KLİMİK

“ADIM ADIM BAKTERİYEL MENENJİT”

BAKTERİYEL MENENJİTTE AŞININ YERİ

Dr. Ayşe Batırel

Kartal Dr. Lütfi Kırdar Eğitim ve Araştırma Hastanesi
İnfeksiyon Hastalıkları ve Klinik Mikrobiyoloji

21 Nisan 2015, İstanbul

PLAN

***S. pneumoniae* aşısı**

***N. meningitidis* aşısı**

***H. influenzae* Tip b aşısı**

- **AŞI ŞEMALARI**
- **EPİDEMİYOLOJİ**
- **ENDİKASYONLAR**
- **KONJUGE vs POLİSAKKARİT AŞILAR**
- **ETKİNLİK**
- **MALİYET - ETKİNLİK**
- **GÜVENLİK – Yan etkiler**

CDC – ACIP Erişkin Aşılama ‡

Recommended Adult Immunization Schedule—United States - 2015

Note: These recommendations must be read with the footnotes that follow containing number of doses, intervals between doses, and other important information.

Figure 1. Recommended adult immunization schedule, by vaccine and age group[1]

VACCINE ▼ / AGE GROUP ▶	19-21 years	22-26 years	27-49 years	50-59 years	60-64 years	≥ 65 years
Influenza*[,2]	1 dose annually					
Tetanus, diphtheria, pertussis (Td/Tdap),*[,3]	Substitute 1-time dose of Tdap for Td booster; then boost with Td every 10 yrs					
Varicella*[,4]	2 doses					
Human papillomavirus (HPV) Female*[,5]	3 doses					
Human papillomavirus (HPV) Male*[,5]	3 doses					
Zoster[6]					1 dose	
Measles, mumps, rubella (MMR)*[,7]	1 or 2 doses					
Pneumococcal 13-valent conjugate (PCV13)*[,8]	1-time dose					
Pneumococcal polysaccharide (PPSV23)[8]	1 or 2 doses					1 dose
Meningococcal*[,9]	1 or more doses					
Hepatitis A*[,10]	2 doses					
Hepatitis B*[,11]	3 doses					
Haemophilus influenzae type b (Hib)*[,12]	1 or 3 doses					

*Covered by the Vaccine Injury Compensation Program

For all persons in this category who meet the age requirements and who lack documentation of vaccination or have no evidence of previous infection; zoster vaccine recommended regardless of prior episode of zoster

Recommended if some other risk factor is present (e.g., on the basis of medical, occupational, lifestyle, or other indication)

No recommendation

Report all clinically significant postvaccination reactions to the Vaccine Adverse Event Reporting System (VAERS). Reporting forms and instructions on filing a VAERS report are available at www.vaers.hhs.gov or by telephone, 800-822-7967.

Information on how to file a Vaccine Injury Compensation Program claim is available at www.hrsa.gov/vaccinecompensation or by telephone, 800-338-2382. To file a claim for vaccine injury, contact the U.S. Court of Federal Claims, 717 Madison Place, N.W., Washington, D.C. 20005; telephone, 202-357-6400.

Additional information about the vaccines in this schedule, extent of available data, and contraindications for vaccination is also available at www.cdc.gov/vaccines or from the CDC-INFO Contact Center at 800-CDC-INFO (800-232-4636) in English and Spanish, 8:00 a.m. - 8:00 p.m. Eastern Time, Monday - Friday, excluding holidays.

Use of trade names and commercial sources is for identification only and does not imply endorsement by the U.S. Department of Health and Human Services.

The recommendations in this schedule were approved by the Centers for Disease Control and Prevention's (CDC) Advisory Committee on Immunization Practices (ACIP), the American Academy of Family Physicians (AAFP), the America College of Physicians (ACP), American College of Obstetricians and Gynecologists (ACOG) and American College of Nurse-Midwives (ACNM).

‡

CDC - ACIP

Figure 2. Vaccines that might be indicated for adults based on medical and other indications[1]

VACCINE ▼ INDICATION ▶	Pregnancy	Immunocompromising conditions (excluding human immunodeficiency virus [HIV])[4,6,7,8,13]	HIV infection CD4+ T lymphocyte count[4,6,7,8,13]		Men who have sex with men (MSM)	Kidney failure, end-stage renal disease, receipt of hemodialysi	Heart disease, chronic lung disease, chronic alcoholism	Asplenia (including elective splenectomy and persistent complement component deficiencies)[4,12]	Chronic liver disease	Diabetes	Healthcare personnel
			< 200 cells/µL	≥ 200 cells/µL							
Influenza*[,2]	1 dose IIV annually				1 dose IIV or LAIV annually	1 dose IIV annually					1 dose IIV or LAIV annually
Tetanus, diphtheria, pertussis (Td/Tdap)*[,3]	1 dose Tdap each pregnancy	Substitute 1-time dose of Tdap for Td booster; then boost with Td every 10 yrs									
Varicella*[,4]	Contraindicated			2 doses							
Human papillomavirus (HPV) Female*[,5]		3 doses through age 26 yrs				3 doses through age 26 yrs					
Human papillomavirus (HPV) Male*[,5]		3 doses through age 26yrs				3 doses through age 21 yrs					
Zoster[6]	Contraindicated			1 dose							
Measles, mumps, rubella (MMR)*[,7]	Contraindicated			1 or 2 doses							
Pneumococcal 13-valent conjugate (PCV13)*[,8]				1 dose							
Pneumococcal polysaccharide (PPSV23)[8]				1 or 2 doses							
Meningococcal*[,9]	1 or more doses										
Hepatitis A*[,10]				2 doses							
Hepatitis B*[,11]				3 doses							
Haemophilus influenzae type b (Hib)*[,12]		post-HSCT recipients only		1 or 3 doses							

*Covered by the Vaccine Injury Compensation Program

For all persons in this category who meet the age requirements and who lack documentation of vaccination or have no evidence of previous infection; zoster vaccine recommended regardless of prior episode of zoster

Recommended if some other risk factor is present (e.g., on the basis of medical, occupational, lifestyle, or other indications)

No recommendation

These schedules indicate the recommended age groups and medical indications for which administration of currently licensed vaccines is commonly recommended for adults ages 19 years and older, as of February 1, 2015. For all vaccines being recommended on the Adult Immunization Schedule: a vaccine series does not need to be restarted, regardless of the time that has elapsed between doses. Licensed

WHO - Rutin Aşılama Önerileri

(updated: 27 February 2015)

Table 1: Summary of WHO Position Papers - Recommendations for Routine Immunization

Antigen		Children (see Table 2 for details)		Adolescents	Adults	Considerations (see footnotes for details)
Recommendations for all immunization programmes						
BCG[1]		1 dose				Exceptions HIV
Hepatitis B[2]		3-4-doses (see footnote for schedule options)		3 doses (for high-risk groups if not previously immunized) (see footnote)		Birth dose Premature and low birth weight Co-administration and combination vaccine Definition high-risk
Polio[3]		3-4 doses (at least one dose of IPV) with DTP				OPV birth dose Type of vaccine Transmission and importation risk criteria
DTP[4]		3 doses	Booster (DTP) 1-6 years of age	Booster (Td) (see footnote)	Booster (Td) in early adulthood or pregnancy	Delayed/interrupted schedule Combination vaccine
***Haemophilus influenzae* type b**[5]	**Option 1**	3 doses, with DTP				Single dose if > 12 months of age Not recommended for children > 5 yrs old Delayed/interrupted schedule Co-administration and combination vaccine
	Option 2	2 or 3 doses, with booster at least 6 months after last dose				
Pneumococcal (Conjugate)[6]	**Option 1**	3 doses, with DTP				Vaccine options Initiate before 6 months of age Co-administration HIV+ and preterm neonates booster
	Option 2	2 doses before 6 months of age, plus booster dose at 9-15 months of age				
Rotavirus[7]		Rotarix: 2 doses with DTP RotaTeq: 3 doses with DTP				Vaccine options Not recommended if > 24 months old
Measles[8]		2 doses				Combination vaccine; HIV early vaccination; Pregnancy
Rubella[9]		1 dose (see footnote)		1 dose (adolescent girls and/or child bearing aged women if not previously vaccinated; see footnote)		Achieve and sustain 80% coverage Combination vaccine and Co-administration Pregnancy
HPV[10]				2 doses (females)		Target 9-13 year old girls Pregnancy Older age groups ≥ 15 years 3 doses HIV and immunocompromised

WHO - Rutin Aşılama Önerileri

‡

(updated: 27 February 2015)

Table 1: Summary of WHO Position Papers - Recommendations for Routine Immunization

Antigen		Children (see Table 2 for details)	Adolescents	Adults	Considerations (see footnotes for details)
Recommendations for certain regions					
Japanese Encephalitis[11]		*Inactivated Vero cell-derived vaccine: generally 2 doses* *Live attenuated vaccine: 1 dose* *Live recombinant vaccine: 1 dose*			Vaccine options and manufacturer's recommendations; Pregnancy; Immunocompromised
Yellow Fever[12]		1 dose, with measles containing vaccine			
Tick-Borne Encephalitis[13]		3 doses (> 1 yr FSME-Immun and Encepur; > 3 yrs TBE-Moscow and EnceVir) with at least 1 booster dose (every 3 years for TBE-Moscow and EnceVir)			Definition of high-risk Vaccine options; Timing of booster
Recommendations for some high-risk populations					
Typhoid[14]		*Vi polysaccharide vaccine*: 1 dose; *Ty21a live oral vaccine*: 3-4 doses (see footnote). Booster dose 3-7 years after primary series			Definition of high-risk Vaccine options
Cholera[15]		*Dukoral (WC-rBS)*: 3 doses ≥ 2-5 yrs, booster every 6 months; 2 doses adults/children > 6 yrs, booster every 2nd year; *Shanchol & mORCVAX*: 2 doses ≥1 yrs, booster dose after 2 yrs			Minimum age Definition of high-risk
Meningococcal[16]	**MenA conjugate**	1 dose 9-18 months (5µg)			2 doses if < 9 months with 8 week interval
	MenC conjugate	2 doses (2-11 months) with booster 1 year after 1 dose (≥12 months)			Definition of high-risk; Vaccine options
	Quadrivalent conjugate	2 doses (9-23 months) 1 dose (≥2 years)			
Hepatitis A[17]		At least 1 dose ≥ 1 year of age			Level of endemicity; Vaccine options; Definition of high risk groups
Rabies[18]		3 doses			Definition of high-risk; Booster
Recommendations for immunization programmes with certain characteristics					
Mumps[19]		2 doses, with measles containing vaccine			Coverage criteria > 80% Combination vaccine
Seasonal influenza (inactivated tri- and qudri-valent)[20]		First vaccine use: 2 doses Revaccinate annually: 1 dose only (see footnote)	Priority for pregnant women 1 dose ≥ 9 years of age Revaccinate annually		Priority risk groups Lower dosage for children 6-35 months
Varicella[21]		1 - 2 doses	2 doses		Achieve & sustain ≥ 80% coverage Pregnancy Co-admin with other live vaccines

T.C. Sağlık Bakanlığı Çocukluk Dönemi Aşı Takvimi

Aşılar	Doğumda	1. ayın sonu	2. ayın sonu	4. ayın sonu	6. ayın sonu	12. ayın sonu	18. ayın sonu	24. ayın sonu	İlköğretim 1. sınıf	İlköğretim 8. sınıf
Hepatit B	I	II			III					
BCG (Verem)			I							
DaBT - İPA - Hib			I	II	III		R			
KPA			I	II	III	R				
KKK						I			R	
DaBT - İPA									R	
OPA					I		II			
Td										R
Hepatit A							I	II		
Suçiçeği						I				

DaBT-IPA-Hib: Difteri, Aselüler Boğmaca, Tetanoz, İnaktif Polio, Hemofilus Influenza Tip b Aşısı (Beşli Karma Aşı)

KPA: Konjuge Pnömokok Aşısı

KKK: Kızamık, Kızamıkçık, Kabakulak Aşısı

DaBT-İPA: Difteri, Aselüler Boğmaca, Tetanoz, İnaktif Polio Aşısı (Dörtlü Karma Aşı)

OPA: Oral Polio Aşısı (Çocuk Felci Aşısı)

Td: Erişkin Tipi Difteri-Tetanoz Aşısı

R: Rapel (Pekiştirme)

Aşı takvimindeki tüm aşılar ücretsizdir.

