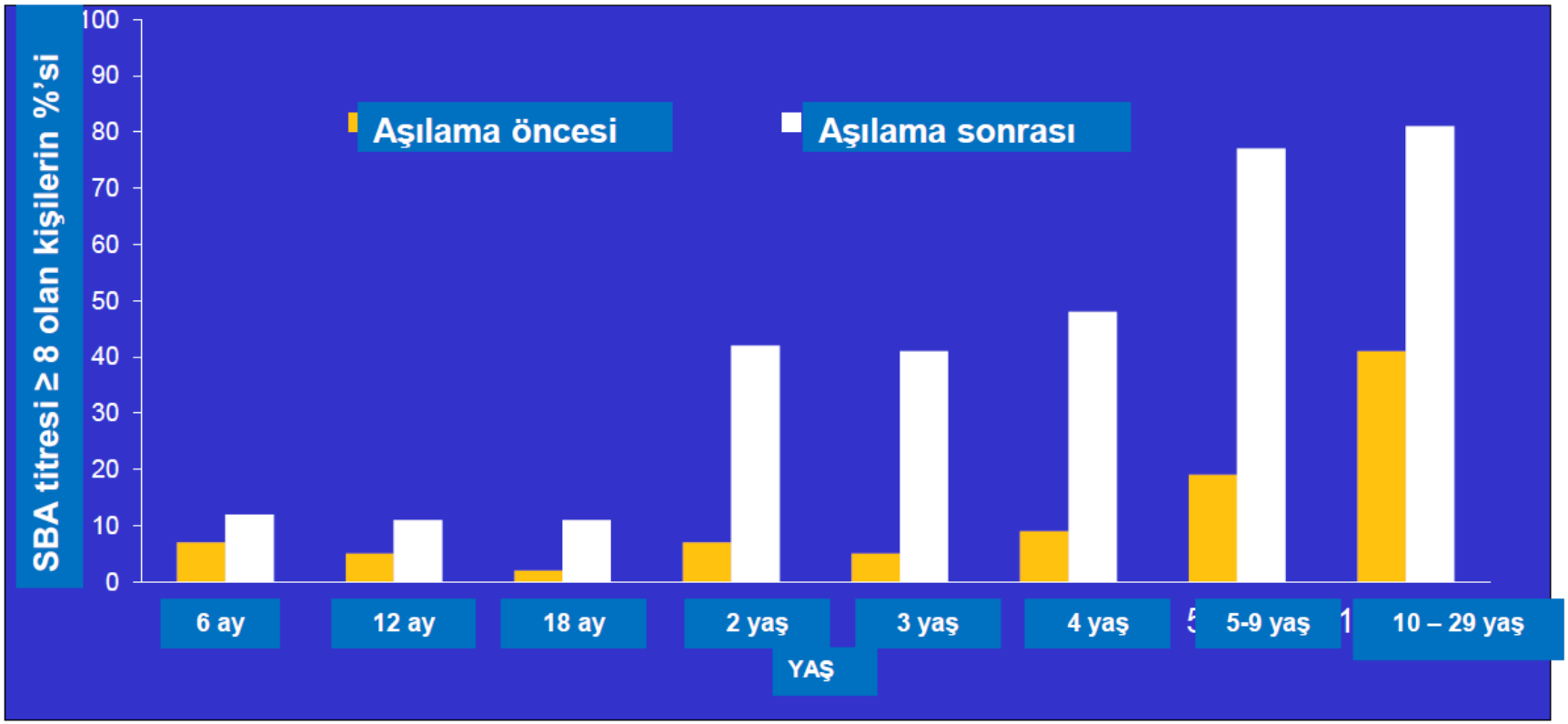
- Tekrarlarda düşük yanıt (hyporesponsiveness) yoktur
- İnfant döneminde immunojeniktir
- Daha yüksek immün yanıt
- Antikor persistansı
- Tekrar aşılamaya ihtiyaç duyulduğunda immün sistemi uyarır (Yüksek Ig G yanıtı)
- Taşıyıcılığı azaltır



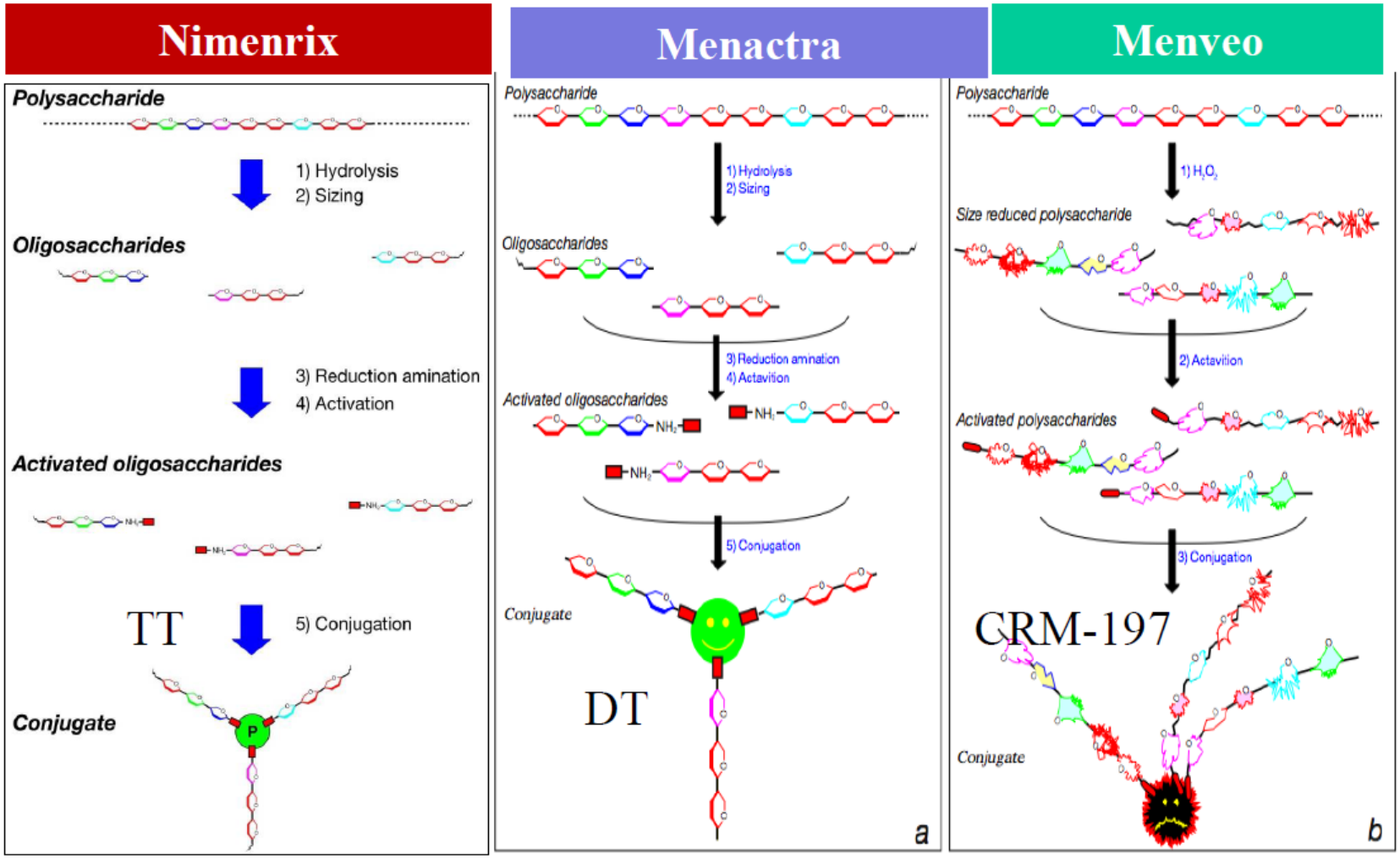
*A. J. Pollard, Nature Reviews Immunology 2009

Polisakkarit Aşılar
yaşla ilgili immunojenisite

Kuadrivalan meningokok aşısıyla aşılanma öncesi ve sonrasında MenC SBA titreleri ≥ 8 olan kişilerin oranı (yaş gruplarına göre)



Konjugasyon işlemi



AŞI IÇIN MUTLAK RISK GRUPLARI

- *N. meningitidis* ile rutin olarak karşılaşan mikrobiyoloji laboratuarı çalışanları
- Askeri birlikler
- Neisseria meningitidis için epidemik yada hiperendemik olan ülke ve bölgelere seyahat edenler
  - Hacılar
- Terminal kompleman komponenti eksikliği olanlar
- Fonksiyonel veya anatomik olarak aspleni
- HIV

Meningokok Aşıları Son Durum

Grup	Ürün adı	FDA	EMEA	Türkiye
Konjuge Menenjit ACWY Aşı	Menveo	2ay-55yaş	2 yaş ve üstü (üst yaş limiti yok)	• 2yaş ve üstü (üst yaş limiti yok) • 2 ay üstü için ruhsat başvurusu yapılmış onay beklenmektedir • 2014 yılında Hacı adayları için kullanılmaya başlanmıştır
	Menactra	9 ay-55 yaş		9 ay- 11 yaş
	Nimenrix	Ruhsat almamıştır	1 yaş üstü	1 yaş üstü
Konjuge Menenjit B Aşı	Bexsero	2ay üstü ruhsat aşamasındadır. Özel izin ile 2014 yılında 2 üniversite gençliğine 10-25 yaş grubuna uygulama için izin verilmiştir	2 ay üstü	Ruhsat başvuru hazırlık aşamasındadır

MEN ACWY-TT (NIMENRIX®)

- Dört değerlikli konjüge meningokok aşısı
- PFIZER VACCINES
- Meningokok serogrup A, C, Y, W135
- Taşıyıcı protein: Tetanos toksoidi (TT)
- Adjuvan içermemektedir.
- İntramüsküler olarak uygulanmaktadır.

MEN ACWY-TT (NIMENRIX®)

- Avrupa' da (Türkiye de dahil) 12 aydan büyük çocuk ve erişkinlerde tek doz intramuskuler olarak uygulanması önerilmektedir.
- EMEA tarafından Nisan 2012' de onaylanmıştır.

Nimenrix Faz II-III Klinik Çalışmaları

Table 4 Phase II and Phase III clinical vaccination trials of MenACWY-TT conjugate vaccine in infants, toddlers, and children

Phase	Author	Year	Age group	Country	Registry number at Clinicaltrials.gov
II	Klein et al[89]	2013	9–12 months	United States	NCT00471081
II	Vesikari et al[90]	2012	12–23 months 2–10 years	Finland Finland	NCT00427908
II	Knuf et al[87]	2010	12–14 months 3–5 years	Germany Austria	NCT00126984
II	Knuf et al[88]	2012	12–14 months 3–5 years	Germany Austria	NCT00126984
II	Dbaibo et al[94]	2012	4.5–10 years	Lebanon	NCT00661557
III	Ruiz-Palacios et al[105]	2013	12–23 months	Taiwan Mexico	NCT00758264
III	Vesikari et al[91]	2011	12–23 months	Finland	NCT00474266
III	Knuf et al[106]	2011	12–23 months	Austria Germany Greece	NCT00508261
III	Memish et al[93]	2011	2–10 years	Philippines India Lebanon Saudi Arabia	NCT00514904
III	Knuf et al[95]	2013	2–10 years	Germany France	NCT00674583

Abbreviation: MenACWY-TT, serogroups A, C, W-135, and Y tetanus toxoid conjugate vaccine.

Nimenrix Faz II-III Klinik Çalışmaları

Table 5 Phase II and phase III clinical vaccination trials of MenACWY-TT conjugate vaccine in adolescents and adults

Phase	Author	Year	Age group	Country	Registry number at Clinicaltrials.gov
II	Dbaibo et al[94]	2012	11–34 years	Lebanon	NCT00661557
II	Ostergaard et al[99]	2013	15–19 years	Denmark	NCT00390143
II	Baxter et al[100]	2011	10–25 years	USA	NCT00454909
II	Ostergaard et al[96]	2009	15–19 years	Belgium	NCT00126945
			18–25 years	Denmark	NCT00196950
II	Borja-Tabora et al[98]	2013	11–55 years	Philippines Saudi Arabia	NCT00356369
III	Ostergaard et al[103]	2012	11–17 years	Sweden Denmark	NCT00465816
III	Bermal et al[97]	2011	11–17 years	Philippines India Taiwan	NCT00464815
III	Dbaibo et al[85]	2012	18–55 years	Lebanon Philippines	NCT00453986
III	Aplasca-De Los Reyes et al[104]	2012	18–55 years	Lebanon Philippines	NCT00453986
III	Dbaibo et al[46]	2013	56–103 years	Lebanon	NCT01235975

Abbreviation: MenACWY-TT, serogroups A, C, W-135, and Y tetanus toxoid conjugate vaccine.

MEN ACWY-TT (NIMENRIX®)

12-24 AY VE 3-5 YAŞ ARASI İNFANT VE ÇOCUKLARDA TEK DOZ MENACWY-TT İMMÜNOJENİK VE GÜVENİLİR

Vaccine 28 (2010) 744–753

Contents lists available at ScienceDirect

Vaccine

journal homepage: www.elsevier.com/locate/vaccine

A dose-range study assessing immunogenicity and safety of one dose of a new candidate meningococcal serogroups A, C, W-135, Y tetanus toxoid conjugate (MenACWY-TT) vaccine administered in the second year of life and in young children

M. Knuf[a], D. Kieninger-Baum[a], P. Habermehl[a], P. Muttonen[b], H. Maurer[c], P. Vink[d], J. Poolman[d], D. Boutriau[d,*]

MEN ACWY-TT (NIMENRIX®)

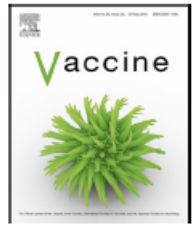
12-15 AY ARASI İNFANTLARDA TEK DOZ MENACWY-TT İMMÜNOJENİK VE GÜVENİLİR

Vaccine 34 (2016) 3363–3370

Contents lists available at ScienceDirect

Vaccine

journal homepage: www.elsevier.com/locate/vaccine



Safety and immunogenicity of a CRM or TT conjugated meningococcal vaccine in healthy toddlers

Gianni Bona[a], Paolo Castiglia[b], Giorgio Zoppi[c], Maurizio de Martino[d], Annaelisa Tasciotti[e], Diego D'Agostino[f], Linda Han[g], Igor Smolenov[f,*]

MEN ACWY-TT (NIMENRIX®)

2-10 YAŞ ARASI ÇOCUKLARDA TEK DOZ MENACWY-TT İMMÜNOJENİK VE GÜVENİLİR

Eur J Pediatr (2013) 172:601–612
DOI 10.1007/s00431-012-1924-0

ORIGINAL ARTICLE

Immunogenicity and safety of the quadrivalent meningococcal serogroups A, C, W-135 and Y tetanus toxoid conjugate vaccine (MenACWY-TT) in 2–10-year-old children: results of an open, randomised, controlled study

Markus Knuf · Olivier Romain · Klaus Kindler · Uta Walther · Phu-My Tran · Heidemarie Pankow-Culot · Thomas Fischbach · Dorothee Kieninger-Baum · Véronique Bianco · Yaela Baine · Jacqueline Miller

MEN ACWY-TT (NIMENRIX®)