Sağlık Bakanlığı Erişkin Aşılama Rehberi - 2009

Tablo 6. Normal ve risk grubu yetişkinlerde aşılama şeması

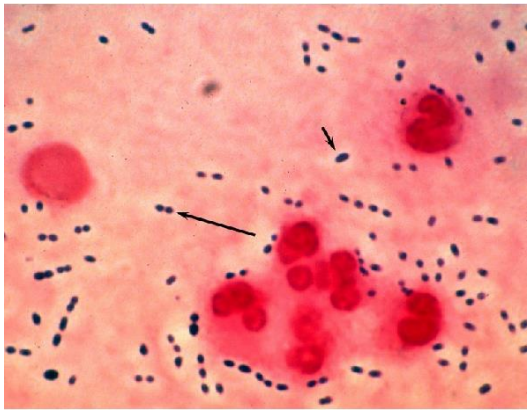
Aşı	18-49 yaş	50-64 yaş	65 ≥ yaş
[1] Tetanoz, difteri (Td)	Her 10 yılda bir rapel doz aşı		
[2,3] Kızamık (K)/ Kızamık, kızamıkçık, kabakulak (KKK)	1 veya 2 doz aşı		
Hepatit B	3 doz aşı (0, 1, 6. aylar)		
İnfluenza	Yılda 1 doz aşı		Yılda 1 doz aşı
[4] Pnömokok (polisakkarid)	1-2 doz aşı		1 doz aşı
Hepatit A	2 doz aşı (0, 6 ya da 18. aylar)		
[2] Suçiçeği	2 doz aşı (0, 1 ya da 2. aylar)		
[5] Meningokok	1 ya da daha fazla doz aşı		

İmmünitesi ve kontrendikasyonu olmayan tüm bireyleri kapsar.

Risk faktörü olan ve kontrendikasyonu olmayan bireyleri kapsar.

[1] Tetanoz aşısı için primer immünizasyonu tamamlamış kişilerdeki şemadır.
[2] Gebelikte kontrendikedir.
[3] Bir ya da iki doz kızamık aşısı yapıldı ise bir doz KKK aşısı yapılır. İlk doz KKK aşısı olarak yapıldı ise 2. doz kızamık aşısı olarak yapılır. İki doz KKK aşısı yapıldı ise tekrar aşıya gerek yoktur.
[4] Beş yıl ara ile risk gruplarına yapılır (her risk grubu özel olarak değerlendirilir).
[5] Koruyuculuk süresi 2 yıldır.


Join hands in the fight against meningitis
WORLD MENINGITIS DAY 24 APRIL
Join hands against meningitis by registering your support for governments worldwide to include meningitis preventing vaccines in their country's National Immunisation Programme today!
join hands
AGAINST MENINGITIS
24 APRIL



S. pneumoniae AŞISI

Pnömokokal Hastalık Yükü

- **Yıllık insidans- ABD: 15-30 / 100.000**

  >65 yaş: 35-80 / 100.000

- **İnvazif pnömokokal hastalık (IPH): <1 yaş ve >65 yaş en sık**
  - **<1 y: 43.3 / 100.000**
  - **>65 y: 39.6 / 100.000**
  - **≥ 50 yaş mortalite: 6200 kişi / yıl**

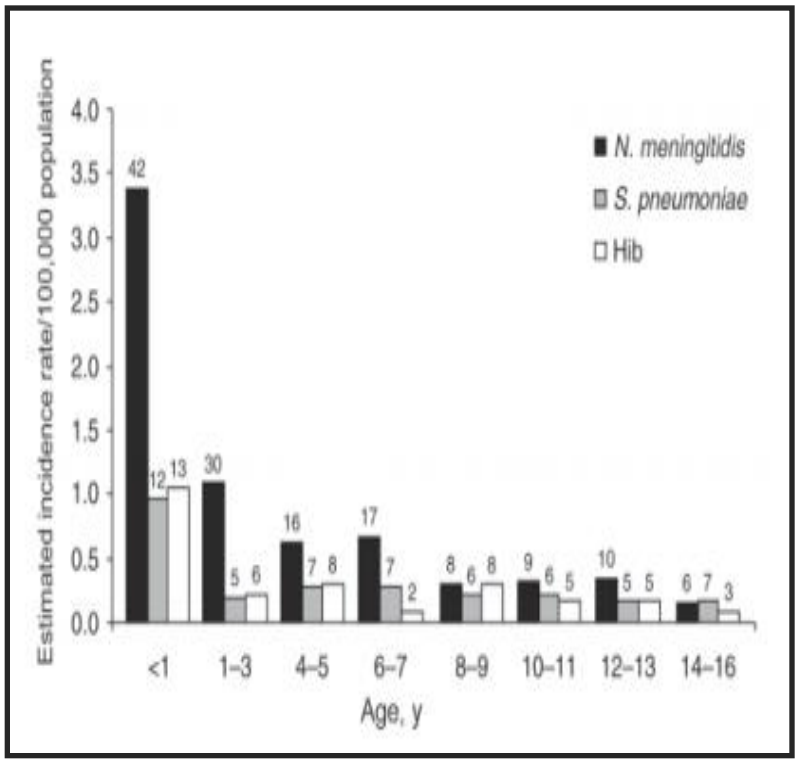
- **Pnömokokal hastalık tahmini yıllık yük- ABD**:
  - 500,000 pnömoni
    - 175,000 pnömoni nedeniyle hospitalizasyon
    - 40,000 mortalite
  - 50,000 bakteremi
  - **3,000 menenjit (Mortalite:%30-40)**

CDC. In: Atkinson W et al. Epidemiology and Prevention of Vaccine-Preventable Diseases The Pink Book. Pneumococcal Disease. 10th ed. Public Health Foundation; 2007:255–268.
Weycker D et al. Vaccine 2010;28:4955–60.

A Prospective Study of Etiology of Childhood Acute Bacterial Meningitis, Turkey

Mehmet Ceyhan,* Inci Yildirim,* Paul Balmer,† Ray Borrow,† Bunyamin Dikici,‡ Mehmet Turgut,§ Nese Kurt,§ Aysel Aydogan,¶ Cigdem Ecevit,¶ Yasar Anlar,# Ozlem Gulumser,# Gonul Tanir,** Nuran Salman,†† Nezahat Gurler,†† Nevin Hatipoglu,†† Mustafa Hacimustafaoglu,‡‡ Solmaz Celebi,‡‡ Yavuz Coskun,§§ Emre Alhan,¶¶ Umit Celik,¶¶ Yildiz Camcioglu,†† Gulten Secmeer,* Deniz Gur,## and Steve Gray†

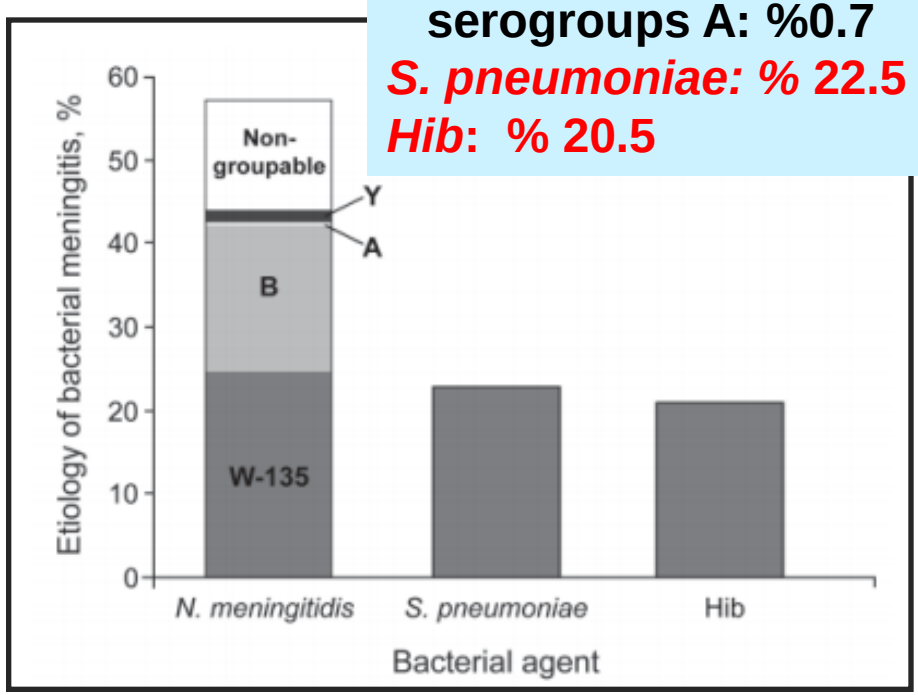
408 BOS örneği, 243'ünde bakteriyel etken



***N. meningitidis*: % 56.5**
- serogroups W-135: %43
- serogroups B: %31
- serogroups Y: %2.2
- serogroups A: %0.7

S. pneumoniae: % 22.5

***Hib*: % 20.5**



Ceyhan M, et al. Emerging Infectious Diseases, 14 (7), July 2008,1089-96

Ülkemizde Menenjit etkenleri: ≤18 yaş

‡

- **2005-2012 menenjit etkenleri, çok merkezli prospektif sürveyans çalışması**
- >1 ay - ≤18 yaş menenjit şüpheli çocukların BOS örnekleri
- Multiplex PCR
- **1452 BOS örneği**, 645 **(%44.4)**'sinde **etken tanımlı**
- ***N. meningitidis*** : 333 **(%51.6)**
  - 127 (**38.1%**): **serogroup W-135**
  - 87 (**26.1%**) **serogroup B**
  - 28 (**8.4%**) **serogroup A**
  - 3 (**0.9%**) **serogroup Y**
  - 88 (**26.4%**) gruplandırılamayan
- ***S. pneumoniae***: 195 (**%30.2**)
- ***Hib***: 117 (**%18.1**)

***N. meningitidis*: 56.5%**

serogroups W-135: %43

serogroups B: %31

serogroups Y: %2.2

serogroups A: %0.7

***S. pneumoniae:* in 22.5%**

***Hib*: in 20.5%**

Ceyhan M, Hum Vaccin Immunother 2014;10(9):2706-12

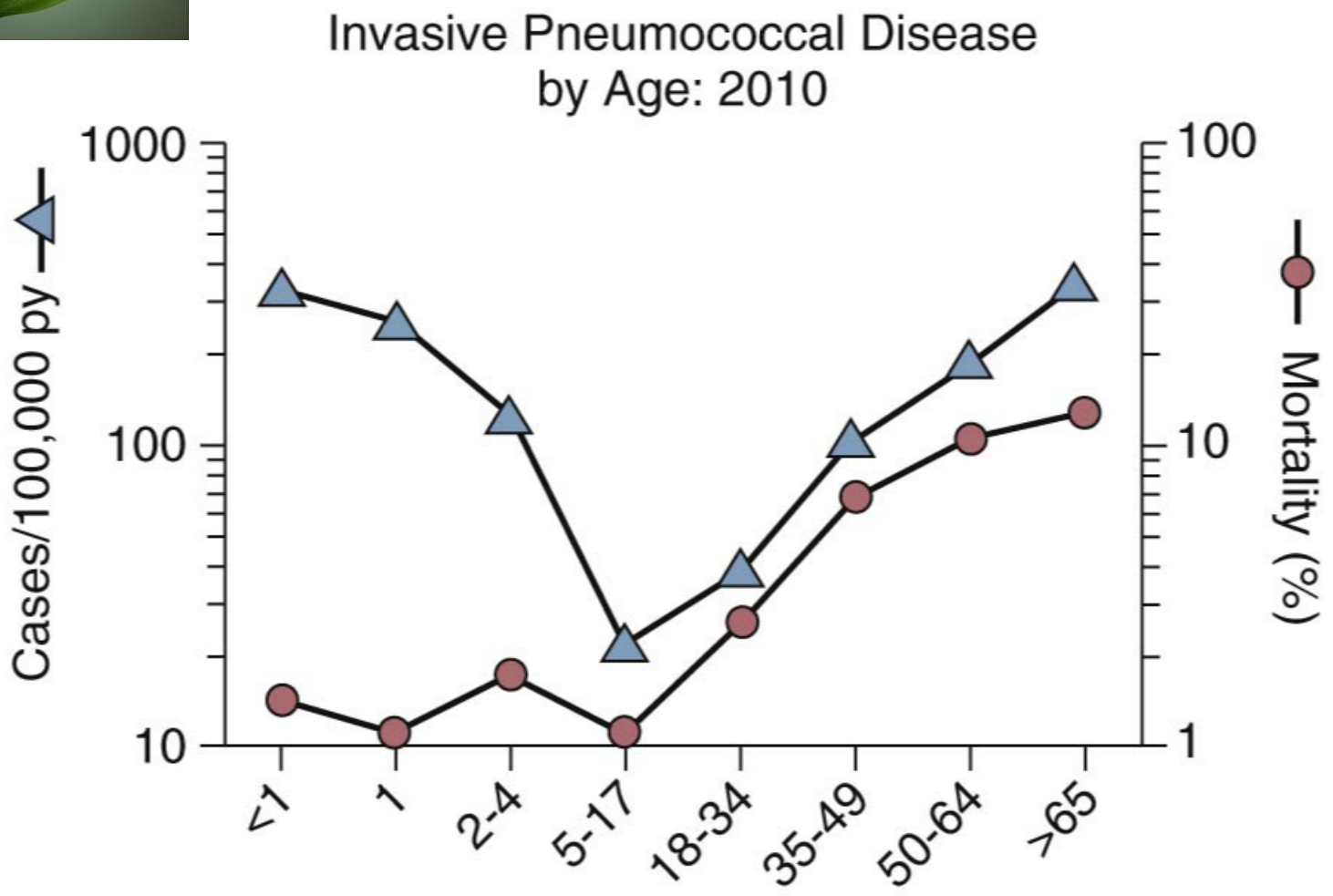
Ülkemizde Menenjit etkenleri

- 841 menenjitli çocuk, 246 etken tanımlı (BOS'da DNA)

- **% 53: *Streptococcus pneumoniae***
  - **En sık serotipler: 1, 19F, 6A/6B, 23F, 5, 14, 18 and 19A**
- **% 19: *Neisseria meningitidis***
  - **86% serogroup B**
  - 6% serogroup C
  - 3% serogroup A
  - 3% serogroup X
  - 3% serogroup W
- **16% *Haemophilus influenzae type b***

Toprak D, et al. Pediatr Infect Dis J, 2014 Oct;33(10):1087-9

İnvazif Pnömokokal Hastalık



Mandell, Douglas, Bennett's Principles and Practice of Infectious Diseases, 2015

ECDC - İNVAZİF PNÖMOKOKAL HASTALIK

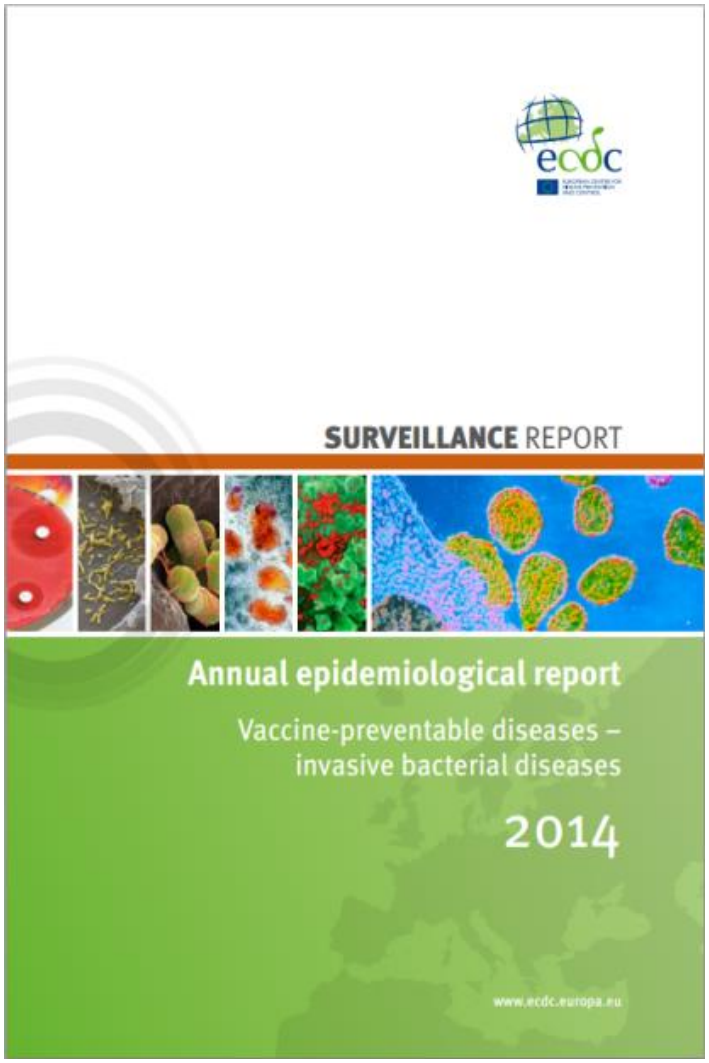
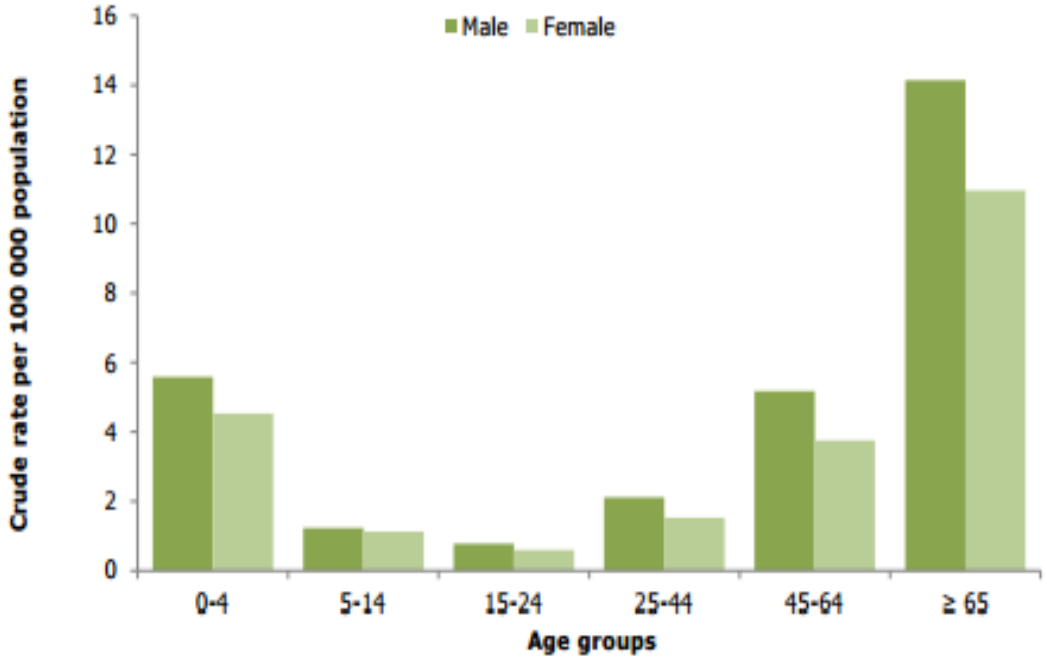


Figure 14. Rates of confirmed invasive pneumococcal disease reported cases by age and gender, EU/EEA, 2012



http://www.ecdc.europa.eu/en/publications/Publications/Annual-Epidemiological-Report-2012.pdf

IPH – En sık 15 Serotip

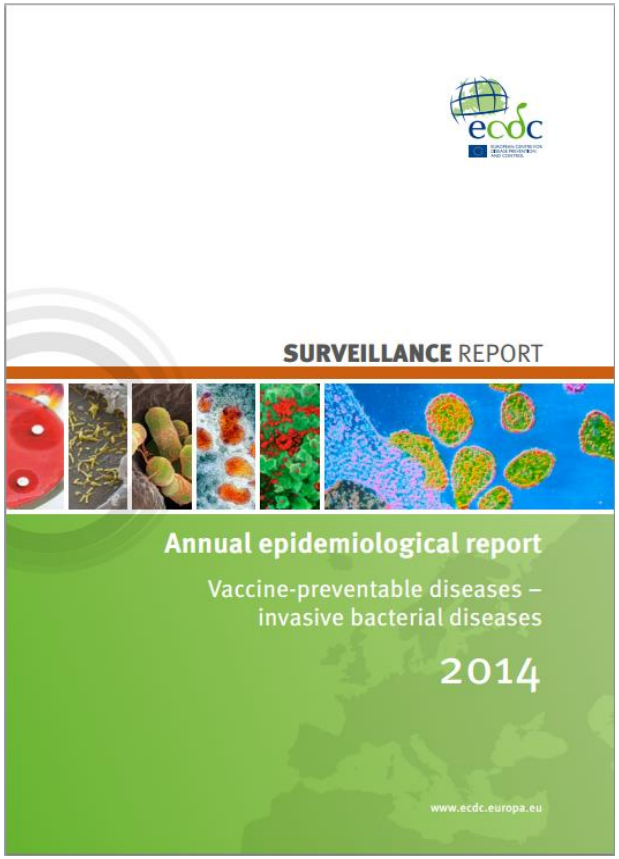
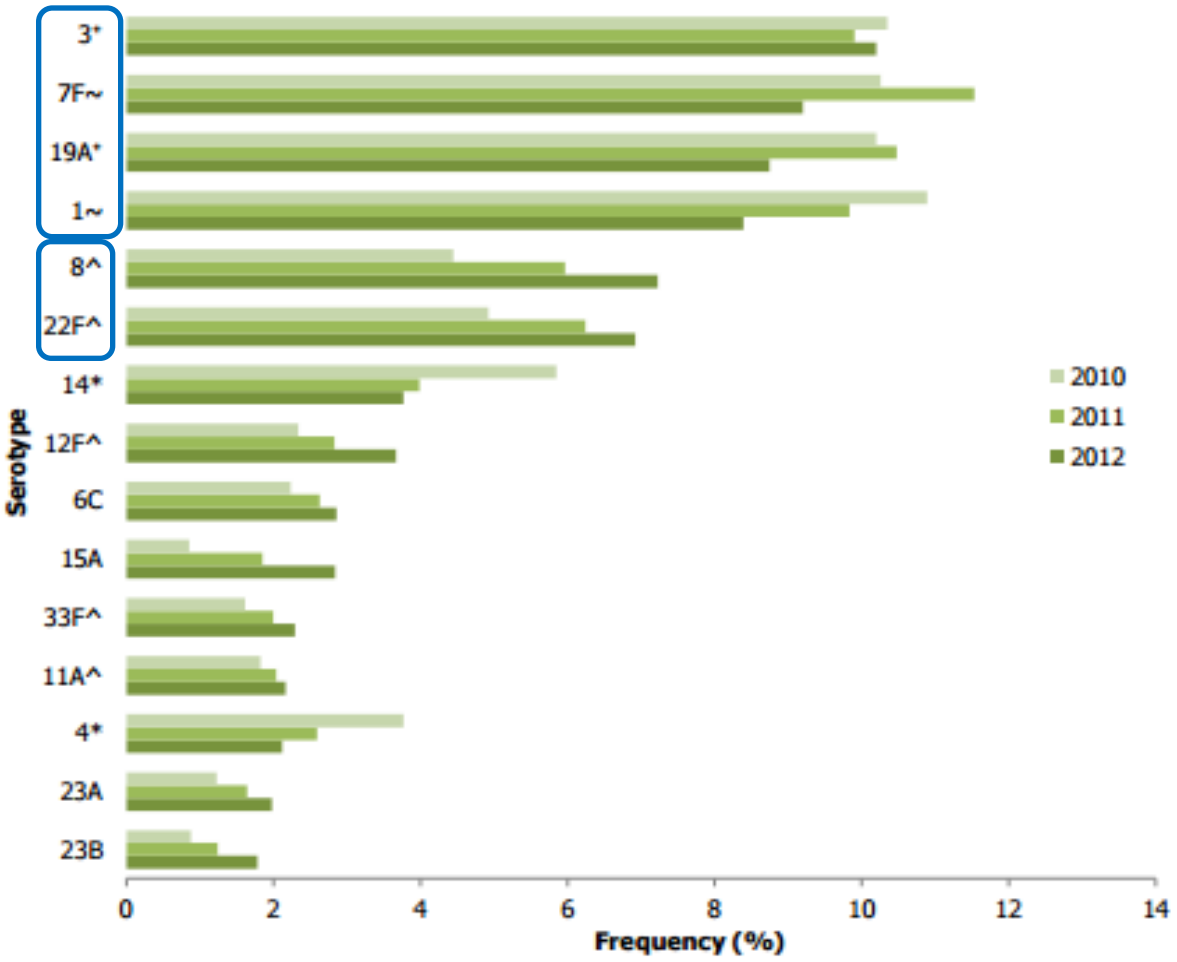


Figure 17. Distribution of confirmed invasive pneumococcal disease reported cases by 15 most common serotypes, EU/EEA, 2010–2012



Source: Country reports.