10-25 YAŞ ARASI ADOLESAN VE GENÇ ERİŞKİNLERDE TEK DOZ MENACWY-TT İMMÜNOJENİK VE GÜVENİLİR

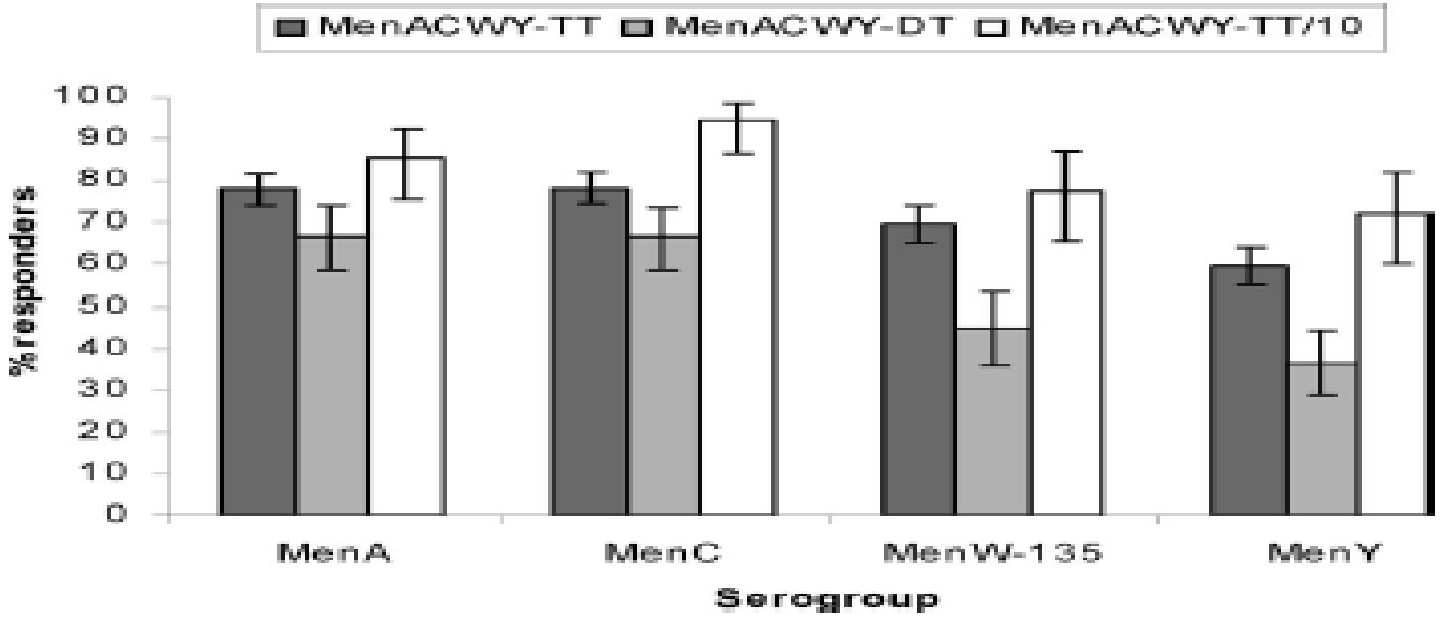


FIGURE 2. Proportion of subjects with a vaccine response for each serogroup by study group with 95% CI (ATP Cohort for Immunogenicity). Vaccine response defined as postvaccination hSBA antibody titer ≥1:16 in subjects with prevaccination hSBA antibody titer <1:4 or ≥4-fold increase in hSBA antibody titer postvaccination in subjects with pre-vaccination hSBA antibody titer ≥1:4

MEN ACWY-TT (NIMENRIX®)

11-55 YAŞ ARASI ÇOCUK VE ERİŞKİNLERDE TEK DOZ MENACWY-TT İMMÜNOJENİK VE GÜVENİLİR

Borja-Tabora *et al. BMC Infectious Diseases* 2013, **13**:116
http://www.biomedcentral.com/1471-2334/13/116

BMC Infectious Diseases

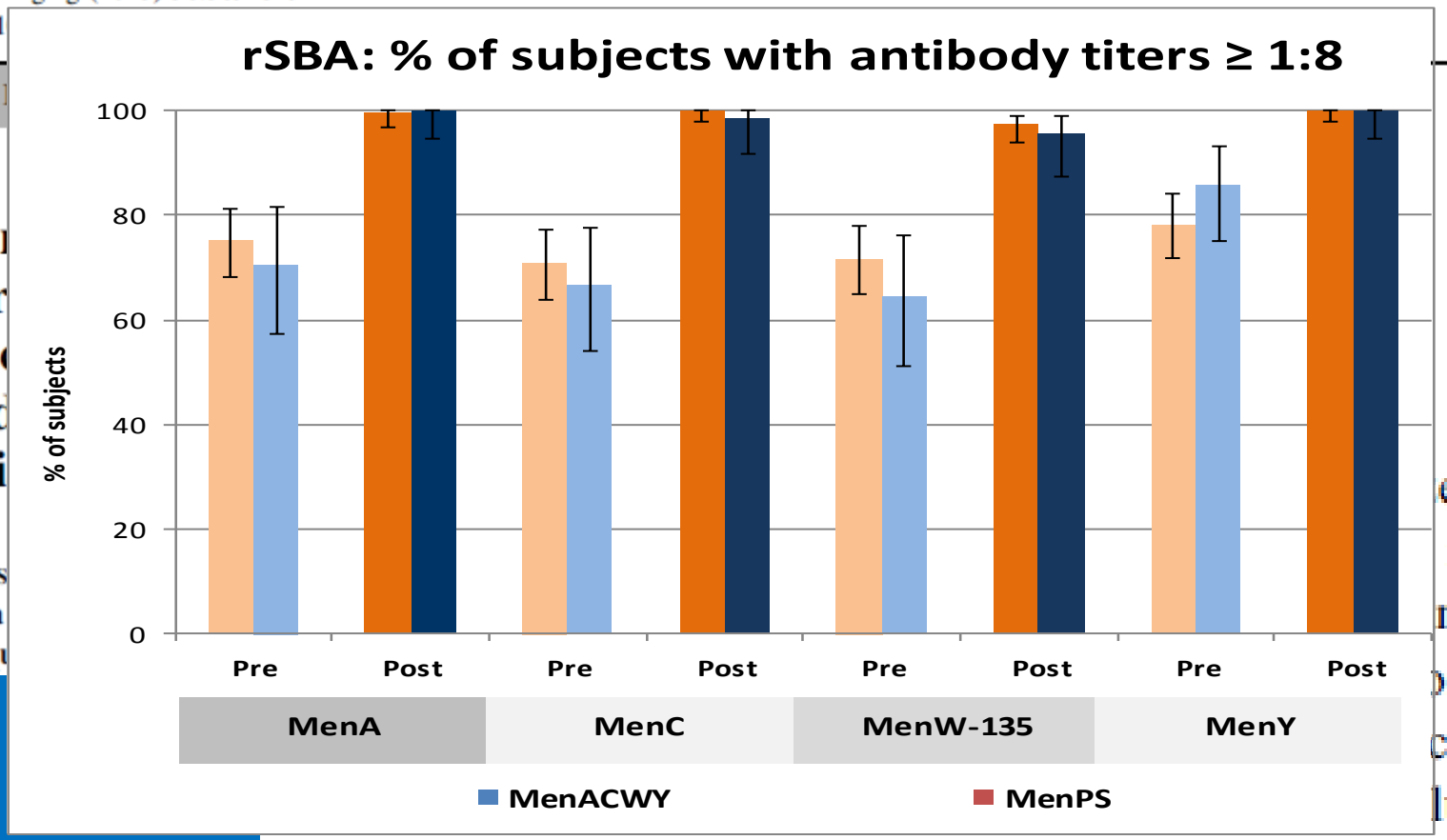
RESEARCH ARTICLE Open Access

Immune response, antibody persistence, and safety of a single dose of the quadrivalent meningococcal serogroups A, C, W-135, and Y tetanus toxoid conjugate vaccine in adolescents and adults: results of an open, randomised, controlled study

Charissa Borja-Tabora[1], Cecilia Montalban[2], Ziad A Memish[3*], Marie Van der Wielen[4], Veronique Bianco[4], Dominique Boutriau[4] and Jacqueline Miller[5]

MEN ACWY-TT (NIMENRIX®)
56-103 YAŞ

Drugs Aging (2013) 30:309–319
DOI 1



ded. They received a single-dose vaccination with Men-

MEN ACWY-TT (NIMENRIX®)

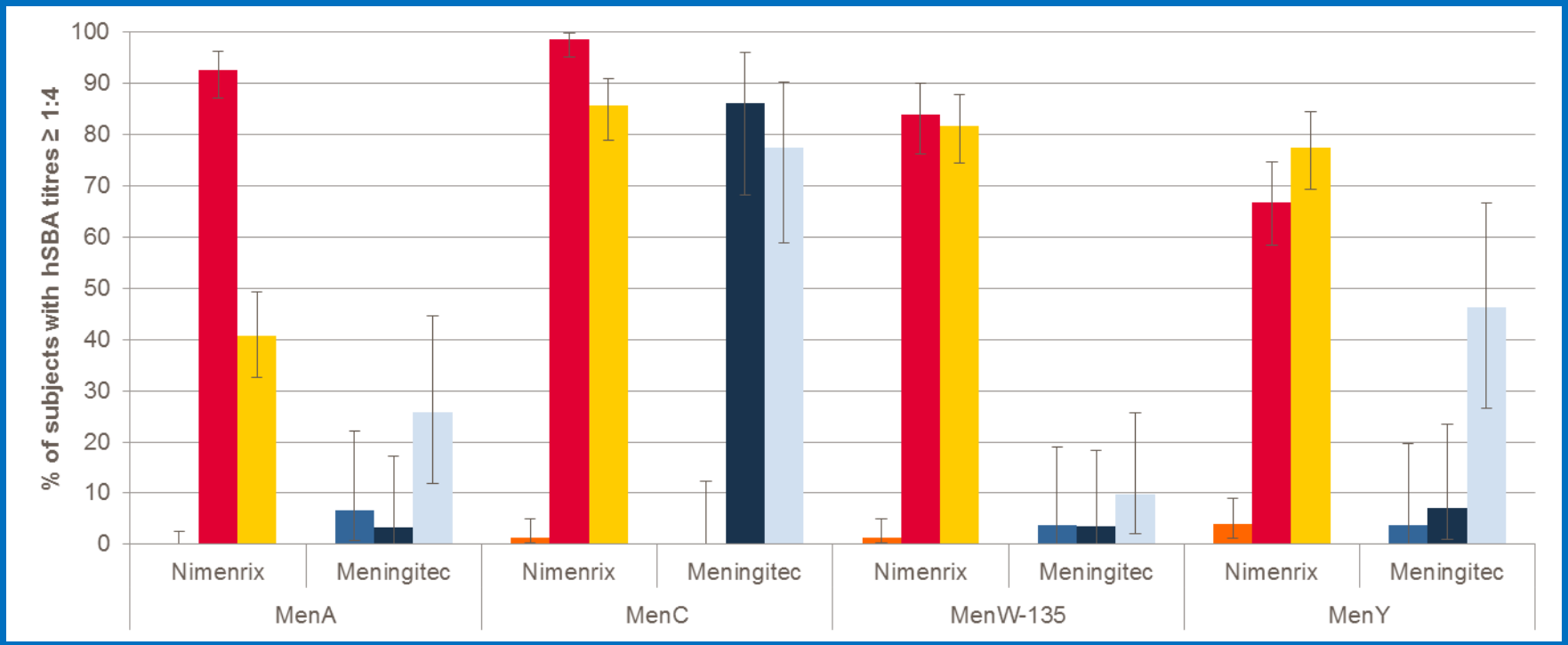
4 yıllık immünojenisite çalışması
MenACWY-TT vs MenC-CRM

Immunogenicity, Safety and Antibody Persistence of a Booster Dose of Quadrivalent Meningococcal ACWY-tetanus Toxoid Conjugate Vaccine Compared with Monovalent Meningococcal Serogroup C Vaccine Administered Four Years After Primary Vaccination Using the Same Vaccines

Timo Vesikari, MD, Aino Forsten, MD,* Veronique Bianco, MS,† Marie Van der Wielen, MD,† and Jacqueline M. Miller, MD‡*

MEN ACWY-TT (NIMENRIX®)
Aşılama sonrası 48.ay verileri

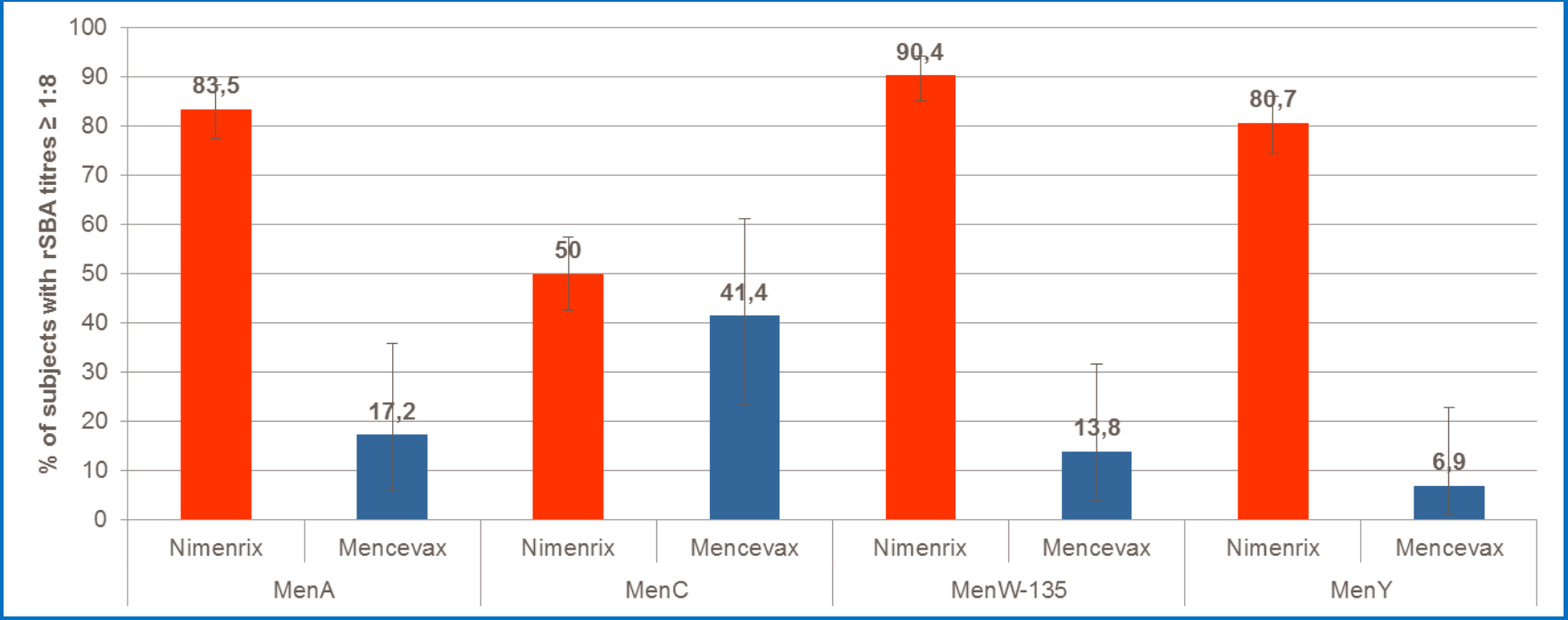
12.Ayda tek doz MenACWY-TT uygulanan çocukların aşılamadan 48 ay sonra %77'de halen yeterli aşı yanıtının devam ettiği gösterilmiştir.