* Protected against by PCV7, PCV10, PCV13 and PPSV23

\+ Protected against by PCV13 and PPSV23

~ Protected against by PCV10, PCV13 and PPSV23

^ Protected against by PPSV23 only

http://ecdc.europa.eu/en/publications/Publications/AER-VPD-IBD-2014.pdf

IPH etkeni serotiplerin yaşa göre dağılımı

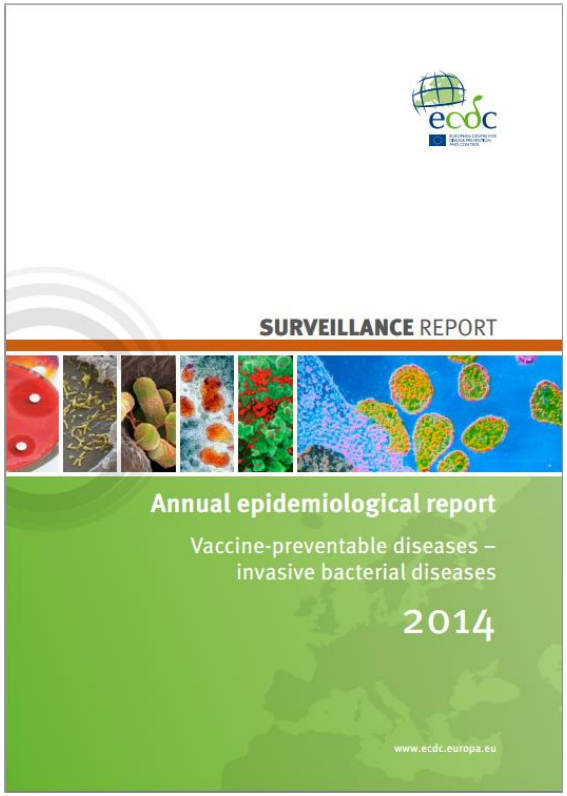
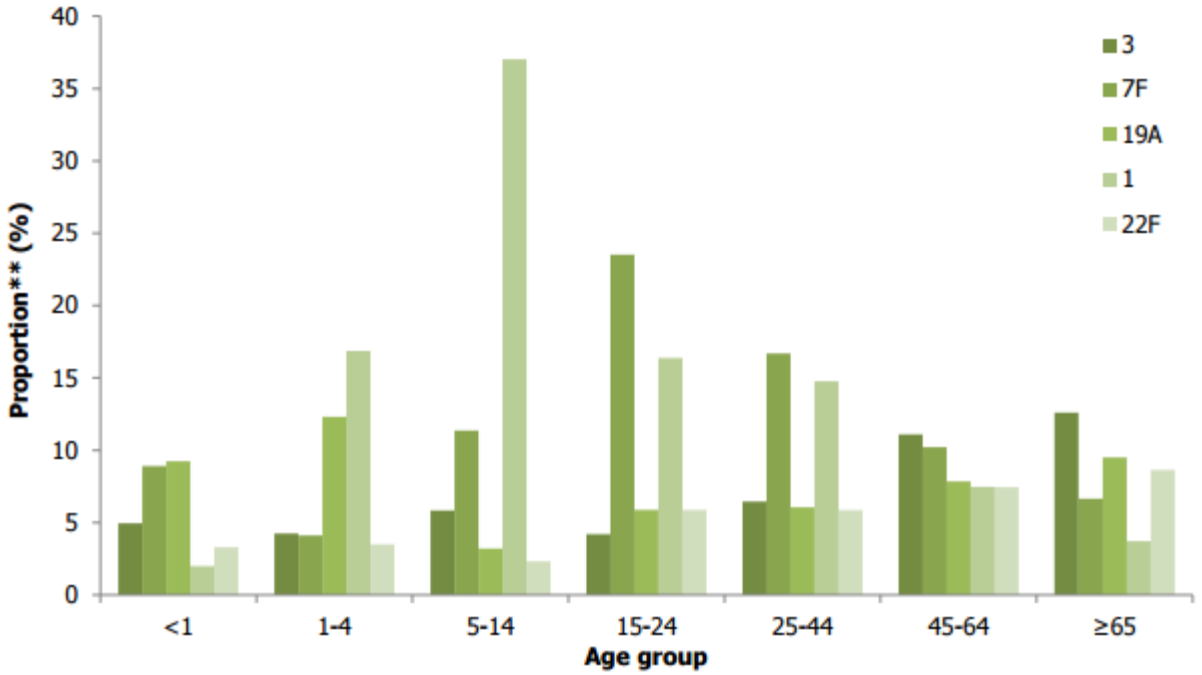


Figure 18. Proportion of confirmed invasive pneumococcal disease reported cases, by age and seven most frequent serotypes, EU/EEA, 2012 (n=12 992*)



http://www.ecdc.europa.eu/en/publications/Publications/Annual-Epidemiological-Report-2012.pdf

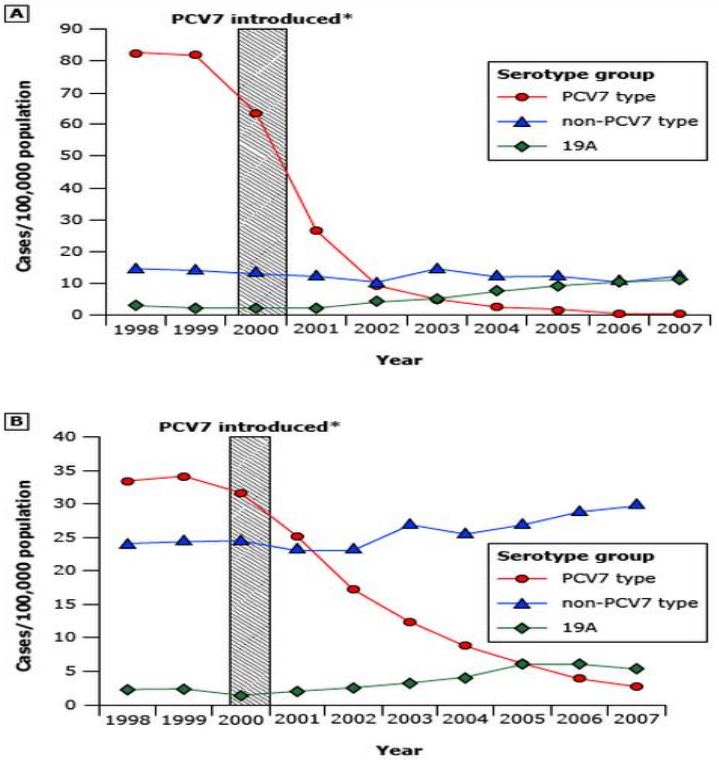
Pnömokok Aşısı - İPH

- *S. pneumoniae:*
  - >90 Pnömokok kapsüler serotipi
- **İnvazif pnömokokal hastalık (IPH):**

  ✓**Bakteremi ± Pnömoni**
  ✓**Menenjit**

- **Aşı endikasyonları:**
  - Tüm çocuklar
  - İPH / pnömoni riski olan erişkinler
  - ≥65 yaş tüm erişkinler

Changes in invasive pneumococcal disease incidence in the era of the conjugate vaccine

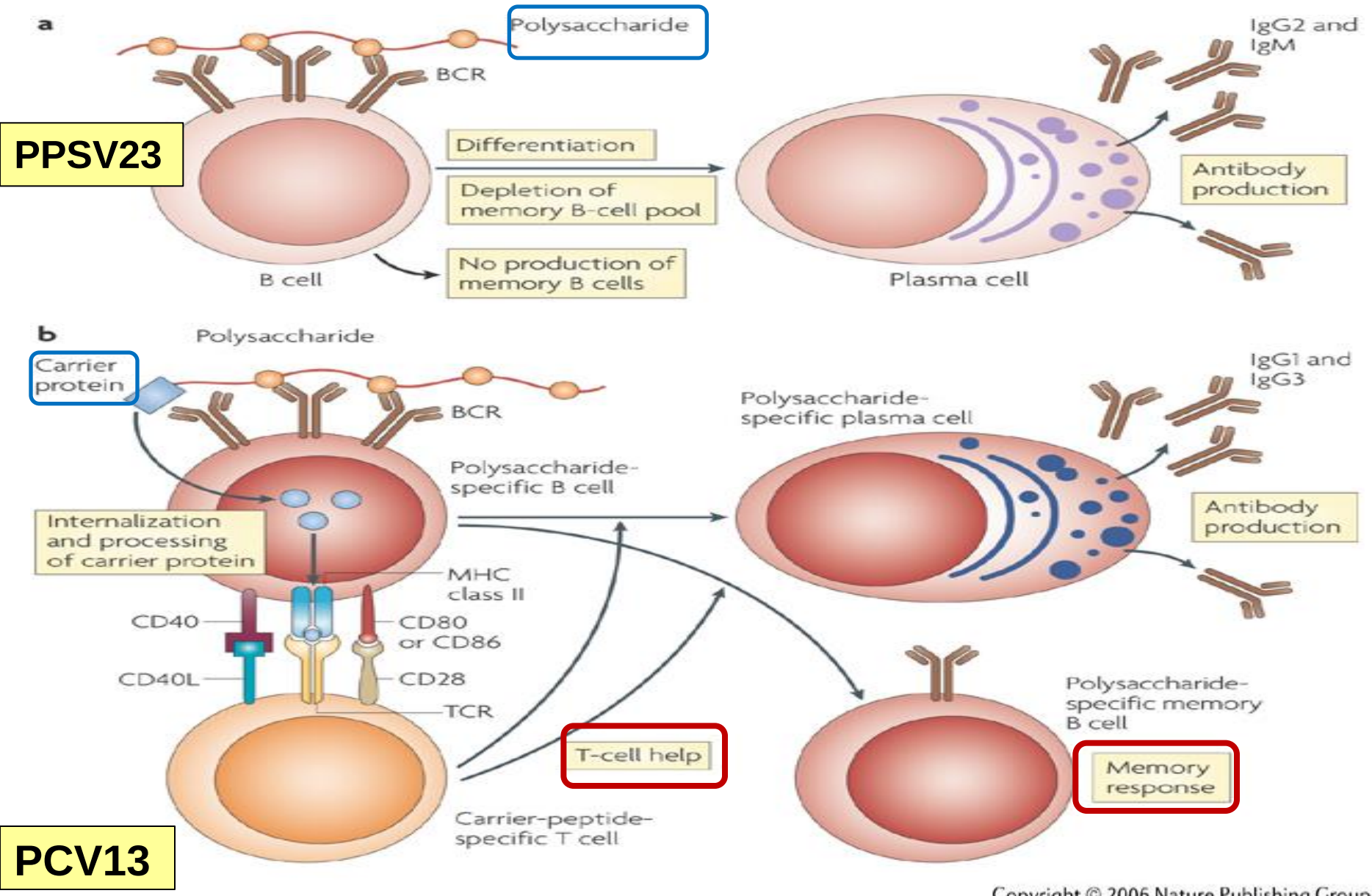


Changes in invasive pneumococcal disease (IPD) incidence by serotype group among children aged <5 years (A) and adults aged ≥65 years (B), 1998 to 2007.

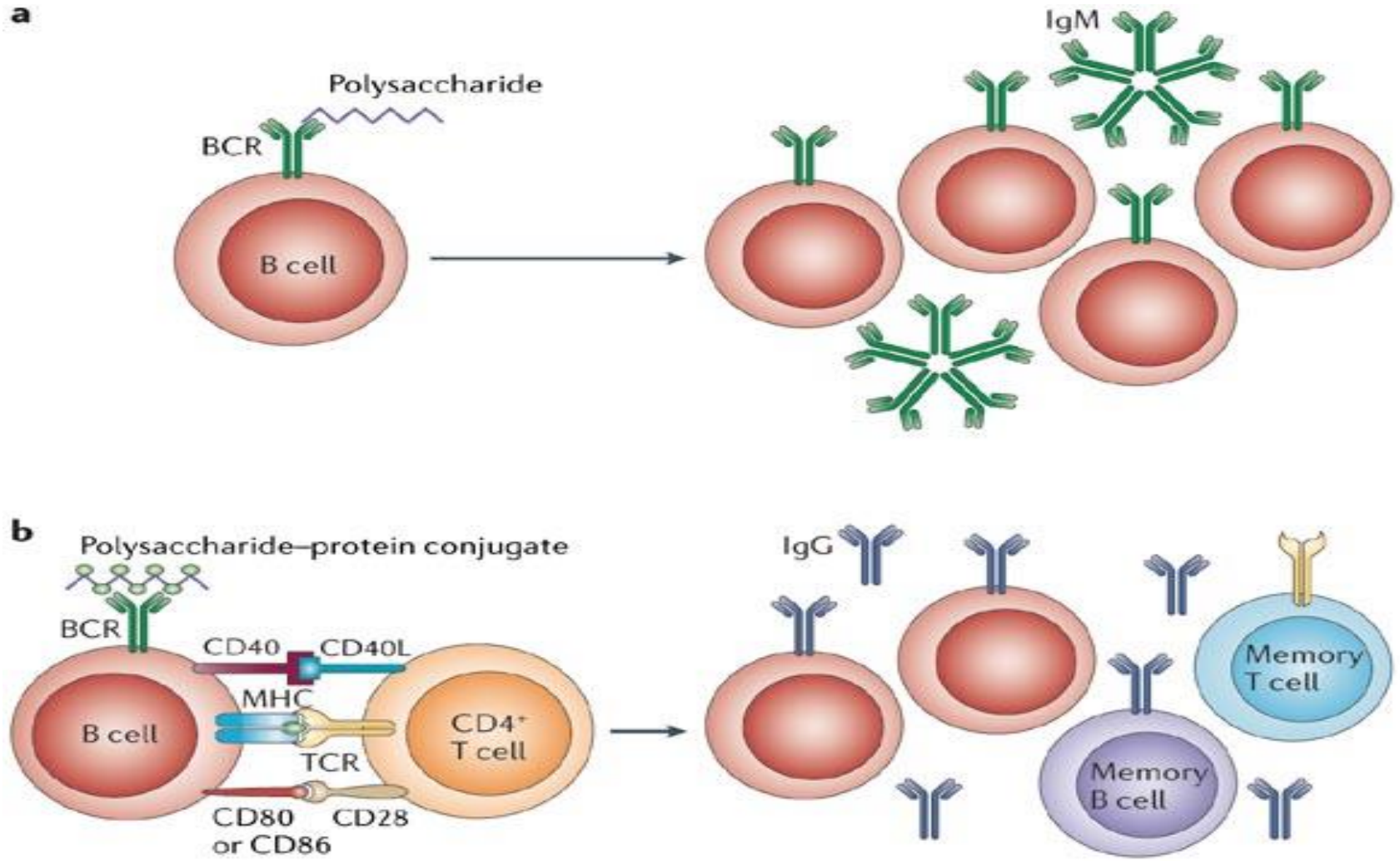
* Seven-valent pneumococcal conjugate vaccine (PCV7) was introduced in the United States for routine use among young children and infants in the second half of 2000.

Polisakkarit vs Konjuge Aşı

‡

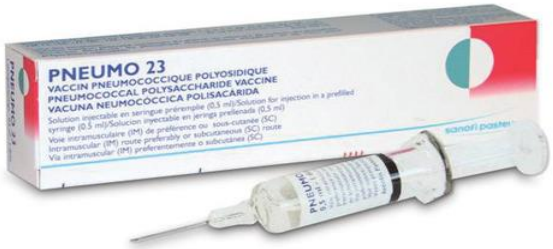


Polisakkarit vs Konjuge Antijen



PNÖMOKOK AŞILARI

- **Pnömokokal polisakkarit aşı (PPSV23)**
- **Pneumovax 23 veya Pneumo 23**
- Pnömokokal hastalık etkeni serotiplerin %**85-90**'ını kapsar
- <2 yaş: zayıf immunojenik
- 0.5 ml IM veya SC



- **Pnömokokal konjuge aşı (PCV7, PCV13)**
- **Prevenar 7 ve Prevenar 13**
- <2 yaş: çok iyi immünojenik
- 0.5 ml IM

Pnömokok aşıları - SEROTİPLER

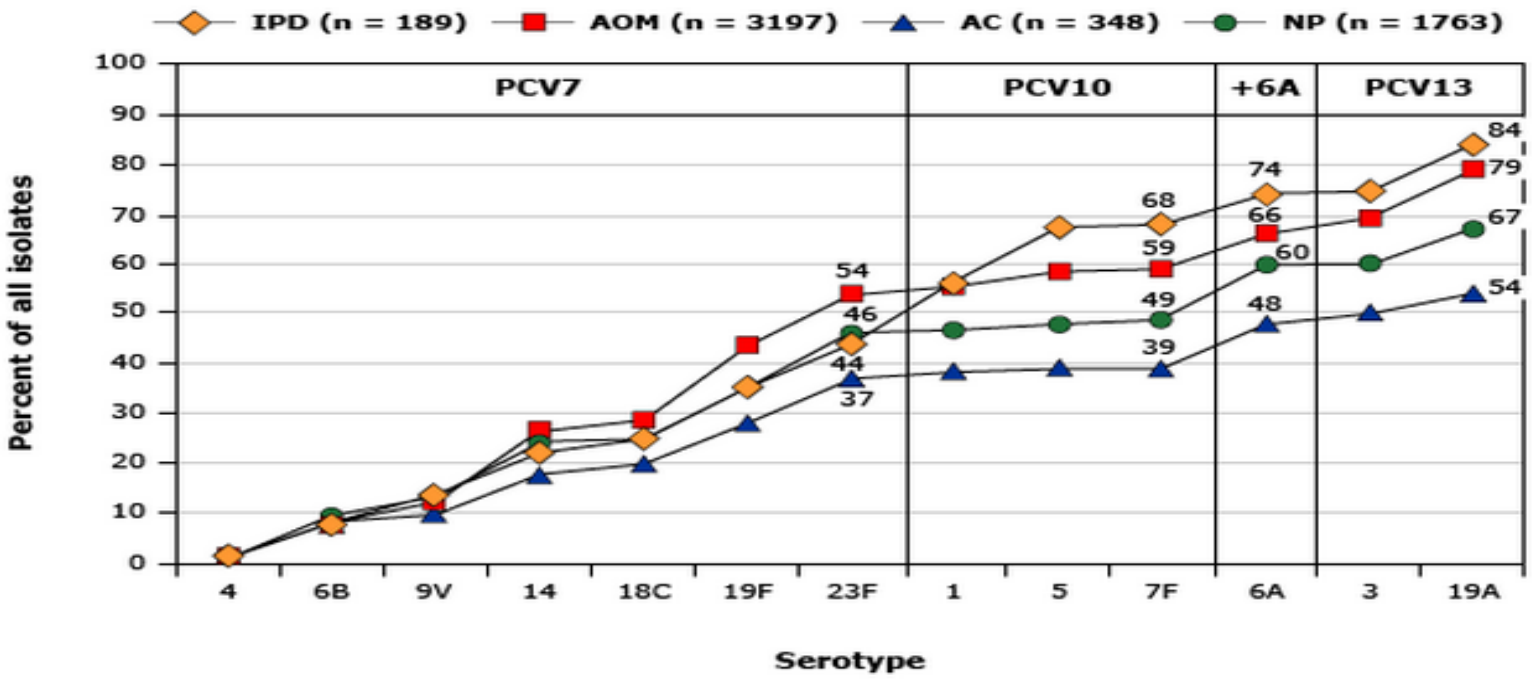
Comparison of serotypes in pneumococcal vaccines

Conjugate vaccines				Polysaccharide vaccine	
PCV7	PCV10*	PCV13	PCV15	PPSV23	
4	4	4	4	4	2
6B	6B	6B	6B	6B	8
9V	9V	9V	9V	9V	9N
14	14	14	14	14	10A
18C	18C	18C	18C	18C	11A
19F	19F	19F	19F	19F	12F
23F	23F	23F	23F	23F	15B
					17F
	1	1	1	1	20
	5	5	5	5	22F
		3	3	3	33F
	7F	7F	7F	7F	
		19A	19A	19A	
		6A	6A		
			22F		
			33F		

www.uptodate.com

Konjuge aşıların serotip kapsayıcılığı

Potential serotype coverage of PCV7, PCV10, and PCV13 of serotypes causing IPD, AOM, AC, and those carried by healthy Israeli children



AC: acute conjunctivitis; AOM: acute otitis media; IPD: invasive pneumococcal disease; NP: nasopharyngeal carriage.