EMGM 2013 (Bad Loipersdorf, Austria, Sept 17-19, 2013)

MEN ACWY-TT (NIMENRIX®)
Aşılama sonrası 48.ay verileri

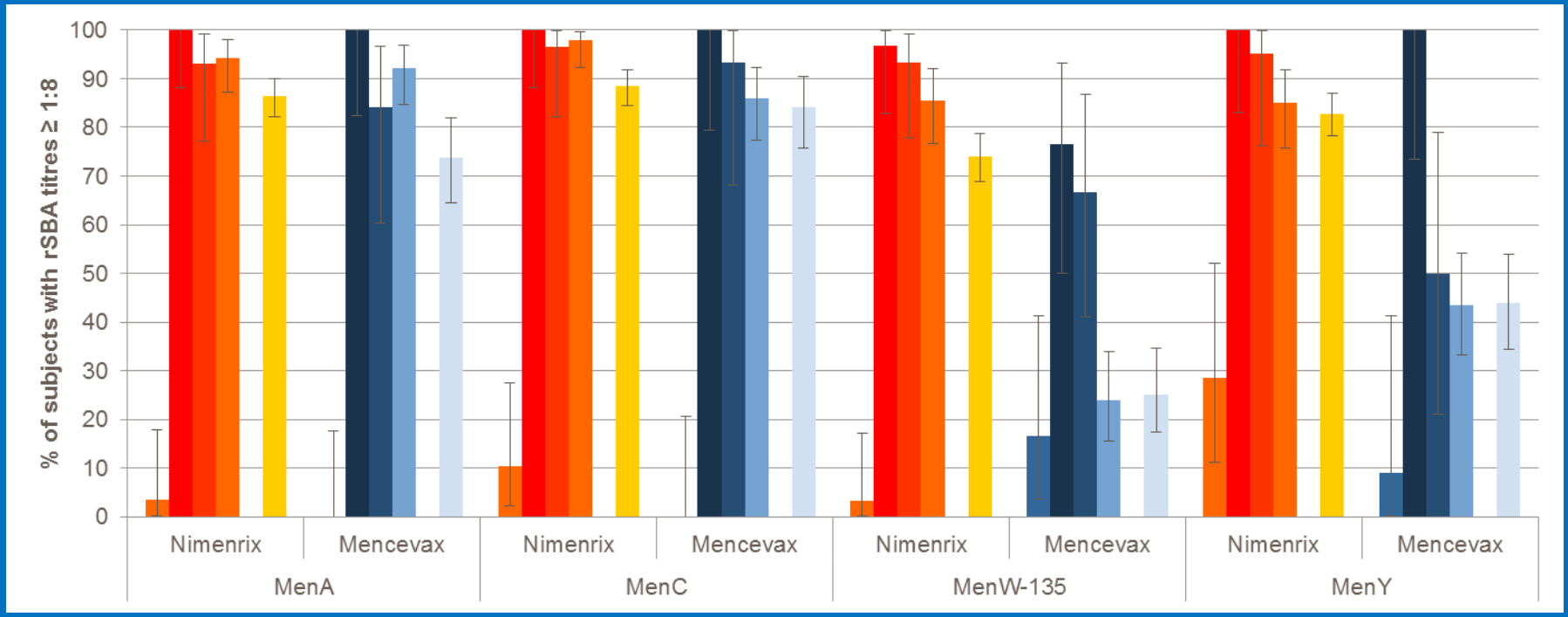
2-10 yaşta tek doz MenACWY-TT uygulanan çocukların aşılamadan 48 ay sonra polisakkarit aşıya göre halen belirgin yüksek antikor yanıtı



EMGM 2013 (Bad Loipersdorf, Austria, Sept 17-19, 2013)

MEN ACWY-TT (NIMENRIX®)
Aşılama sonrası 48.ay verileri

11-50 yaşta tek doz MenACWY-TT uygulanan ADOLESAN VE ERİŞKİNLERDE aşılamadan 48 ay sonra polisakkarit aşıya göre halen belirgin yüksek antikor yanıtı



MEN ACWY-TT (NIMENRIX®)
Aşılama sonrası 60. ay verileri

İNFANTLARDA; tek doz ya da iki doz MenACWY-TT uygulamasından 60 ay sonra halen belirgin yüksek antikor titresi ve tek doz rapel sonrası tüm serogruplara immünojenik ve güvenilir.

VACCINE REPORTS

Five-year Antibody Persistence and Booster Response After 1 or 2 Doses of Meningococcal A, C, W and Y Tetanus Toxoid Conjugate Vaccine in Healthy Children

Nicola P. Klein, MD, PhD, Yaela Baine, PhD,† Devayani Kolhe, MSc,§ Carmen I. Baccarini, MD,‡ Jacqueline M. Miller, MD,‡ and Marie Van der Wielen, MD¶*

The Pediatric Infectious Disease Journal • Volume 35, Number 6, June 2016

MEN ACWY-TT (NIMENRIX®)
Aşılama sonrası 60. ay verileri

İNFANTLARDA; tek doz ya da iki doz MenACWY-TT uygulamasından 60 ay sonra halen belirgin yüksek antikor titresi ve tek doz rapel sonrası tüm serogruplara immünojenik ve güvenilir.

This study found that antibody persistence 5 years after MenACWY-TT vaccination in infancy did not differ substantially between children who received 1 or 2 doses, with the exception of serogroup W. Exploratory analyses found that the percentages of children with hSBA-MenW titers ≥4 and ≥8 and GMTs were higher in the ACWY-2 group than in the ACWY-1 group. We observed no other potentially significant differences with respect to antibody persistence of serogroups A, C and Y. Overall, 5 years after primary vaccination with MenACWY-TT, there was no clear evidence of benefit of receiving 2 versus 1 dose of vaccine in infancy.

The Pediatric Infectious Disease Journal • Volume 35, Number 6, June 2016

MEN ACWY-TT (NIMENRIX®)
Aşılama sonrası 60. ay verileri

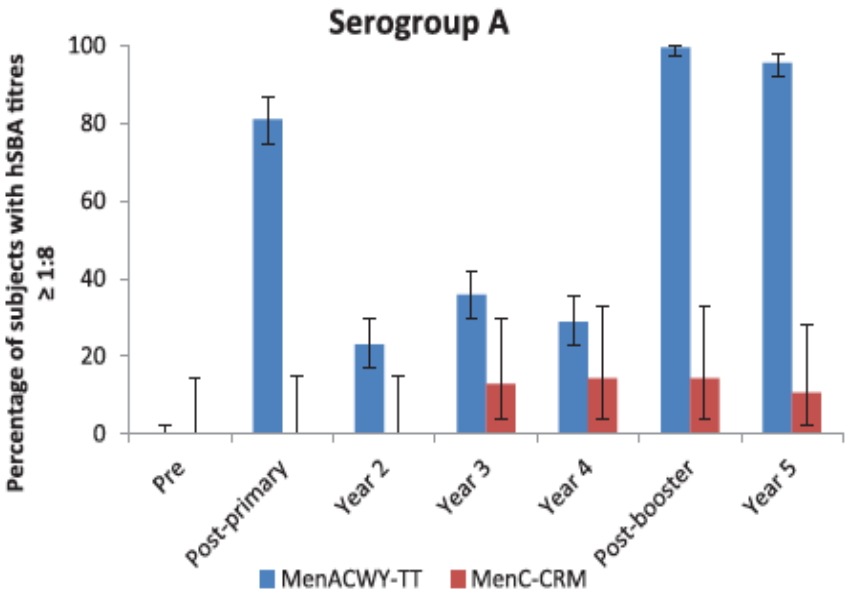
İNFANTLARDA; MenACWY-TT uygulamasından 60 ay sonra halen belirgin yüksek antikor titresi ve tek doz rapel sonrası tüm serogruplara immünojenik ve güvenilir.

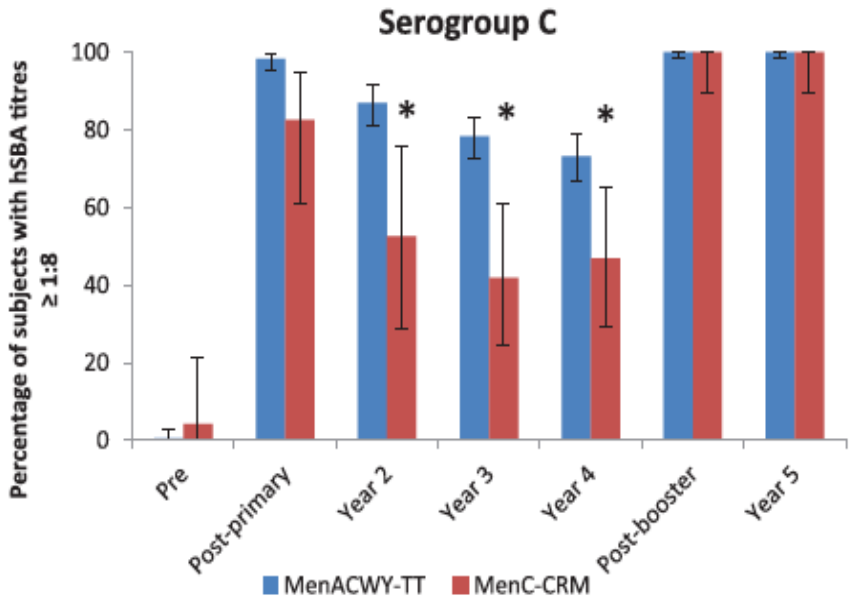
VACCINE REPORTS

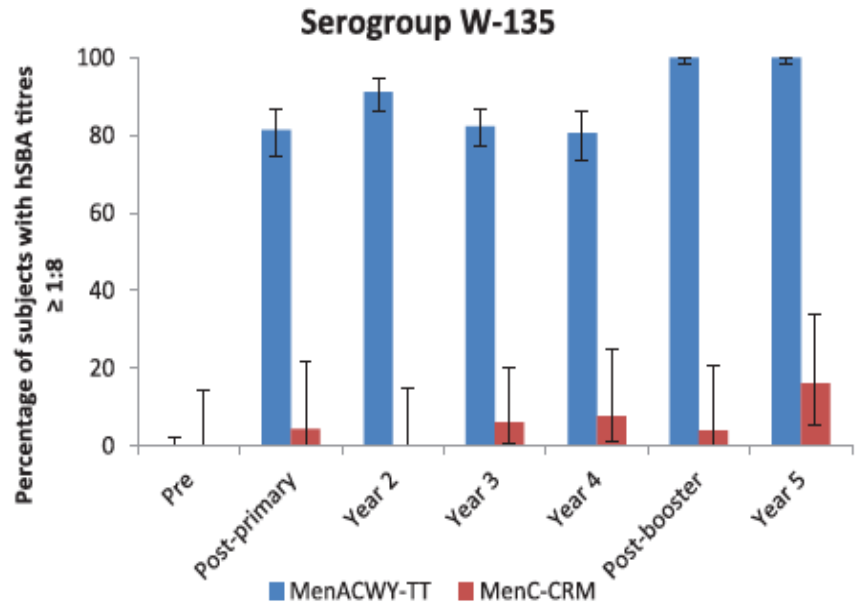
Immunogenicity, Safety and Antibody Persistence of a Booster Dose of Quadrivalent Meningococcal ACWY-tetanus Toxoid Conjugate Vaccine Compared with Monovalent Meningococcal Serogroup C Vaccine Administered Four Years After Primary Vaccination Using the Same Vaccines

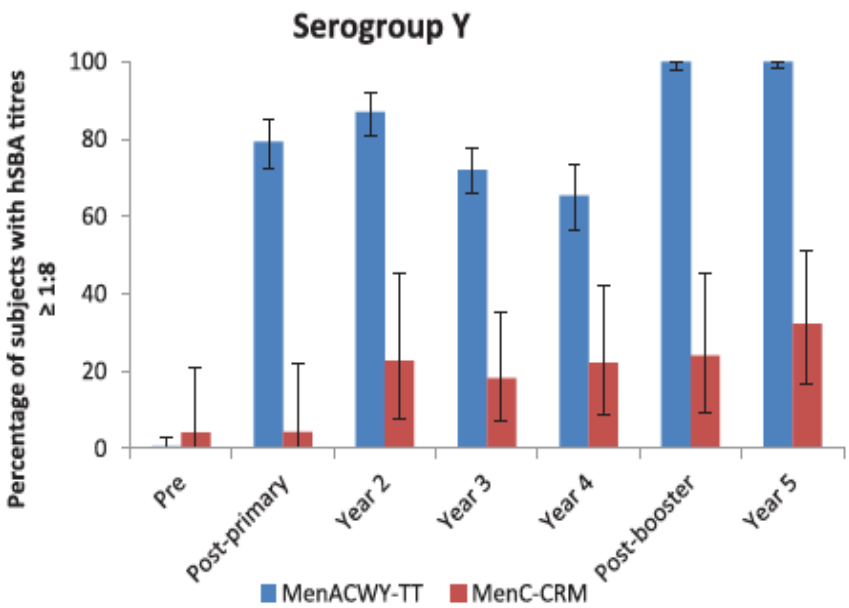
Timo Vesikari, MD, Aino Forsten, MD,* Veronique Bianco, MS,† Marie Van der Wielen, MD,† and Jacqueline M. Miller, MD‡*

(*Pediatr Infect Dis J* 2015;34:e298–e307)


Serogroup A
Percentage of subjects with hSBA titres ≥ 1:8
100
80
60
40
20
0
Pre
Post-primary
Year 2
Year 3
Year 4
Post-booster
Year 5
MenACWY-TT
MenC-CRM

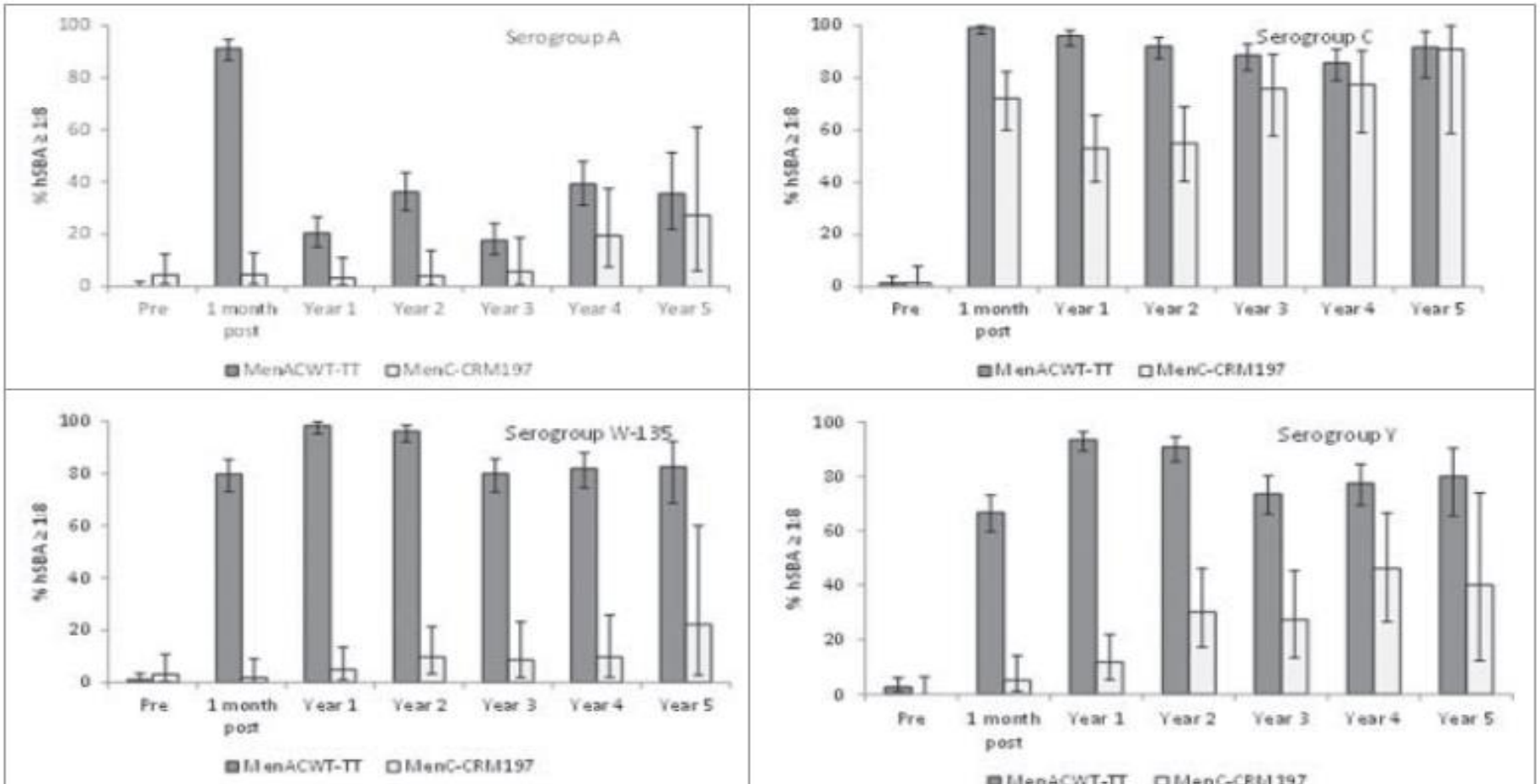

Serogroup C
Percentage of subjects with hSBA titres ≥ 1:8
100
80
60
40
20
0
*
*
*
Pre
Post-primary
Year 2
Year 3
Year 4
Post-booster
Year 5
MenACWY-TT
MenC-CRM


Serogroup W-135
Percentage of subjects with hSBA titres ≥ 1:8
100
80
60
40
20
0
Pre
Post-primary
Year 2
Year 3
Year 4
Post-booster
Year 5
MenACWY-TT
MenC-CRM


Serogroup Y
Percentage of subjects with hSBA titres ≥ 1:8
100
80
60
40
20
0
Pre
Post-primary
Year 2
Year 3
Year 4
Post-booster
Year 5
MenACWY-TT
MenC-CRM

MEN ACWY-TT (NIMENRIX®)
Aşılama sonrası 60. ay verileri

1 AY-10 YAŞ; tek doz MenACWY-TT uygulamasından 60 ay sonra halen belirgin yüksek antikor titresi ve tok doz rapel sonrası tüm serogruplara immünojenik ve güvenilir.



MEN ACWY-TT (NIMENRIX®)
Aşılama sonrası 60. ay verileri

ADOLESAN VE GENÇ ERİŞKİNLERDE MenACWY-TT uygulamasından 60 ay sonra halen belirgin yüksek antikor titresi ve tek doz rapel sonrası tüm serogruplara immünojenik ve güvenilir.

VACCINE REPORTS

Five-year Antibody Persistence and Booster Response to a Single Dose of Meningococcal A, C, W and Y Tetanus Toxoid Conjugate Vaccine in Adolescents and Young Adults

An Open, Randomized Trial

Roger Baxter, MD, Yaela Baine, PhD,† Devayani Kolhe, MSc,‡ Carmen I. Baccarini, MD,† Jacqueline M. Miller, MD,† and Marie Van der Wielen, MD§*

The Pediatric Infectious Disease Journal • Volume 34, Number 11, November 2015

MEN ACWY-TT (NIMENRIX®)
Aşılama sonrası 60. ay verileri

ADOLESAN VE ERİŞKİNLERDE MenACWY-TT uygulamasından 60 ay sonra halen belirgin yüksek antikor titresi

Borja-Tabora *et al. BMC Infectious Diseases* (2015) 15:409
DOI 10.1186/s12879-015-1138-y

BMC

Conclusion: These results suggest that a single dose of MenACWY-TT could protect at least 72 % of vaccinated adolescents and adults against meningococcal disease at least 5 years post-vaccination.

after a single dose of the quadrivalent meningococcal serogroups A, C, W, and Y tetanus toxoid conjugate vaccine in adolescents and adults: 5-year follow-up of an open, randomized trial

Charissa Fay Corazon Borja-Tabora[1*], Cecilia Montalban[2], Ziad A. Memish[3], Dominique Boutriau[4], Devayani Kolhe[5], Jacqueline M. Miller[6] and Marie Van der Wielen[4]

MEN ACWY-TT (NIMENRIX®)
Yan Etki Profili

- LOKAL İSTENMEYEN ETKİLER
- MenACWY-TT' nin güvenirliği 8108 kişide değerlendirilmiş.
- 12 ay -55 yaş grububda en sık lokal reaksiyonlar
  - Ağrı %24.1- %39.9
  - Kızarıklık %14.3- %33
  - Şişlik %11.2-%17.9
  - 55 yaş üzerinde lokal yan etki sıklığı çok düşük: ağrı %2.3, kızarıklı %1.1, şişlik %1.1

MEN ACWY-TT (NIMENRIX®)
Yan Etki Profili

- SİSTEMİK İSTENMEYEN ETKİLER
  - 12-23 ay: irritabilite, halsizlik, ateş, iştahsızlık
  - 2-5 yaş yaş: halsizlik, irritabilite, ateş, iştahsızlık
  - 6-10 yaş: halsizlik, baş ağrısı, GIS bulguları, ateş
  - 11-17 yaş: halsizlik, baş ağrısı, GIS bulguları, ateş
  - 18-55 yaş: baş ağrısı,halsizlik, GIS bulguları, ateş
  - >55 yaş: çok nadiren baş ağrısı

Diğer Aşılarla Birlikte Uygulama

- Hep A/B
- MMRV
- İnfluenza
- PCV10
- DTPa-HBV-IPV/Hib

- **Diğer çocukluk çağı aşıları ile birlikte uygulanmasında sorun bulunmamaktadır.**

EMA. Nimenrix KÜB 2015.

MEN ACWY-D (MENACTRA)

- 0.5 ml tek doz olan aşı
  - Her serogruptan 4 g içermekte (A, C, Y, W135) ve kapsül polisakaritler
  - 4.8 g difteri toksoidine konjuge edilmiştir.
  - Adjuvan ya da prezervatif içermemektedir.
  - İntramuskuler uygulanmaktadır.

- Dünyada 50 ülkede ruhsatlı
- 65 milyon dozdan fazla aşı kullanılmış durumda.

MEN ACWY-D (MENACTRA)

- 2005 yılında FDA tarafından onay almıştır.
- Aynı yıl FDA tarafından 2-55 yaş arası grupta meningokok enfeksiyonu için risk grubu oluşturanlarda kullanımı ve 11-12 yaş grubundaki tüm adolesanlara uygulanmaya başlamıştır.
    - Ülkemizde 9 ay -55 yaş arasında ruhsatlı

MEN ACWY-D (MENACTRA)

- Adolesanlarda yapılan çalışmalarda MenACWY-D sonrasında antikor titrelerinin yüksek olduğu ve rapel doz MenACWY-D yapılan olgularda antikor yanıtının serogrup A dışındaki serogruplara ilk kez aşı uygulanan kişilere göre daha yüksek olduğu gösterilmiştir.
- MenACWY-D ile diğer **Td** aşılarının birlikte uygulanmasında etkinlik ve güvenirlik açısından sorun bulunmamaktadır.
- MenACWY-D ile diğer adolesan dönemde uygulanan aşılar ile ilgili (**Hepatit A ve B, HPV gibi**) henüz veri bulunmamaktadır.

MEN ACWY-D (MENACTRA)

Can J Infect Dis Med Microbiol 2014;25(4):211-216.

ORIGINAL ARTICLE

Safety and immunogenicity of two doses of quadrivalent meningococcal conjugate vaccine or one dose of meningococcal group C conjugate vaccine, both administered concomitantly with routine immunization to 12- to 18-month-old children

Percent of patients with protective (≥8 [1/dilution]) antimeningococcal antibody titres (full analysis set)

Serogroup	Group 1 (n=52) before 18-month MenACYW-D	Group 1 (n=49 to n=51)* one month after 18-month MenACYW-D	Group 2 (n=60) one month after 12-month MCC	Group 2 (n=58) seven months after 12-month MCC
A	34.6 (22.0–49.1)	100 (93–100)	1.7 (0.04–8.9)	3.4 (0.4–11.9)
C	26.9 (15.6–41.0)	96.1 (86.5–99.5)	66.7 (53.3–78.3)	25.9 (15.3–39.0)
Y	82.7 (69.7–91.8)	100 (93–100)	60 (46.5–72.4)	67.2 (53.7–79.0)
W	71.2 (56.9–82.9)	98 (89.6–100)	8.3 (2.8–18.4)	19 (9.9–31.4)

*Data presented as % (95% CI). Antibody titres determined by serum bactericidal assay in the presence of baby rabbit complement. *Sample size varies depending on available data; MenACYW-D Quadrivalent meningococcal conjugate vaccine; MCC Meningococcal conjugate group C vaccine; n Values based on all participants available*

MEN ACWY-D (MENACTRA)

Can J Infect Dis Med Microbiol 2014;25(4):211-216.

ORIGINAL ARTICLE

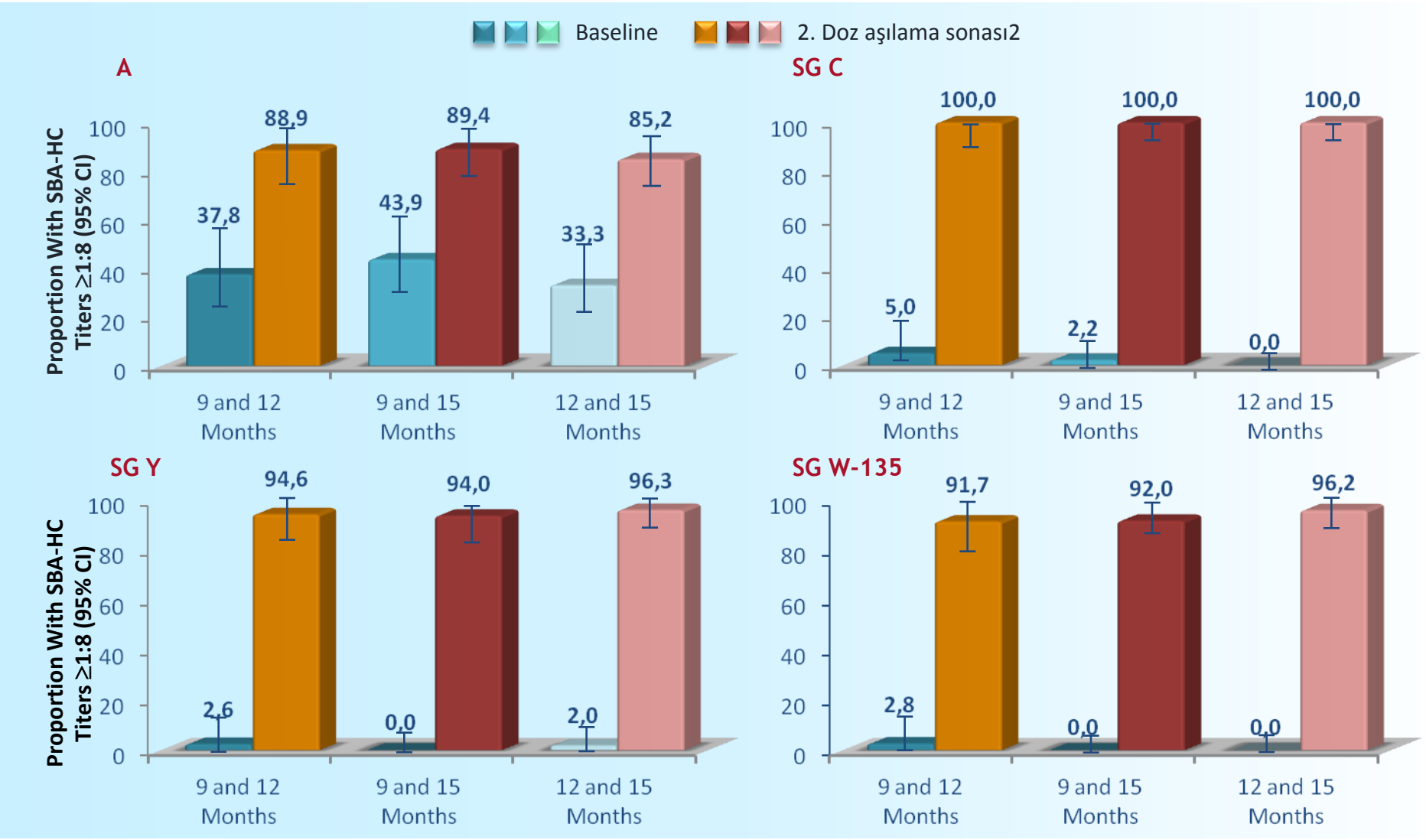
Safety and immunogenicity of two doses of quadrivalent meningococcal conjugate vaccine or one dose of meningococcal group C conjugate vaccine, both administered concomitantly with routine immunization to 12- to 18-month-old children

Overview of safety data after each and any meningococcal dose

Participants with ≥1:	Group 1: Dose 1 (n=60)	Group 1: Dose 2 (n=58)	Group 2 (n=62)
Immediate adverse event	0 (0–6.0)	0 (0–6.2)	1.6 (0–8.7)
Solicited adverse reaction	90.0 (79.5–96.2)	93.1 (83.3–98.1)	91.7 (81.6–97.2)
Injection site adverse reaction	55.0 (41.6–67.9)	67.2 (53.7–79.0)	55.0 (41.6–67.9)
Systemic adverse reaction	88.3 (77.4–95.2)	84.5 (72.6–92.7)	80.0 (67.7–89.2)
Unsolicited adverse event	71.7 (58.6–82.5)	55.2 (41.6–68.3)	59.7 (46.4–71.9)
Unsolicited adverse reaction	5.0 (1.0–13.9)	0 (0–6.2)	4.8 (1.0–13.5)
Serious adverse event	1.7 (0–8.9)	0 (0–6.2)	3.2 (0.4–11.2)
Adverse event-related withdrawal	0 (0–6.0)	0 (0–6.2)	0 (0–5.8)

Data presented as % (95% CI). n Values based on all participants available

MEN ACWY-D (MENACTRA)



MEN ACWY-D (MENACTRA)

	Menactra® 9.ay	Menactra® + Çocukluk Çağı Aşıları 12.ay				Çocukluk Çağı Aşıları 12.ay	
	Menactra® Alone	Menactra® Alone	Menactra® + MMRV	Menactra® + PCV	Menactra® + MMRV + PCV + HepA	MMRV + PCV	MMRV + PCV + HepA
MTA44	1,247	407	293	418	–	–	–
MTA37	2,253	257	664	246	–	476	–
MTA48	1,374	–	–	–	1,053	–	321
Total	4,874	664	957	664	1,053	476	321

Pina LM. *Pediatr Infect Dis J.* 2012;31(11):1173.

MEN ACWY-D (MENACTRA)

Int J Infect Dis. 2016 Feb 24;45:59-64. doi: 10.1016/j.ijid.2016.02.010. [Epub ahead of print]

Safety and immunogenicity of a single dose of a quadrivalent meningococcal conjugate vaccine (MenACYW-D): a multicenter, blind-observer, randomized, phase III clinical trial in the Republic of Korea.