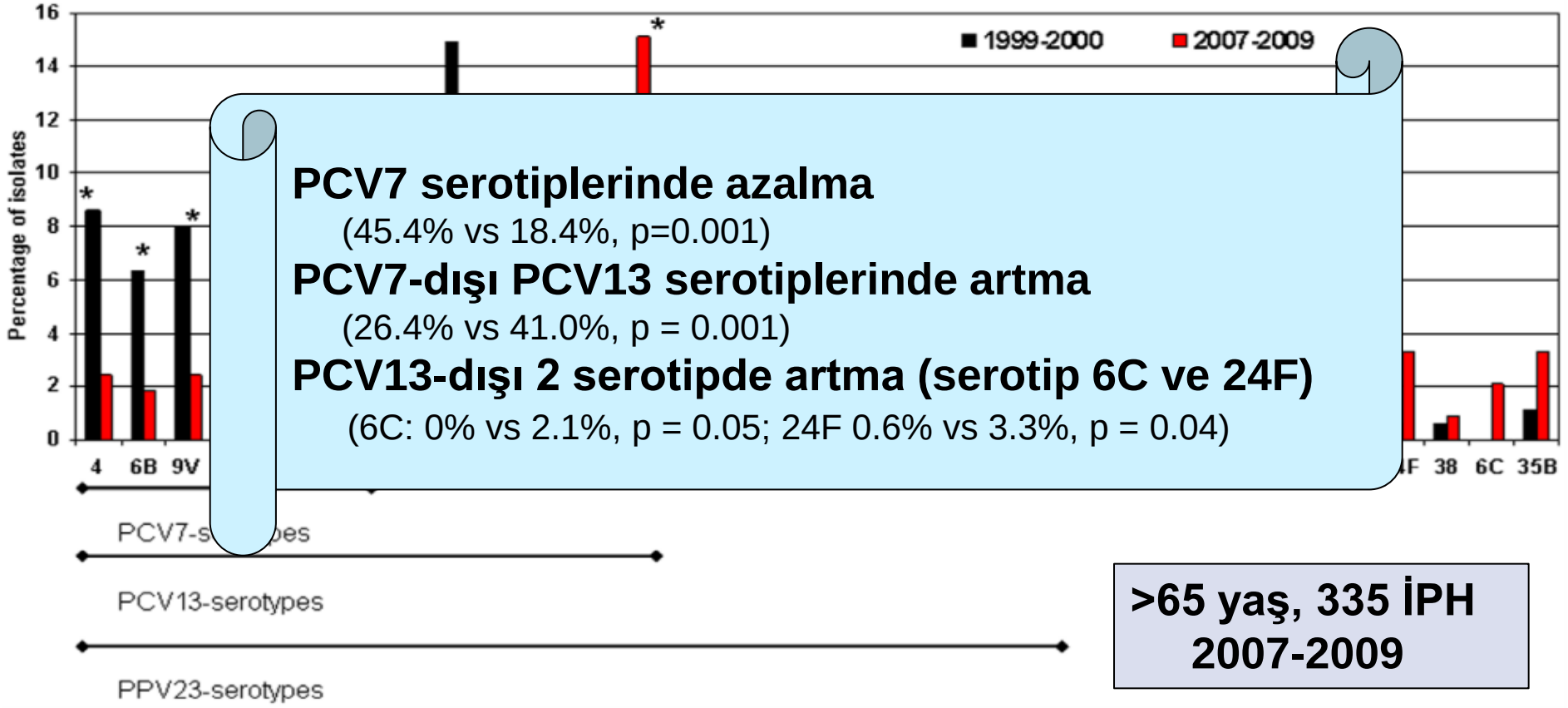
Shouval DS, et al. Pediatr Infect Dis J 2009; 28: 277
www.uptodate.com

OPEN ACCESS Freely available online August 2012, 7(8), e43619 PLOS ONE

‡

Epidemiology of Invasive Pneumococcal Disease in Older People in Spain (2007–2009): Implications for Future Vaccination Strategies

Carmen Ardanuy[1,2]*, José María Marimón[2,3], Laura Calatayud[1,2], Montserrat Giménez[2,4], Marta Alonso[2,3], Immaculada Grau[2,5], Román Pallarés[2,5], Emilio Pérez-Trallero[2,3], Josefina Liñares[1,2]



PCV7 serotiplerinde azalma
(45.4% vs 18.4%, p=0.001)
PCV7-dışı PCV13 serotiplerinde artma
(26.4% vs 41.0%, p = 0.001)
PCV13-dışı 2 serotipde artma (serotip 6C ve 24F)
(6C: 0% vs 2.1%, p = 0.05; 24F 0.6% vs 3.3%, p = 0.04)

>65 yaş, 335 İPH 2007-2009

Figure 1. Serotype distribution of invasive pneumococci collected from adults over 65 by period. The serotype distribution in the two

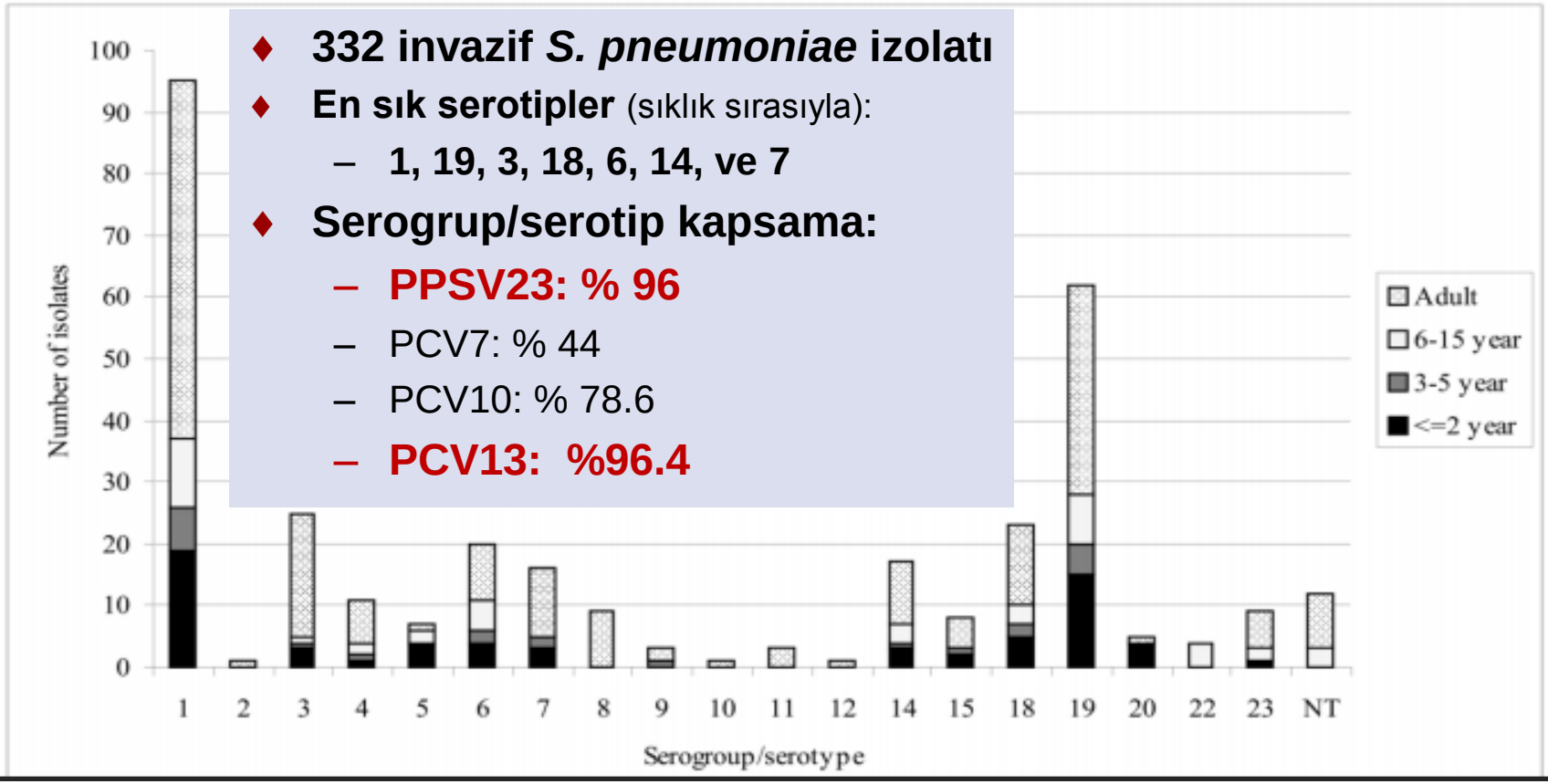
Original Article

Ten-year surveillance of invasive *Streptococcus pneumoniae* isolates in central Turkey prior to the introduction of a conjugate vaccine

Duygu Percin[1], Yasemin Ay Altintop[1], Bulent Sumerkan[1]

[1]*Department of Microbiology and Clinical Microbiology, Faculty of Medicine, Erciyes University, 38039-Kayseri/Turkey*

Figure 1. Age distrubution of serogroups/serotypes (NT: Non-typable)



- **332 invazif *S. pneumoniae* izolatı**
- **En sık serotipler** (sıklık sırasıyla):
  - **1, 19, 3, 18, 6, 14, ve 7**
- **Serogrup/serotip kapsama:**
  - **PPSV23: % 96**
  - PCV7: % 44
  - PCV10: % 78.6
  - **PCV13: %96.4**

J Infect Dev Ctries 2010; 4(9):560-565

‡

PCV7 → PCV13

- **Pnömokokal konjuge aşı** (**PCV7**, **PCV13**)
- **Konjugasyon proteinleri:**
  - **CRM197** (nontoxic mutant of diphtheria toxin)
  - **OMP** (*Neisseria meningitidis*'in OMP)
- **<2 yaş: çok iyi immünojenik**
- **Mukozal immunite, NF kolonizasyon ↓**

- **2000: PCV7 FDA onayı**
- **2010: PCV13 FDA onayı**
- ACIP: 6 hafta - 71 ay tüm çocuklar
- **30 Aralık 2011: PCV13 → ≥ 50 yaş erişkin aşılaması için FDA onayı**
  - 2012 ACIP: yüksek riskli erişkinler
  - **2014 ACIP: ≥ 65 yaş tüm erişkinler**
- 2018: ACIP Tekrar değerlendirme

ACIP: Advisory Committee on Immunization Practices

‡

Centers for Disease Control and Prevention

MMWR

Morbidity and Mortality Weekly Report

Weekly / Vol. 63 / No. 37

September 19, 2014

Use of 13-Valent Pneumococcal Conjugate Vaccine and 23-Valent Pneumococcal Polysaccharide Vaccine Among Adults Aged ≥65 Years: Recommendations of the Advisory Committee on Immunization Practices (ACIP)

Sara Tomczyk, MSc[1,2], Nancy M. Bennett, MD[3,4], Charles Stoecker, PhD[5], Ryan Gierke, MPH[2], Matthew R. Moore, MD[2], Cynthia G. Whitney, MD[2], Stephen Hadler, MD[2], Tamara Pilishvili, MPH[2] (Author affiliations at end of text)

PCV13 : ACIP Çocuk- Genç aşılama

- **Universal aşılama: < 60 ay tüm çocuklar** (Grade 1A)
  - **2 - 23 ay tüm çocuklar**
  - **24 - 59 ay: eksik aşılanmış çocuklar** (Grade 1A)
  - **14 - 59 ay: PCV7 ile aşılaması tamamlanmış sağlıklı çocuklar**

- **İPH riski olan < 72 ay çocuklar** (PPSV23 aşılanmışlar dahil)
- **6 - 18 yaş:** (Grade 1A)
  - Anatomik veya fonksiyonel aspleni (Orak hücreli anemi)
  - HIV veya diğer immunosupresyon nedenleri
  - Kronik renal yetmezlik
  - Nefrotik sendrom
  - Kohlear implant
  - Serebrospinal sıvı kaçağı

PNÖMOKOK AŞISI – RİSK GRUBU

Indications for the administration of the 13-valent pneumococcal conjugate vaccine (PCV13) and the 23-valent pneumococcal polysaccharide vaccine (PPSV23) for adults in the United States

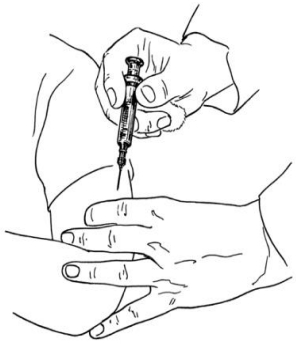
Risk group	Underlying condition	PCV13	PPSV23	
		Recommended	Recommended	Revaccination
Immunocompetent persons	Chronic heart disease*		X	
	Chronic lung disease•		X	
	Diabetes mellitus		X	
	Cerebrospinal fluid leak	X	X	
	Cochlear implant	X	X	
	Alcoholism		X	
	Chronic liver disease, cirrhosis		X	
	Cigarette smoking		X	
	Age ≥65	X	X	Δ
Persons with functional or anatomic asplenia	Sickle cell disease/other hemaglobinopathy	X	X	X◇
	Congenital or acquired asplenia	X	X	X◇
Immunocompromised persons	Congenital or acquired immunodeficiency§	X	X	X◇
	Human immunodeficiency virus infection	X	X	X◇
	Chronic renal failure	X	X	X◇
	Nephrotic syndrome	X	X	X◇
	Leukemia	X	X	X◇
	Lymphoma	X	X	X◇
	Hodgkin disease	X	X	X◇
	Generalized malignancy	X	X	X◇
	Iatrogenic immunosuppression¥	X	X	X◇
	Solid organ transplant	X	X	X◇
	Multiple myeloma	X	X	X◇