Kim DS[1], Kim MJ[2], Cha SH[3], Kim HM[4], Kim JH[5], Kim KN[6], Lee JS[7], Choi JY[8], Castells VB[9], Kim HS[10], Bang J[10], Oster P[9].

Author information

Abstract

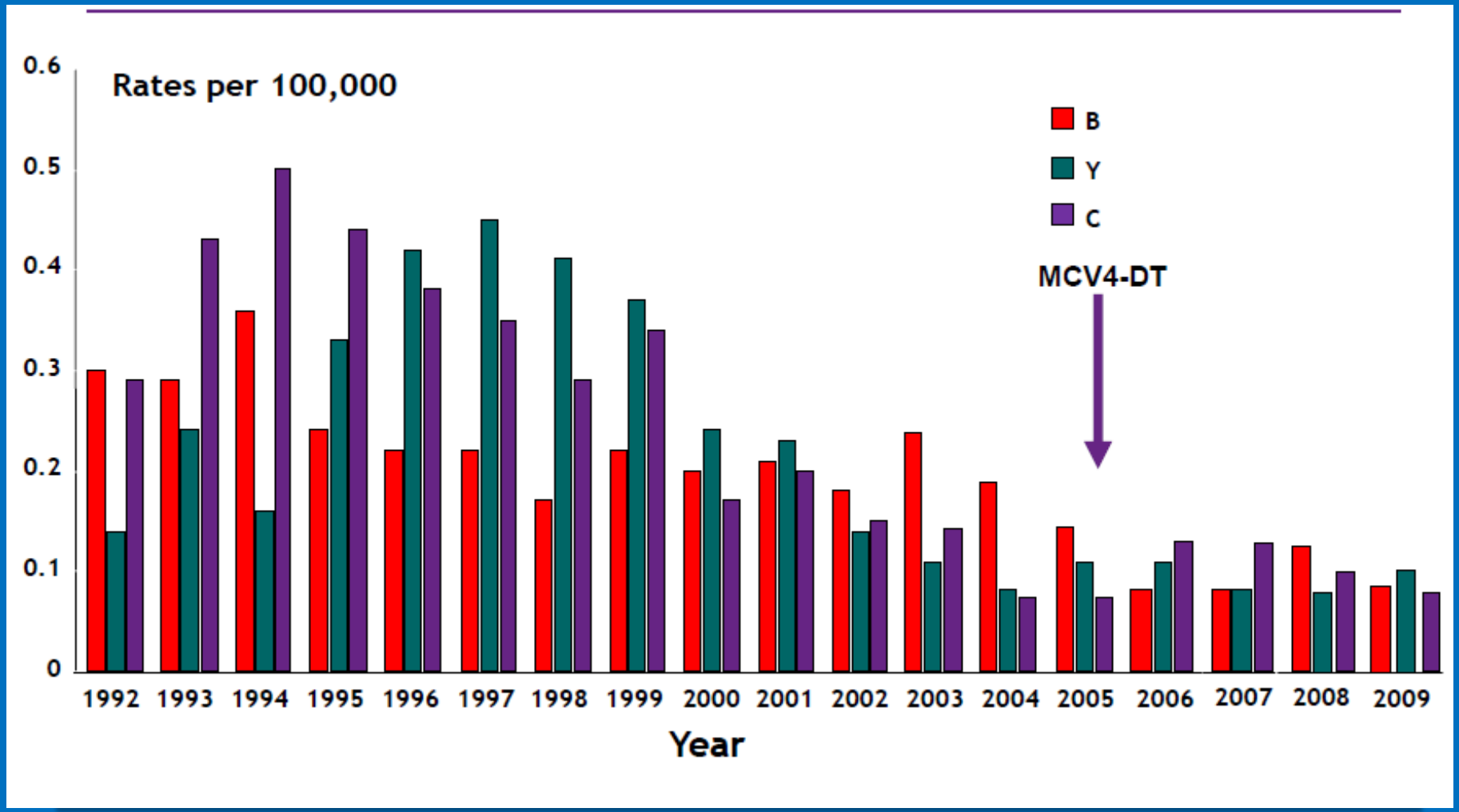
OBJECTIVES: To assess the safety and immunogenicity of a meningococcal polysaccharide diphtheria toxoid conjugate vaccine (MenACYW-D) in a Korean population.

METHODS: This was a phase III, blind-observer, controlled study in which participants aged 11-55 years were randomized (2:1 ratio) to a single dose of MenACYW-D or tetanus/diphtheria/acellular pertussis (Tdap) vaccine. Outcomes included rates of seroconversion against all serogroups (≥4-fold increase in antibody titer from pre-vaccination), geometric mean titers (GMTs) at days 0 and 28 based on a serum bactericidal assay using baby rabbit complement, rates of seroprotection (titer ≥1:128) at day 28, and safety.

RESULTS: A total of 300 participants were enrolled in the study (200 MenACYW-D and 100 Tdap). Seroconversion rates for serogroups A, C, Y, and W-135 were 77.8%, 88.3%, 74.6%, and 92.4%, respectively, for the MenACYW-D group and 9.3%, 8.1%, 12.2%, and 8.2%, respectively, for the Tdap group. The proportions of participants with pre-vaccination titers ≥1:128 were 57.3%, 12.6%, 51.5%, and 22.2% for serogroups A, C, Y, and W-135, respectively; post-vaccination rates were 98.5%, 89.4%, 96.0%, and 95.0% for the MenACYW-D group. A lower proportion of participants reported solicited reactions with MenACYW-D (46.2%) compared with Tdap (76.8%).

CONCLUSION: A single dose of MenACYW-D was well tolerated and elicited a robust immune response in Korean adolescents and adults.

AMERİKA BİRLEŞİK DEVLETLERİ



MENİNGOKO

Plan Nacional de Inmunizaciones

Calendario de VACUNACIÓN 2014

EDAD	VACUNA	PROTEGE CONTRA
Recién Nacido	BCG	Tuberculosis
2, 4 Meses	Pentavalente	Hepatitis B Difteria, Tétanos, Tos Convulsiva H. Influenza B
	Polio oral	Poliomielitis
	Neumocócica conjugada	Enfermedades por Neumococo
6 Meses	Pentavalente	Hepatitis B Difteria, Tétanos, Tos Convulsiva H. Influenza B
	Polio oral	Poliomielitis
12 meses	Antimeningocócica	Enfermedad Meningocócica
	Tres vírica	Sarampión, Rubéola, Paperas
	Neumocócica conjugada	Enfermedades por Neumococo
18 Meses	Pentavalente	Hepatitis B Difteria, Tétanos, Tos Convulsiva H. Influenza B
	Polio oral	Poliomielitis
	Hepatitis A*	Hepatitis A
1º Básico	Tres vírica	Sarampión, Rubéola, Paperas
	dTp (acelular)	Difteria, Tétanos, Tos Convulsiva
Niñas de 4º Básico	VPH	Infección por Virus Papiloma Humano
8º Básico	dTp (acelular)	Difteria, Tétanos, Tos Convulsiva
Adultos de 65 años	Neumocócica Polisacárida	Enfermedades por Neumococo

*Sólo para la Región de Arica y Parinacota y Tarapacá

SALUD RESPONDE
600·360·7777
www.minsal.cl
Búscanos en

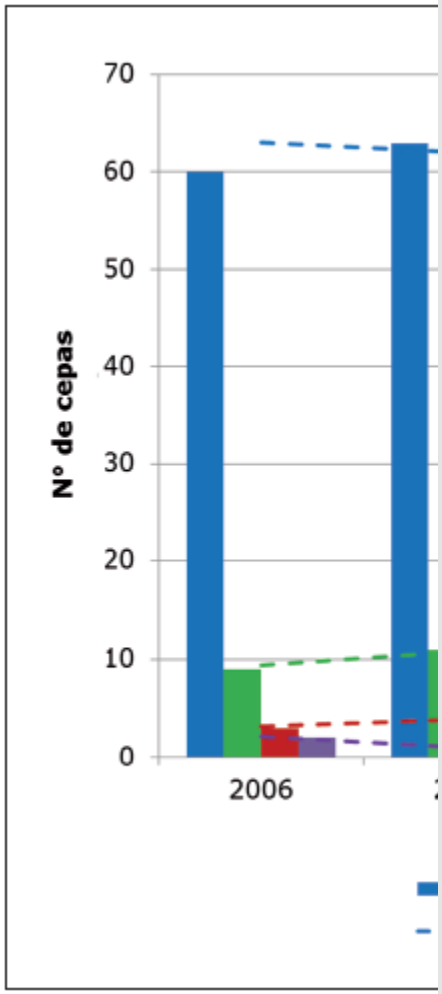
Organización Panamericana de la Salud
Oficina Regional de la Organización Mundial de la Salud

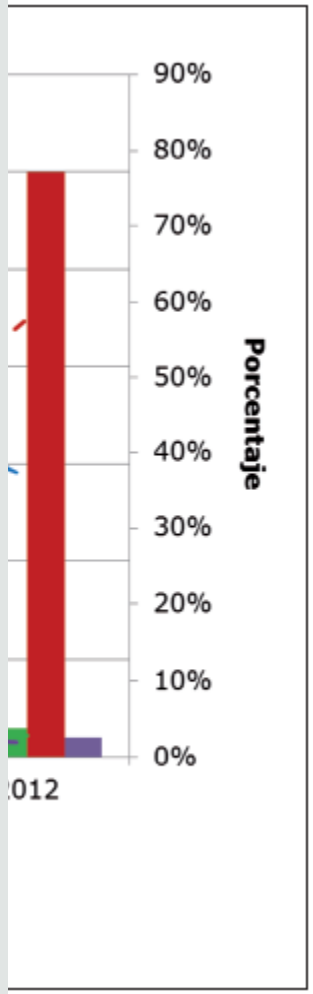
Ministerio de Salud
Gobierno de Chile

5,0

27,8

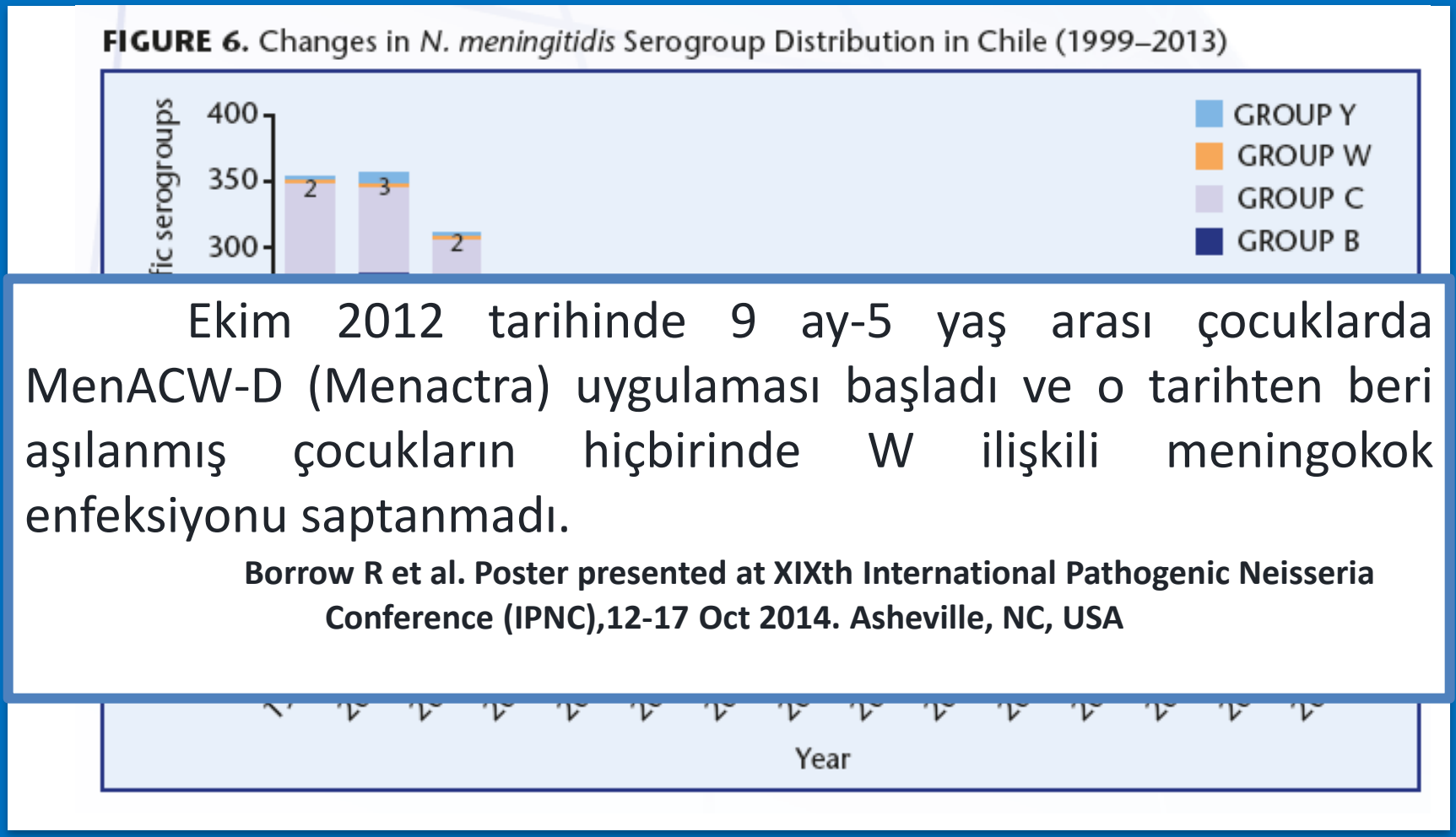
30





5

ŞİLİ TECRÜBESİ



Ekim 2012 tarihinde 9 ay-5 yaş arası çocuklarda MenACW-D (Menactra) uygulaması başladı ve o tarihten beri aşılanmış çocukların hiçbirinde W ilişkili meningokok enfeksiyonu saptanmadı.

Borrow R et al. Poster presented at XIXth International Pathogenic Neisseria Conference (IPNC),12-17 Oct 2014. Asheville, NC, USA

GÜVENLİK

- **Menactra**
  - **uygulama yeri reaksiyonlarının çoğu hafif veya orta dereceli yoğunlukta**
  - **7 yıldan uzun süredir 50 milyondan fazla doz sonrası tecrübe**
  - **Diğer aşılarla birlikte kullanılabilir**
  - **Şubat 2008: 15 milyon doz sonrası 26 konfirme GBS vakası**
    - **Haziran 2010: ACIP (CDC) veritabanı analizleri Menactra sonrası artmış GBS riski saptamadı**

Pina. Pediatr Infect Dis J 2012;31(11): 1173–83

Menactra® Endikasyon

- Endikasyon ve kullanım
  - Menactra *N. meningitidis* A, C, Y ve W-135 serogruplarının neden olduğu invaziv meningokokal hastalığın aktif bağışıklamasında endikedir.
  - **Menactra ABD'de 9 ay – 55 yaş arasındaki kişilerde kullanım için onaylanmıştır.** *
- Dozaj ve Uygulama
  - 0,5 mL'lik doz intamusküler enjeksiyon yoluyla uygulanır.
  - Menactra, 9 ay – 23 ay arasındaki çocuklarda **en az üç ay arayla 2 dozluk seri** halinde uygulanır
  - 2 – 55 yaş arasındaki kişilerde **tek doz** olarak uygulanır

* Menactra, Türkiye'de 9 ay – 11 yaş arası için ruhsatlandırılmıştır
(ruhsatın erişkin yaşları da kapsaması için çalışmalar sürmektedir)

MEN ACWY-CRM197 (MENVEO)

- **MEN ACWY-CRM$_{197}$**
  - **MENVEO (GSK®)**
  - **10 µg MenA, 5 µg MenC, 5 µg, MenW135, 5 µg MenY**
  - **Adjuvan ya da koruyucu içermemektedir.**
  - **+2 ile + 8 C'de 36 ay raf ömrü bulunmaktadır.**
  - **İntramuskuler uygulanmaktadır.**

MEN ACWY-CRM197 (MENVEO)

İNFANT

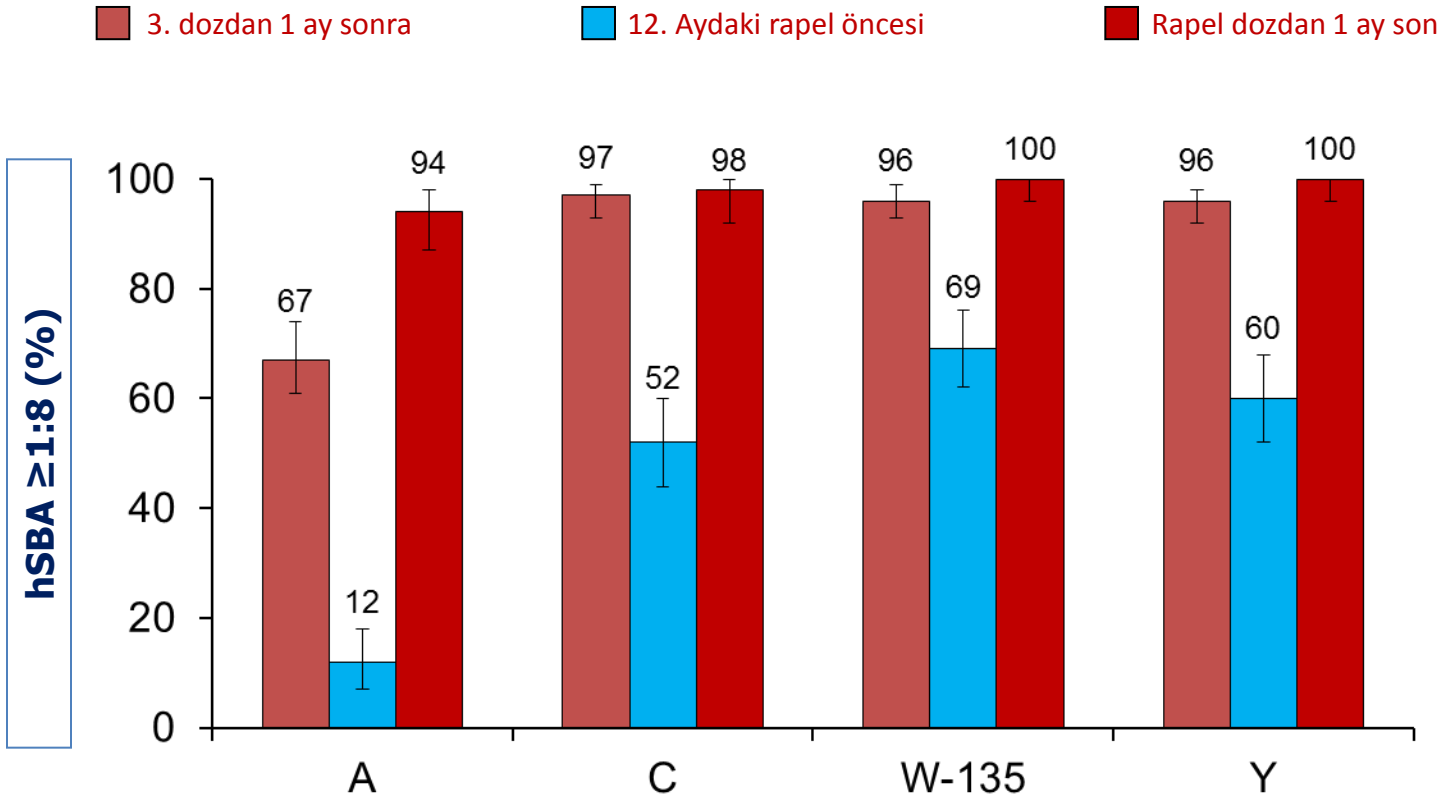
Safety and Immunogenicity of a Novel Quadrivalent Meningococcal CRM-conjugate Vaccine Given Concomitantly With Routine Vaccinations in Infants

Nicola P. Klein, MD, PhD, Keith S. Reisinger, MD,† William Johnston, MD,‡ Tatjana Odrljin, MD,§ Christopher J. Gill, MD,¶ Lisa Bedell, MA,** and Peter Dull, MD§*

Methods: In this open-label phase III study, we randomized full-term 2-month-old infants to 4 doses of MenACWY-CRM coadministered with routine vaccines at 2, 4, 6, and 12 months of age or with routine vaccines alone. We monitored for local and systemic reactions and serious adverse events among all study participants and evaluated for sufficiency of the immune responses to MenACWY-CRM through serum bactericidal activity assay with human complement.

MEN ACWY-CRM197 (MENVEO)

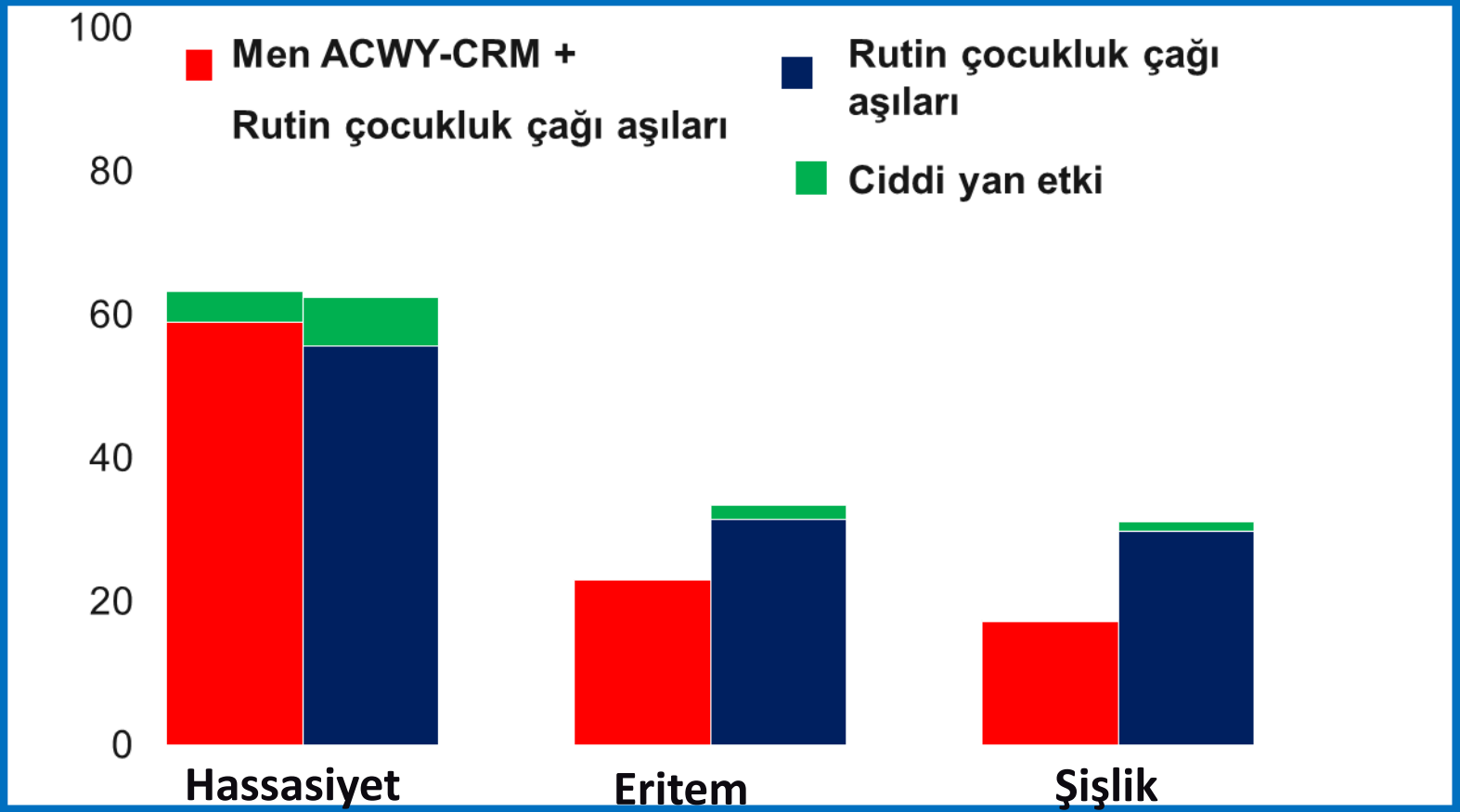
İNFANT 2. 4. 6. ay-12. ay rapel



Klein NP, et al. *Pediatr Infect Dis J.* 2012;31:64-71.

MEN ACWY-CRM197 (MENVEO)

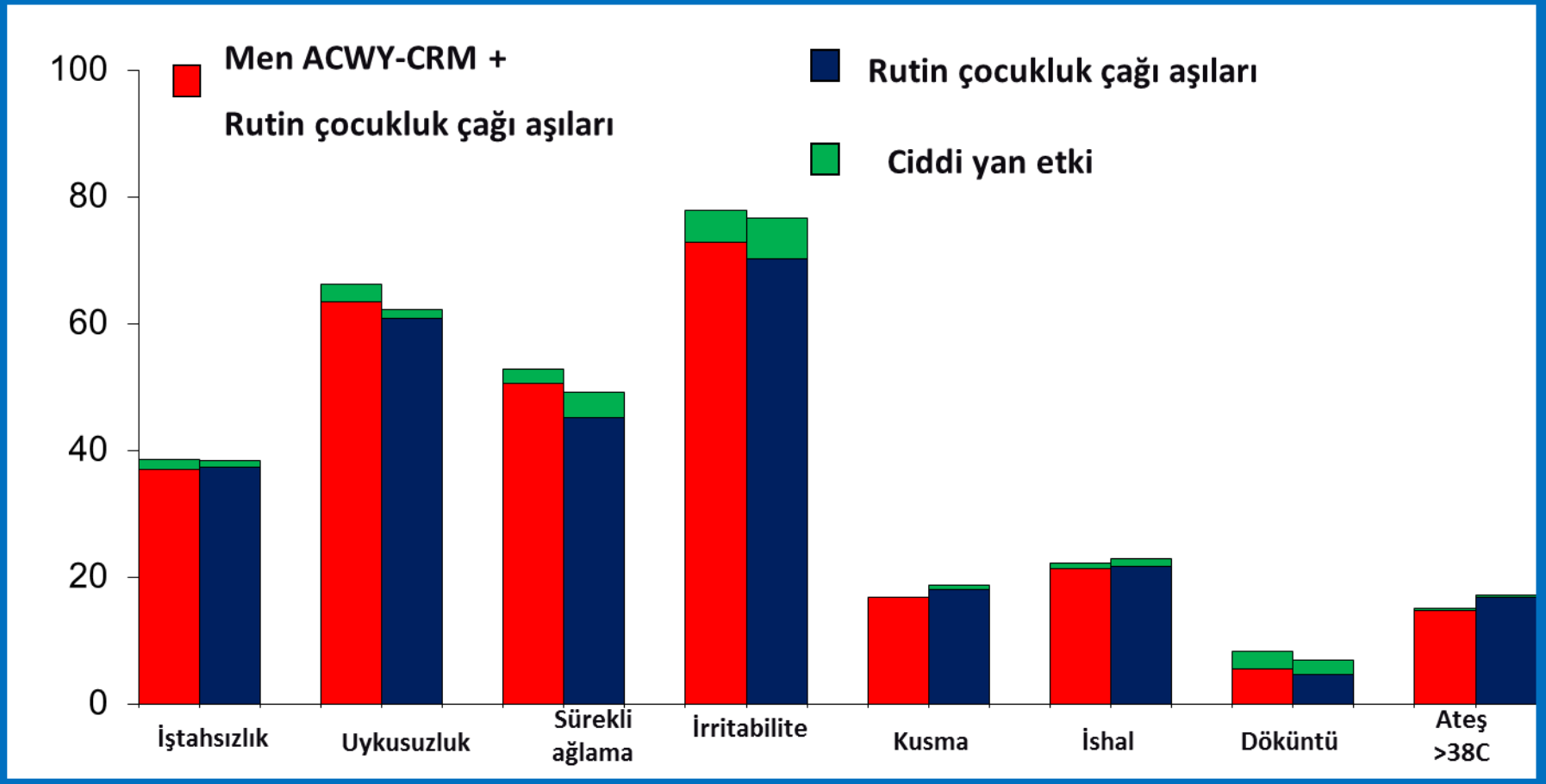
İNFANT 2. 4. 6. ay-12. ay rapel vs. 12.ay



Klein NP, et al. *Pediatr Infect Dis J.* 2012;31:64-71.

MEN ACWY-CRM197 (MENVEO)

İNFANT 2. 4. 6. ay-12. ay rapel vs. 12.ay



Klein NP, et al. *Pediatr Infect Dis J.* 2012;31:64-71.

MEN ACWY-CRM197 (MENVEO)
İNFANT

- 3 Faz 3 çalışma sonuçları
- MenACWY-CRM ve rutin 2-24 ay aşıları
  - (DTaP-HBV-IPV, +HIB or DTP-HIB-IPV+HBV, +Rotavirus, +PCV7 or PCV13, +MMR/MMRV)
- **12.818 çocuk**
  - Amerika, Avustralya, Kanada, Tayvan, Latin Amerika
- 3 + 1 doz şemasından 1 ay sonra hSBA titresi ≥8 olan olgu yüzdesi serogrup A için %89-95, C için %95-98, W135 için %97-100, Y için %96-100
  - Latin Amerika'da 2,4,6, 16.ay, diğer ülkelerde 2,4, 12 ay)
- Birlikte uygulandığı aşıların immün yanıtı üzerine olumsuz etkisi yok.
- İyi tolere edilmiş ve yan etki profili kabul edilebilir düzeyde

Smolenov I et al. International Pathogenic Neisseria Conference 2012..

MEN ACWY-CRM197 (MENVEO)

Vaccine 30 (2012) 2831–2838

Contents lists available at SciVerse ScienceDirect

Vaccine

journal homepage: www.elsevier.com/locate/vaccine

Persistence of the immune response at 5 years of age following infant immunisation with investigational quadrivalent MenACWY conjugate vaccine formulations☆

Ameneh Khatami[a,*], Matthew D. Snape[a], Elizabeth Davis[a], Helen Layton[a], Tessa John[a], Ly-Mee Yu[b], Peter M. Dull[c], Christopher J. Gill[c], Tatjana Odrjlin[c], Simon Dobson[d], Scott A. Halperin[e], Joanne M. Langley[e], Shelly A. McNeil[e], Andrew J. Pollard[a]

Conclusions: Serogroup-specific bactericidal antibody wane following infant immunisation with MenACWY-CRM$_{197}$, most markedly against serogroup A. Best persistence against serogroup C is observed with MenC conjugate vaccine priming and MenACWY-CRM$_{197}$ at 12 months, compared to schedules using only MenACWY-CRM$_{197}$, with the potential for providing broader protection compared to monovalent MenC vaccines alone.