ACIP 2015 - Pnömokok Aşısı Önerileri

‡

Risk Grubu	Altta yatan hastalık	KPV13	PPV 23	
		Önerilir	Önerilir	İlk dozdan 5 yıl sonra yeniden aşılama
Bağışıklığı yeterli bireyler	Kronik kalp hastalığı†		✓	
	Kronik akciğer hastalığı§		✓	
	Diyabet		✓	
	BOS sızıntısı	✓	✓	
	Koklear implant	✓	✓	
	Alkolizm		✓	
	Kronik karaciğer hastalığı		✓	
	Sigara kullanımı		✓	
Fonksiyonel veya anatomik aspleni bulunan bireyler	Orak hücre hastalığı/diğer hemoglobinopatiler	✓	✓	✓
	Konjenital veya edinilmiş aspleni	✓	✓	✓
Bağışıklık yetmezliği olan bireyler	Konjenital veya edinilmiş bağışıklık yetmezliği¶	✓	✓	✓
	HIV enfeksiyonu	✓	✓	✓
	Kronik böbrek yetmezliği	✓	✓	✓
	Nefrotik sendrom	✓	✓	✓
	Lösemi	✓	✓	✓
	Lenfoma	✓	✓	✓
	Hodgkin hastalığı	✓	✓	✓
	Jeneralize malignite	✓	✓	✓
	İatrojenik immünosüpresyon‡	✓	✓	✓
	Solid organ nakli	✓	✓	✓
	Multipl miyelom	✓	✓	✓

http://www.cdc.gov/vaccines/schedules/



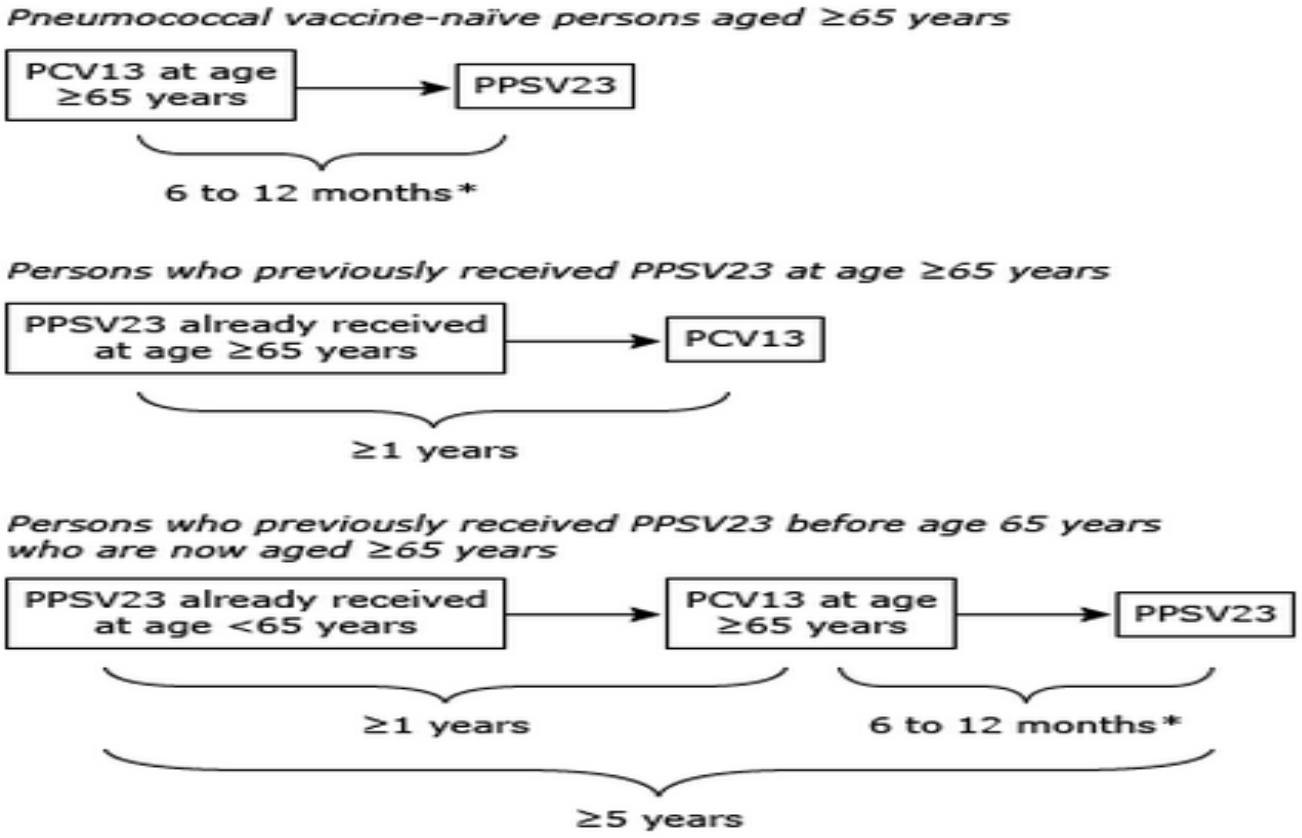
PPSV23 – ACIP Önerileri

- **19 - 64 yaş risk grubu**

- **<u>Sadece PPSV23</u> endikasyonları olanlar:**
  - **Kronik kalp hastalığı (KKY, KMP)**
  - **Kronik akciğer hastalığı (Astım, KOAH)**
  - **Kronik karaciğer hastalığı**
  - **Diabetes mellitus**
  - **Alkolizm**
  - **Sigara içenler**

ACIP 2014

Sequential administration and recommended intervals for PCV13 and PPSV23 for adults aged ≥65 years — Advisory Committee on Immunization Practices, United States



Tomczy S, et al. MMWR Morb Mortal Wkly Rep 2014; 63: 822

PCV13 ve PPSV23 ardışık aşılama

- **Tercihen önce PCV13, en az 8 hafta sonra PPSV23**
- **19-64 yaş ve ≥65 yaş**
- **BOS kaçakları**
- **Kohlear implant**
- **Fonksiyonel veya anatomik aspleni**
- **Immunokompromize durumlar**:
  - •Congenital or acquired immunodeficiency
  - •HIV infection
  - •Chronic renal failure
  - •Nephrotic syndrome
  - •Leukemia
  - •Lymphoma
  - •Hodgkin disease
  - •Multiple myeloma
  - •Generalized malignancy
  - •Iatrogenic immunosuppression (glucocorticoids or radiation)
  - •Solid organ transplant

PPSV23 – Sistematik Derleme ve Meta-analiz, 2013 ‡

- **Erişkinde PPSV23 etkinliği**
- 18 RKÇ, 64.852 katılımcı, 7 randomize olmayan KÇ, 62.294 katılımcı

- **İPH riskini anlamlı düzeyde azaltmıştır**
  (OR 0.26, 95% CI 0.14-0.45)

- Aşı serotipleriyle oluşan hastalık insidansında bu etki daha belirgin (OR 0.18, 95% CI 0.10-0.31)

- **İnvazif pnömokokal pnömoni**
  (OR 0.26, 95% CI 0.15-0.46)
- **Non-invazif pnömokokal pnömoni**
  (OR 0.46, 95% CI 0.25-0.84)

} **insidansda azalma**

Moberley S, et al. Cochrane Database Syst Rev 2013; 1:CD000422.

ETKİNLİK

‡

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Effects of Vaccination on Invasive Pneumococcal Disease in South Africa

Anne von Gottberg, M.B., B.Ch., Ph.D., Linda de Gouveia, N.D., M.T., Stefano Tempia, D.V.M., Ph.D., Vanessa Quan, M.B., B.Ch., M.P.H., Susan Meiring, M.B., Ch.B., Claire von Mollendorf, M.B., B.Ch., Shabir A. Madhi, M.B., B.Ch., Ph.D., Elizabeth R. Zell, M.Stat., Jennifer R. Verani, M.D., M.P.H., Katherine L. O'Brien, M.D., M.P.H., Cynthia G. Whitney, M.D., M.P.H., Keith P. Klugman, M.B., B.Ch., Ph.D., and Cheryl Cohen, M.B., B.Ch., for the GERMS-SA Investigators*

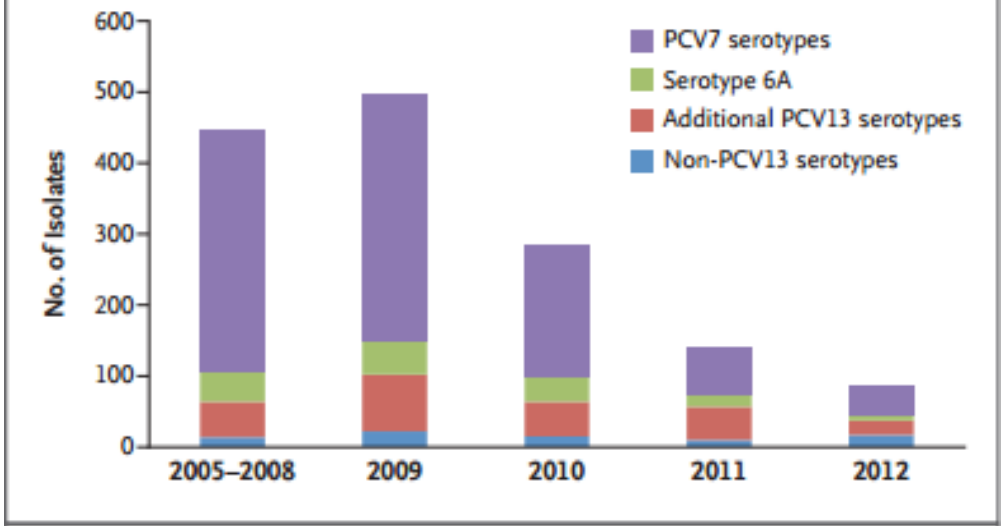
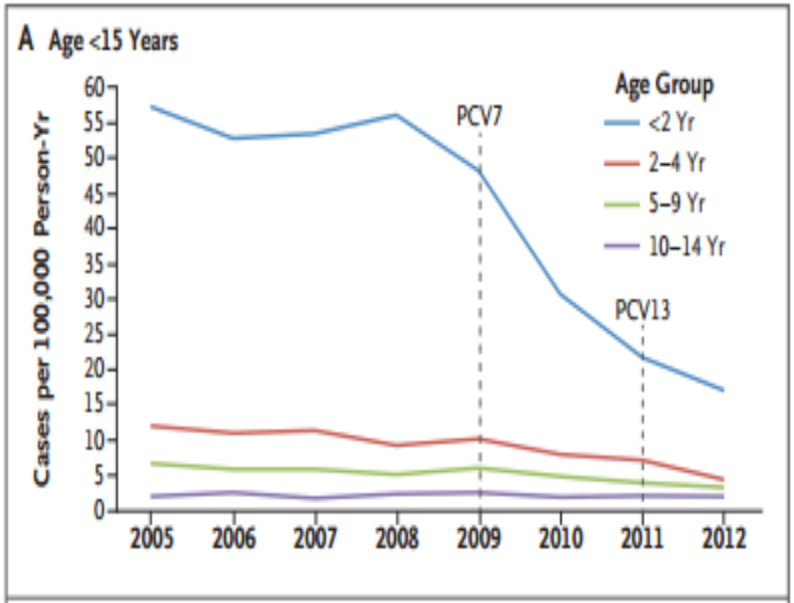
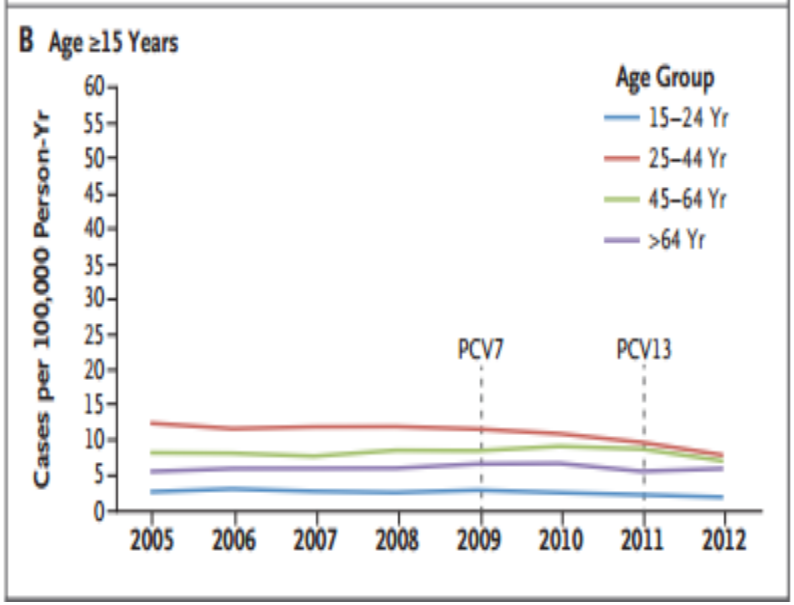


Figure 4. Number of Penicillin-Nonsusceptible Isolates Causing Invasive Pneumococcal Disease among Children Younger than 2 Years of Age, According to Serotype.