MEN ACWY-CRM197 (MENVEO)

2-10 YAŞ

Table 3
Percentage of children experiencing local and/or systemic reactions.

	MenACWY-CRM	MPSV4	
Subjects (2–10-year-olds) experiencing local reactions (severe reactions), %	*n* = 308	*n* = 310	*P*
Pai			
Ery			
Ind			
Subjects experiencing systemic reactions (severe reactions), %			
Irritability	19(0)	17(0)	
Sleepiness	17(1)	16(1)	
Anorexia	12(0)	11(0)	
Vo			
Dia			
Art			
He			
Fev			
Analg			

	6–10-year-olds	
	n = 157	*n* = 157
Headache	19(2)	11(1)
Malaise	8(2)	6(1)
Chills	8(1)	3(1)
Myalgia	8(2)	3(1)
Nausea	4(0)	4(1)
Arthralgia	3(1)	2(0)
Fever, oral temp. ≥38 °C (≥40 °C)	2(0)	2(0)
Analgesic/antipyretic use	23	15

MenACWY-CRM, investigational quadrivalent meningococcal CRM_{197}-conjugated vaccine; MPSV4, quadrivalent meningococcal polysaccharide vaccine.

MEN ACWY-CRM ile MPSV4 KARŞILAŞTIRMASINDA, MEN ACWY-CRM İYİ TOLERE EDİLMİŞ, LOKAL VE SİSTEMİK YAN ETKİLER KABUL EDİLEBİLİR DÜZEYDEDİR.

MEN ACWY-CRM ile MEN ACWY-D KARŞILAŞTIRMASINDA, MEN ACWY-CRM İYİ TOLERE EDİLMİŞ, LOKAL VE SİSTEMİK YAN ETKİLER KABUL EDİLEBİLİR DÜZEYDEDİR.

Table 3b
Percent (95% confidence interval) of 6–10-year-olds with solicited reactions by vaccine group.

Induration	13 (10–16)	17 (14–20)
Pain	45 (41–49)[a]	39 (35–43)
Systemic reactions		
Arthralgia	4 (3–6)	6 (5–9)
Headache	13 (11–17)	18 (15–21)[a]
Rash	3 (2–5)	5 (3–7)
Fever ≥38 °C	2 (1–3)	2 (1–4)

Percentages are based on numbers of children for whom diary card data were available.

[a] $p < 0.05$ vs. comparator; no other statistically significant differences were observed.

MEN ACWY-CRM197
2-10 YAŞ 5 YIL SONRA??

Vaccine. 2015 Apr 27;33(18):2175-82. doi: 10.1016/j.vaccine.2015.02.049. Epub 2015 Mar 2.

Antibody persistence 5 years after vaccination at 2 to 10 years of age with Quadrivalent MenACWY-CRM conjugate vaccine, and responses to a booster vaccination.

Block SL[1], Christensen S[2], Verma B[3], Xie F[3], Keshavan P[4], Dull PM[3], Smolenov I[4].

Author information

Abstract

BACKGROUND: In a multi-center extension study, children 2-10 years of age, initially vaccinated with one or two doses (2-5 year-olds) or one dose (6-10 year-olds) of quadrivalent meningococcal CRM197-conjugate vaccine (MenACWY-CRM), were assessed five years later for antibody persistence and booster response using serum bactericidal assay with human complement (hSBA).

METHODS: Children 7-10 and 11-15 years of age, who received MenACWY-CRM in the original study, and age-matched vaccine-naïve children, were enrolled in this extension study. After an initial blood draw, children received one dose of MenACWY-CRM as booster or primary dose, with a second blood draw 28 days later.

RESULTS: hSBA titers decreased five years after primary vaccination, but were higher than in non-vaccinated controls against serogroups C, W and Y, with substantial proportions having titers ≥8: 7-22% for A, 32-57% for C, 74-83% for W, and 48-54% for Y. Previously-vaccinated children demonstrated booster responses to revaccination against all four serogroups. Responses to primary vaccination in vaccine-naïve controls were lower and similar to primary responses observed in the original study. All vaccinations were generally well tolerated, with no safety concern raised.

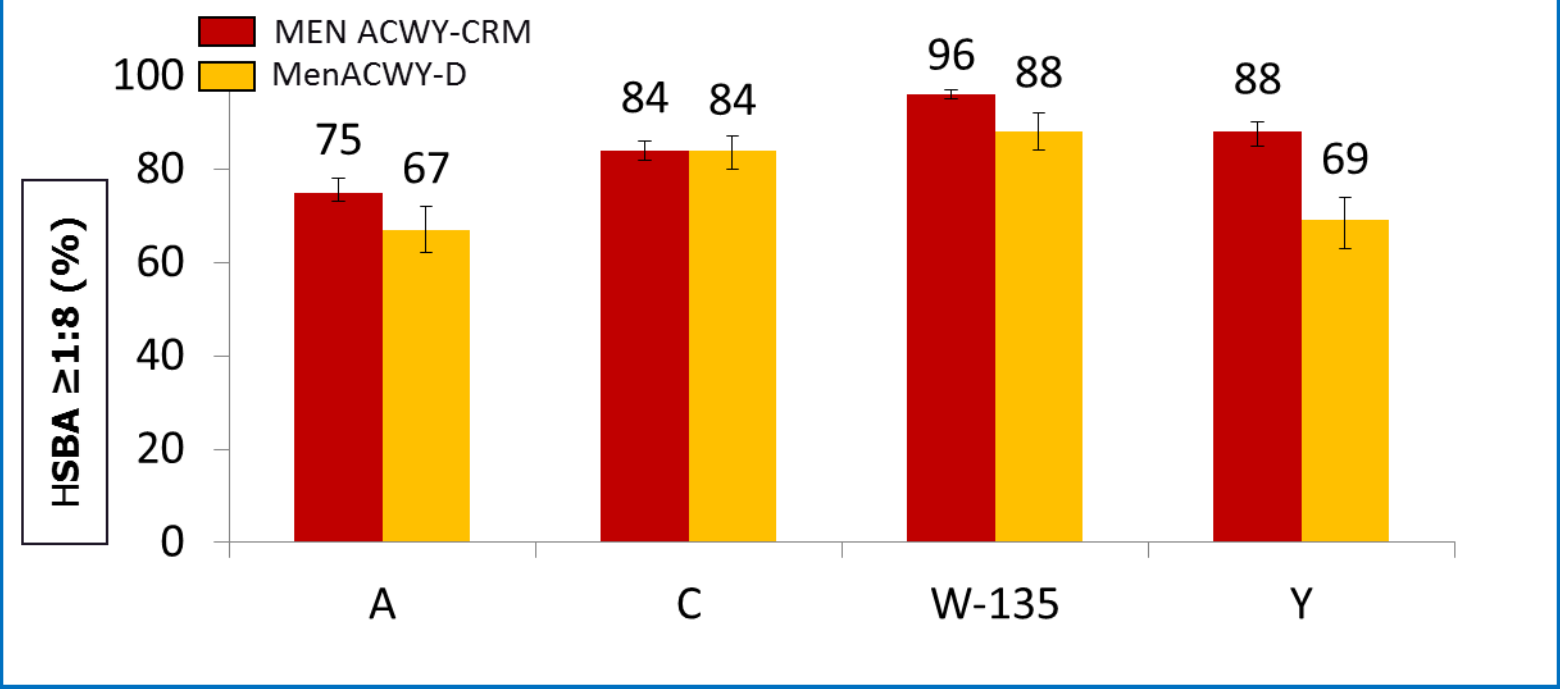
CONCLUSIONS: Approximately half the children vaccinated as 2-10 year-olds maintained protective antibodies against serogroups C, W and Y five years later, but fewer did against serogroup A. Declining titers five years after vaccination and robust booster responses suggest that five years may be an appropriate interval to revaccinate children, subject to epidemiology and delivery considerations.

MEN ACWY-CRM197 (MENVEO)

ADOLESAN

A Randomized Trial to Determine the Tolerability and Immunogenicity of a Quadrivalent Meningococcal Glycoconjugate Vaccine in Healthy Adolescents

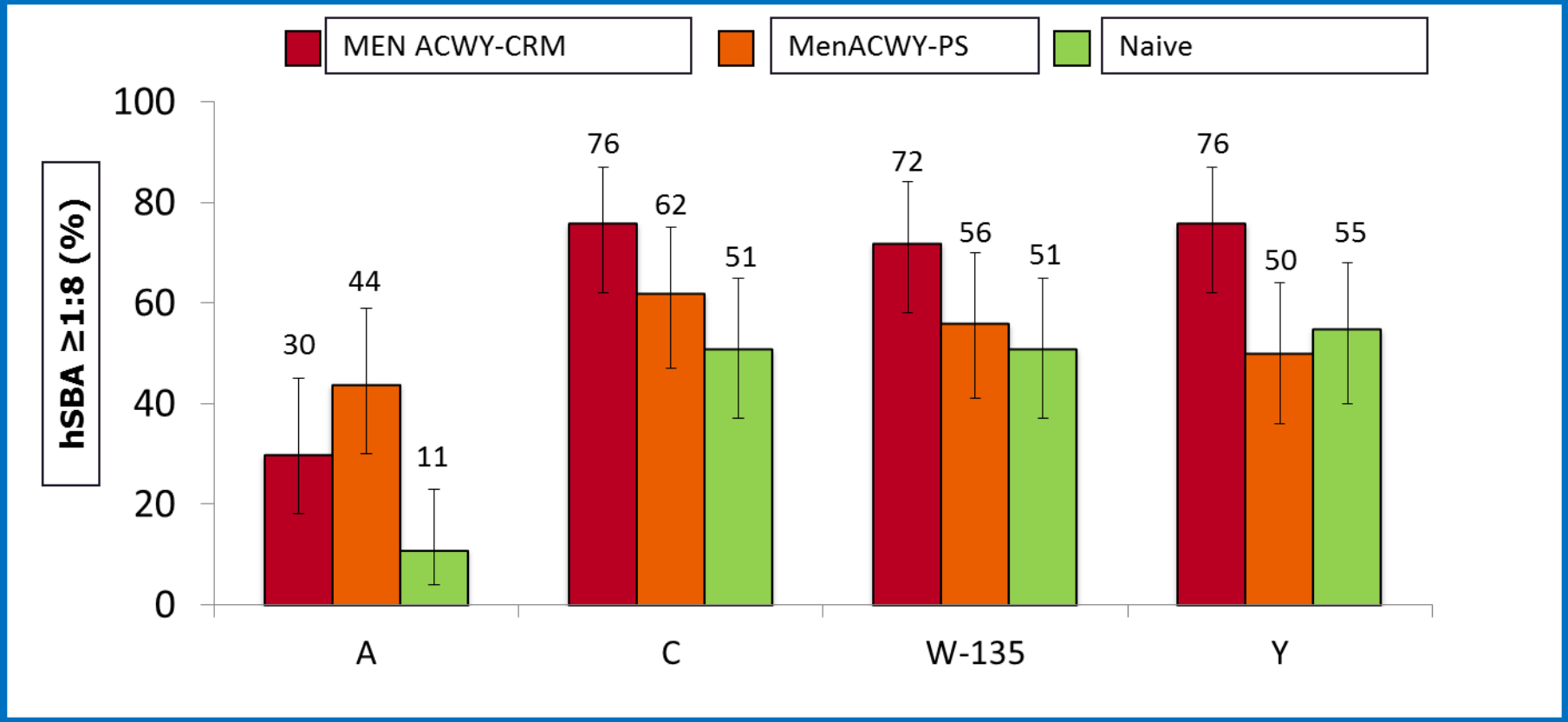
Lisa A. Jackson, MD, MPH, Robert M. Jacobson, MD,† Keith S. Reisinger, MD, MPH,‡ Alessandra Anemona, DStat,§ Lisa E. Danzig, MD,§ and Peter M. Dull, MD§*



MEN ACWY-CRM197 (MENVEO)

ADOLESAN

Aşılamanın **5**. yılı, hSBA >1:8(%); 11-17 YAŞ MENACWY-CRM vs. MPSV4



Jacobson RM, et al. *Pediatr Infect Dis J*. 2013;32:e170-177.

MEN ACWY-CRM197

ADOLESAN

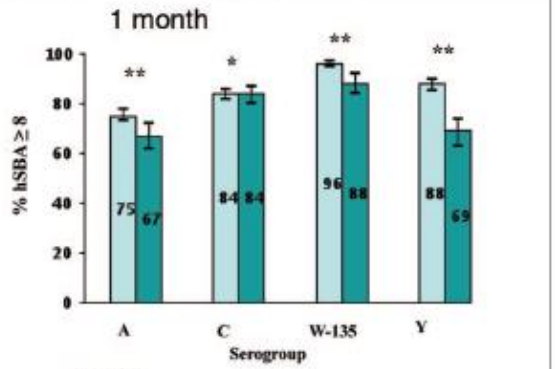
SHORT REPORT

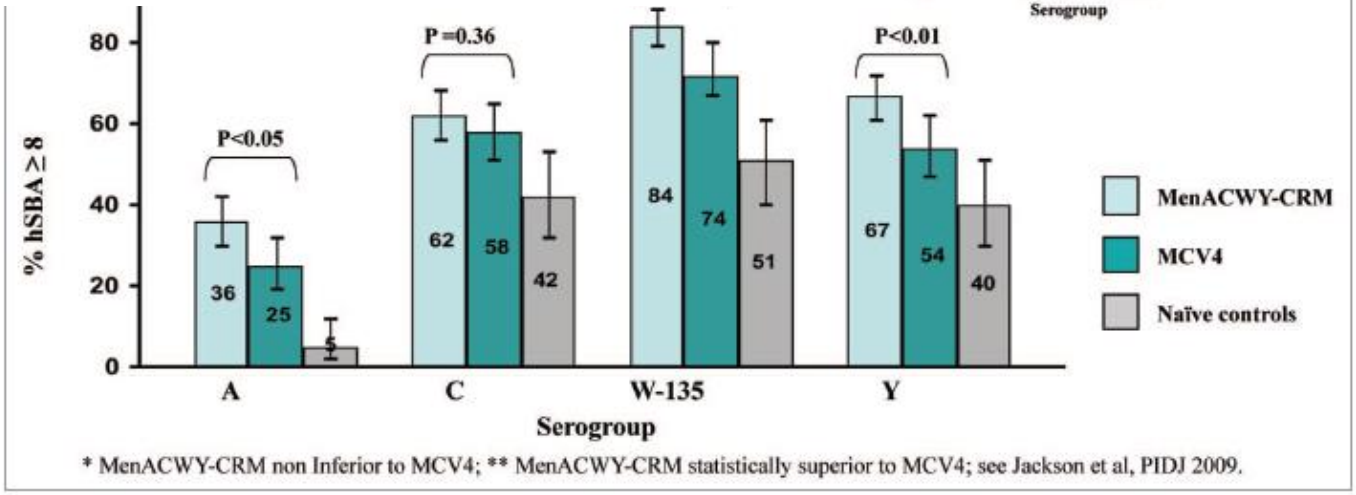
Human Vaccines 6:11, 881-887; November 2010; © 2010 Landes Bioscience

Persistence of immune responses after a single dose of Novartis meningococcal serogroup A, C, W-135 and Y CRM-197 conjugate vaccine (Menveo®) or Menactra® among healthy adolescents

Christopher J. Gill,[1]* Roger Baxter,[2] Alessandra Anemona,[1] Giuseppe L. Ciavarro[1] and Peter M. Dull[1]

In summary, recipients of the MenACWY-CRM was immunogenic at the post-primary (1 month) and demonstrated strong persistence at a median of 22 months post vaccination, and led to a statistically higher proportion of subjects with hSBA titers ≥8 for serogroups A, W-135 and Y than did MCV4. Given that hSBA titers have been correlated with protection against invasive meningococcal disease due to serogroup C,[5,16] these results may infer a potential advantage of the MenACWY-CRM vaccine over time, and may be relevant in determining the need for,

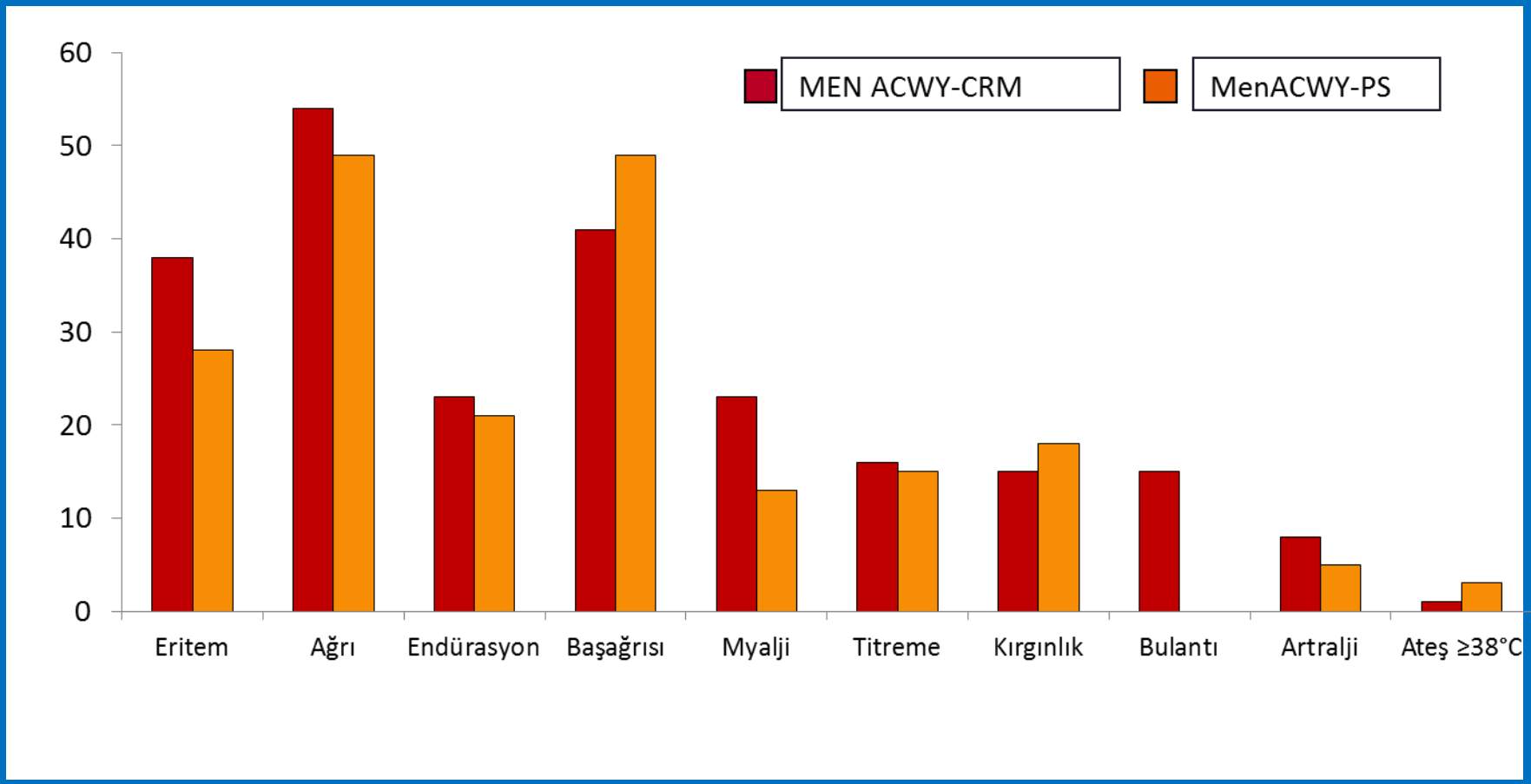




* MenACWY-CRM non Inferior to MCV4; ** MenACWY-CRM statistically superior to MCV4; see Jackson et al, PIDJ 2009.

MEN ACWY-CRM197
ADOLESAN

Yan etki profili yönünden MenACWY-CRM ile polisakarit aşı benzer bulunmuştur.



Jackson LA, et al. *Pediatr Infect Dis J*. 2009;28:86-91.

MEN ACWY-CRM197 (MENVEO)

ADOLESAN

MenACWY-CRM ile HPV ve TDAP birlikte uygulamada antikor yanıtında değişme olmamış, yan etki profili ayrı ayrı uygulama ile benzer olarak bulunmuş.

Vaccine 28 (2010) 3171–3179

Contents lists available at ScienceDirect

Vaccine

journal homepage: www.elsevier.com/locate/vaccine

Safety and immunogenicity of one dose of MenACWY-CRM, an investigational quadrivalent meningococcal glycoconjugate vaccine, when administered to adolescents concomitantly or sequentially with Tdap and HPV vaccines☆

A. Arguedas[a,*], C. Soley[a], C. Loaiza[a], G. Rincon[a], S. Guevara[a], A. Perez[a], W. Porras[a], O. Alvarado[a], L. Aguilar[a], A. Abdelnour[a], U. Grunwald[b], L. Bedell[c], A. Anemona[c,d], P.M. Dull[c]

MEN ACWY-CRM197 (MENVEO)

2 AY-18 YAŞ

Infection and Drug Resistance

Dovepress
open access to scientific and medical research

Open Access Full Text Article

REVIEW

Critical appraisal of a quadrivalent CRM_{197} conjugate vaccine against meningococcal serogroups A, C W-135 and Y (Menveo®) in the context of treatment and prevention of invasive disease

Table 2 Overview of published clinical studies of MenACWY-CRM in children and adolescents

Age group	Immunogenicity among MenACWY-CRM recipients	Safety and tolerability among MenACWY-CRM recipients
Infants from 2 months of age*	60%–92% of two-dose and 81%–99% of three-dose recipients had protective hSBA titers (≥4)[52]	Most common reactions were injection site redness and irritability[52]
Infants from 6 months of age	86%–100% of two-dose recipients had protective hSBA titers (≥4)[54]	Most common reactions were injection site redness and irritability[54]
Toddlers	86%–100% of two-dose primed and 94%–100% of three-dose primed toddlers had protective hSBA titers (≥4)[52] 65%–100% of unprimed toddlers had protective hSBA titers (≥4) after two doses[54]	Most common reactions were injection site redness and irritability[52]
Children aged 2–10 years	83%–95% of two-dose recipients had protective hSBA titers (≥4)[56]	Most common reactions were injection site pain, headache, and irritability[56]
Adolescents	75%–96% of adolescents had protective hSBA titers (≥4)[58,59]	Most common reactions were injection site pain and headache[58,59]

MEN ACWY-CRM197 (MENVEO)
ERİŞKİN

56-65 YAŞ ARASINDA MEN ACWY-CRM ile MPSV4 KARŞILAŞTIRMASINDA, MEN ACWY-CRM İYİ TOLERE EDİLMİŞ, LOKAL VE SİSTEMİK YAN ETKİLER KABUL EDİLEBİLİR DÜZEYDEDİR.

*.

Stamboulian D, et al. *Int J Infect Dis.* 2010;14:e868-e875;

19-55 YAŞ ARASINDA MEN ACWY-CRM ile MEN ACWY-D KARŞILAŞTIRMASINDA, MEN ACWY-CRM İYİ TOLERE EDİLMİŞ, LOKAL VE SİSTEMİK YAN ETKİLER KABUL MEN ACWY-D İLE BENZERDİR

Reisinger KS, et al. *Clin Vaccine Immunol*. 2009;16:1810-1815.

MEN ACWY-CRM197 (MENVEO)

ERİŞKİN 75 YAŞ??

Int J Infect Dis. 2015 Sep;38:36-42. doi: 10.1016/j.ijid.2015.07.003. Epub 2015 Jul 9.

Safety and immunogenicity of an investigational meningococcal ACWY conjugate vaccine (MenACWY-CRM) in healthy Indian subjects aged 2 to 75 years.

Lalwani S[1], Agarkhedkar S[2], Gogtay N[3], Palkar S[1], Agarkhedkar S[2], Thatte U[3], Vakil H[4], Jonnalagedda R[4], Pedotti P[5], Hoyle M[6], Bhusal C[6], Arora A[7].

Author information

Abstract

BACKGROUND: This phase 3, multi-center, open-label study evaluated the immunogenicity and safety of a quadrivalent meningococcal conjugate vaccine (MenACWY-CRM, Menveo(®); Novartis Vaccines and Diagnostics S.r.l., Siena, Italy) in healthy Indian subjects aged 2-75 years, to provide data for licensure in India.

METHODS: A total of 180 subjects were enrolled (60 subjects 2-10 years, 60 subjects 11-18 years, and 60 subjects 19-75 years) and received one dose of MenACWY-CRM. Serum bactericidal activity with human complement (hSBA) was measured before and 1 month after vaccination. Adverse events were collected throughout the 29-day study period.

RESULTS: Percentages of subjects with post-vaccination hSBA ≥8 were 72%, 95%, 94%, and 90% for serogroups A, C, W, and Y, respectively. Geometric mean titers rose 7-fold to 42-fold against the four serogroups. Similar immune responses were observed for the age subgroups 2-10 years, 11-18 years, and 19-75 years. Seroresponse rates at 1 month following vaccination were 72%, 88%, 55%, and 71% for serogroups A, C, W, and Y, respectively. The vaccine was well tolerated with no safety concerns.

CONCLUSION: A single dose of MenACWY-CRM induced a robust immune response against all four meningococcal serogroups and was well tolerated in an Indian population 2-75 years of age.

MEN ACWY-CRM197 (MENVEO)
2016 DİĞER AŞILAR İLE BİRLİKTE?

Pediatr Infect Dis J. 2016 Jan;35(1):81-93. doi: 10.1097/INF.0000000000000930.

Safety and Immunogenicity of a Quadrivalent Meningococcal Conjugate Vaccine and Commonly Administered Vaccines After Coadministration.

Gasparini R[1], Tregnaghi M, Keshavan P, Ypma E, Han L, Smolenov I.

Author information

Abstract

BACKGROUND: Given the broad age range across which the quadrivalent meningococcal conjugate vaccine MenACWY-CRM is used, coadministration with routine vaccines should be evaluated across age groups for possible immunologic interference and impact on vaccine reactogenicity and safety.

METHODS: We summarize data from a large population of infants, adolescents and international travelers from 10 phase 3 or 4 clinical studies to evaluate coadministration of MenACWY-CRM with commonly administered vaccines. Noninferiority analyses of immune responses were performed across studies and age groups for each vaccine. Reactogenicity and safety were also assessed.

RESULTS: In infants, MenACWY-CRM coadministered with routine vaccines did not reduce immune responses to diphtheria, tetanus, poliovirus, hepatitis B, Haemophilus influenzae type b, pneumococcal conjugate, measles-mumps-rubella, varicella or pertussis antigens. Noninferiority criteria were not met for some pneumococcal conjugate serotypes at 7 months of age, but no consistent trends were observed. In adolescents, coadministration did not reduce immune responses to tetanus, diphtheria and human papilloma virus vaccine antigens. Noninferiority criteria for pertussis antigens were not uniformly met in infant and adolescent studies, although the clinical relevance is unclear. In adults, coadministration did not reduce immune responses to hepatitis A/B, typhoid fever, yellow fever, Japanese encephalitis and rabies antigens. Immune responses to MenACWY-CRM were not impacted by coadministration of commonly administered vaccines. Coadministration did not increase frequencies of postvaccination adverse events in any age group.

CONCLUSIONS: With no clinically relevant vaccine interactions or impact on vaccine reactogenicity or safety, these results support the coadministration of MenACWY-CRM with routine vaccines in all age groups.

MEN ACWY-CRM197 (MENVEO)
TAŞIYICILIK ÜZERİNE ETKİLİLİK

Impact of a Quadrivalent Conjugate (MenACWY-CRM) or a Serogroup B (4CMenB) Meningococcal Vaccine on Meningococcal Carriage in English University Students

R.C. Read, *D. Baxter, D.R. Chadwick, S.N. Faust, A. Finn, S. Gordon, P.T. Heath, D.J.M. Lewis, A.J. Pollard, D.P.J. Turner, R. Bazaz, T. Ganguli, T. Havelock, K.R. Neal, I. Okike, B. Morales-Aza, K. Patel, M.D. Snape, J. Williams, S. Gilchrist, S.J. Gray, D. Toneatto, C. Kittel, M. McCarthy, P.M. Dull, R. Borrow*

31st ESPID 28 MAY, 1 JUNE, 2013, MILAN

MEN ACWY-CRM197
TAŞIYICILIK ÜZERİNE ETKİLİLİK

MenACWY-CRM İLE AŞILAMADAN 3 AY SONRA

		Çalışma Grubu		Efficacy % (95% CI)
		MenACWY-CRM	Kontrol	
A, C, W, Y	n	193	260	**36.2%** (15.6 – 51.7)
	%	**5.5%**	**7.4%**	
	N	3520	3504	
Y	n	157	227	**39.0%** (17.3 – 55.0)
	%	**4.5%**	**6.5%**	
	N	3520	3504	

MEN ACWY-CRM197
TAŞIYICILIK ÜZERİNE ETKİLİLİK

Read et al. Vaccine 2017

MenACWY-CRM İLE AŞILAMADAN 1 YIL SONRA

- Fonksiyonel antikor düzeylerinin halen yüksek olduğu gösterişmiş.
- Aşı immünojenik
- hSBA titeleri ile nazofaringeal taşıyıcılık arasında bir ilişki saptanmamış.

,

MEN ACWY-CRM197
2017

Pediatrics. 2017 Jan;139(1). pii: e20162084. doi: 10.1542/peds.2016-2084.

1. **Safety of Quadrivalent Meningococcal Conjugate Vaccine in 11- to 21-Year-Olds.**

Tseng HF[1], Sy LS[2], Ackerson BK[3], Hechter RC[2], Tartof SY[2], Haag M[4], Slezak JM[2], Luo Y[2], Fischetti CA[2], Takhar HS[2], Miao Y[5], Cunnington M[6], Solano Z[2], Jacobsen SJ[2].

- **48.899 MENVEO** uygulanmış, 11-21 yaş arasındaki genç 1 yıl süre ile takip edilmiş.
- 21 farklı klinik durum izlenmiş (nörolojik, romatolojik, hematolojik, endokrin, renal, infeksiyon hastalıkları).
- Hiçbir yan etki bildirimi olmamış.
- Sadece geçici yüz felci (Bell's Palsy) ile istatistik ilişki? Diğer aşılar ile birlikte uygulanması durumunda saptanmış, tek başına uygulamada rastlanmamış.
- Şans? Altta yatan hastalık?

SONUÇ

- Meningokok hastalıkları çocukluk çağında ve ergenlik döneminde önemli morbidite ve mortaliteye neden olmaktadır.
- 4 valanlı konjüge aşılar ülkemizde de mevcuttur ve güvenle kullanılabilmektedir.
- Her 3 aşı da diğer çocukluk çağı aşıları ile birlikte uygulanabilir.