NEJM 371;20, November 13, 2014, 1889,1899

ETKİNLİK

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Effect of Pneumococcal Conjugate Vaccine on Pneumococcal Meningitis

Heather E. Hsu, M.P.H., Kathleen A. Shutt, M.S., Matthew R. Moore, M.D., M.P.H., Bernard W. Beall, Ph.D., Nancy M. Bennett, M.D., Allen S. Craig, M.D., Monica M. Farley, M.D., James H. Jorgensen, Ph.D., Catherine A. Lexau, Ph.D., M.P.H., Susan Petit, M.P.H., Arthur Reingold, M.D., William Schaffner, M.D., Ann Thomas, M.D., Cynthia G. Whitney, M.D., M.P.H., and Lee H. Harrison, M.D.

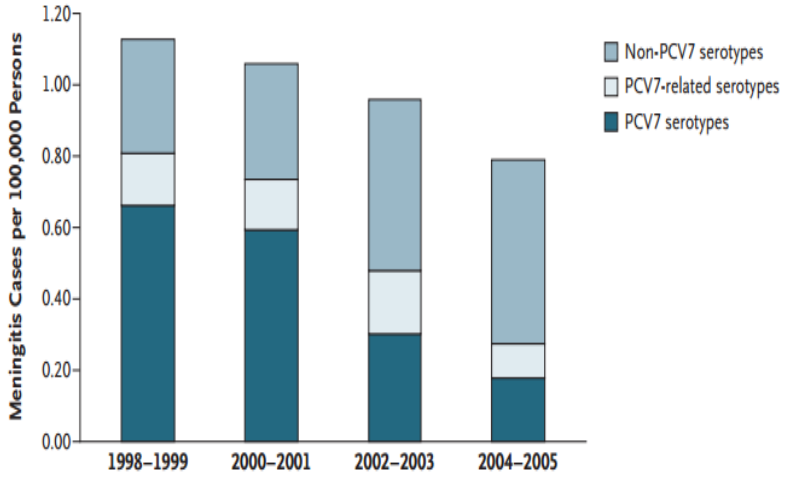


Figure 1. Mean Annual Incidence of Pneumococcal Meningitis, According to Serotype Group and Time Period.

Serotypes of the heptavalent pneumococcal conjugate vaccine (PCV7) were 4, 6B, 9V, 14, 18C, 19F, and 23F. PCV7-related serotypes were 6A, 9A, 9L, 9N, 18A, 18B, 18F, 19B, 19C, 23A, and 23B. Non-PCV7 serotypes were 3, 7F, 10A, 11A, 12F, 15A, 15B/C, 16F, 19A, 22F, 33F, 35B, 35F, and 38.

- 1998 – 2005, 1379 OLGU, ABD
- **İnsidans: %30 azalma,**
- **<2 yaş: %64 azalma, >65 yaş: %54 azalma** (P<0.001)
- 1.13 cases/100.000 (1998–1999) → 0.79 cases/100,000 (2004–2005)
- **Tüm yaş grubunda PCV7-serotipi menenjit hızı: % 73 azaldı** (P<0.001)
- **PCV7- aşı serotipi hastalık %32 azaldı** (P = 0.08)
- **Aşı-dışı serotiplerle hastalık % 60.5 arttı** (P<0.001) (19A, 22F, 35B)

NEJM 360;3 January 15, 2009, 244, 256

ETKİNLİK

Davis *et al. BMC Public Health* 2013, **13**(Suppl 3):S21
http://www.biomedcentral.com/1471-2458/13/S3/S21

BMC Public Health

REVIEW Open Access

The effect of *Haemophilus influenzae* type B and pneumococcal conjugate vaccines on childhood meningitis mortality: a systematic review

Stephanie Davis, Daniel Feikin, Hope L Johnson*

- Düşük-orta gelirli ülkelerde < 5 yaş çocuklarda menenjit insidansı ve mortalitesi üzerine doza-özgül etkisi

- Çocuklarda menenjite bağlı ölümlerin önlenebilir oranı ?
- Hib konjuge aşısı: 18 çalışma (2 RKÇ, 16 gözlemsel çalışma)
- PCV Konjuge pnömokok aşısı : 2 RKÇ

- **Menenjite bağlı ölümlerin ¾'ü aşılarla önlenebilir**!

İmmunojenite: PCV13 vs PPSV23

The Potential Role for Protein-Conjugate Pneumococcal Vaccine in Adults: What Is the Supporting Evidence?

Daniel M. Musher, Rahul Sampath, and Maria C. Rodriguez-Barradas

The Medical Care Line (Infectious Disease Section), Michael E. DeBakey Veterans Affairs Medical Center and the Departments of Medicine and Molecular Virology and Microbiology, Baylor College of Medicine, Houston, Texas

Vaccination with protein-conjugate pneumococcal vaccine (PCV) provides children with extraordinary protection against pneumococcal disease, although the protective effect may be blunted by the emergence of replacement strains. Studies in adults have compared PCV with pneumococcal polysaccharide vaccine (PPV) using surrogate markers of protection, namely, serum anticapsular IgG antibody and opsonic activity. Results suggest that PCV is at least as effective as PPV for the strains covered, but a definitive and consistent advantage has not been demonstrated. Unfortunately, persons who are most in need of vaccine do not respond as well as otherwise healthy adults to either vaccine. Newer formulations of PCV will protect against the most prevalent of the current replacement strains, but replacement strains will create a moving target for PCVs. Unless an ongoing trial comparing 13-valent PCV with placebo (not to PPV) demonstrates a clearly better effect than that seen in the past with PPV, cost-effectiveness considerations are likely to prevent widespread use of PCV in adults.

Musher DM, CID 2011:52 (1 March); 633-640

October 8-12 • Philadelphia, PA • www.idweek.org

IDWeek 2014™

Advancing Science, Improving Care

CAPITA TRIAL

PROGRAM SCHEDULE

Navigation

Search

Print Page

Interactive Planning Tool (create your schedule here)

Abstracts in PDF

At-A-Glance

Browse by Day:

Tuesday, October 7th

Wednesday, October 8th

Thursday, October 9th

Friday, October 10th

Saturday, October 11th

Sunday, October 12th

Browse by Track:

- Adult ID
- Global ID
- HIV-STD-TB
- Investigative ID

595

COMMUNITY ACQUIRED PNEUMONIA IMMUNIZATION TRIAL IN ADULTS (CAPITA)

• **Session:** Oral Abstract Session: Adult Vaccines

Friday, October 10, 2014: 8:30 AM

Room: The Pennsylvania Convention Center: 111-AB

Background: Conjugate vaccines have shown efficacy against invasive pneumococcal disease (IPD) and otitis media in children, but have not been evaluated in the healthy elderly.

Methods: This was a randomized, double-blind clinical trial in 84,496 participants 65 years of age and older in the Netherlands The CAPiTA study was designed to demonstrate the efficacy of 13-valent pneumococcal conjugate vaccine (13vPnC) in the prevention of a first episode of vaccine-type (VT) pneumococcal community-acquired pneumonia (CAP) (primary objective). The secondary objectives were to demonstrate efficacy in prevention of a first episode of nonbacteremic/noninvasive (NB/NI) VT pneumococcal CAP and a first episode of VT-IPD. Key eligibility criteria were no previous pneumococcal vaccination and immune competence. Participants were randomized 1:1 to receive either 13vPnC or placebo. They were enrolled at community-based sites and home visits, and surveillance for CAP and IPD was conducted at hospitals in the areas of enrollment. Isolation of pneumococcus from blood or other normally sterile site and/or a serotype-specific urinary antigen detection assay were used to identify episodes of vaccine-type CAP. Safety was also evaluated.

Results: In the per protocol analysis vaccine efficacy of 45.56% (95.2% 21.82%-62.49%, p=0.0006) was demonstrated for the first episode VT-CAP; 45.00% (95.2% 14.21%-65.31%, p=0.0067) for the first episode of NB/NI VT-CAP, and 75.00% (95.2% 41.43%-90.78%, p=0.0005) for the first episode of VT-IPD. Safety findings were consistent with prior adult experience.

Conclusion: 13vPnC was effective in preventing vaccine-type pneumococcal CAP and vaccine-type IPD in adults >65 years of age.

(Funded by Pfizer, Inc.; ClinicalTrials.govnumber NCT00744263.)

Marc Bonten, MD PhD[1,2], *Susanne M Huijts, MD*[2], *Marieke Bolkenbaas, MD*[2], *Chris Webber, MD, PhD*[3], *Samantha Gault, Msc*[3], *William Gruber, MD*[4], *Scott D. Patterson, PhD*[5], *Diederick E. Grobbee, MD, PhD*[2,6] *and CAPiTA study team, (1)Department of Medical Microbiology, University Medical Center Utrecht, Utrecht, Netherlands, (2)Julius Center for Health Sciences and Primary Care, University Medical Center Utrecht, Utrecht, Netherlands, (3)Pfizer Vaccine Clinical Research, Maidenhead, United Kingdom, (4)Pfizer Vaccine Clinical Research, Pearl River, NY, (5)Pfizer Vaccine Clinical Research, Collegeville, PA, (6)Julius Clinical, Zeist, Netherlands*

PCV13 – ETKİNLİK: CAPITA Çalışması

- RKÇ, Hollanda, **2008 – 2013**
- ≥65 yaş, daha önce PPSV23 ile aşılanmamış 85,000 kişi
- **Aşı-tipi pnömokokal pnömoniyi önleme: % 45 etkinlik**

  (95% CI: %22- 63)
- **Aşı-tipi non-bakteremik pnömokokal pnömoniyi önleme: % 45 etkinlik**

  (95% CI: %14-65)
- **Aşı-tipi invazif pnömokokal hastalıkları önleme: % 75 etkinlik** (95% CI: %41-91)

PCV7 – Nazofarengeal taşıyıcılık

‡

The Turkish Journal of Pediatrics 2013; 55: 575-583 *Original*

Risk factors for nasopharyngeal carriage of *Streptococcus pneumoniae* in healthy Turkish children after the addition of heptavalent pneumococcal conjugate vaccine (PCV7) to the national vaccine schedule

Halil Özdemir[1], Ergin Çiftçi[1], Rıza Durmaz[2], Haluk Güriz[3], Ahmet Derya Aysev[3], Adem Karbuz[1], Refik Gökdemir[3], Bülent Acar[2], Selin Nar-Ötgün[2], Mustafa Ertek[2], Serdal Kenan Köse[4], Erdal İnce[1]

- 1 ay-18 yaş, **1101 sağlıklı çocuk**
- ***S. pneumoniae***: in 241/1101 (**21.9%**)
- **Risk faktörleri:**
  - <5 yaş
  - Kreş/yuvaya giden çocuk varlığı
  - Son 1 ayda solunum yolu infeksiyonu geçirmiş olmak
  - Düşük sosyo-ekonomik düzey
  - Ailede fazla çocuk sayısı
- **PCV7 sağlıklı çocuklarda nazofarengeal pnömokok taşıyıcılığını etkilememiş**

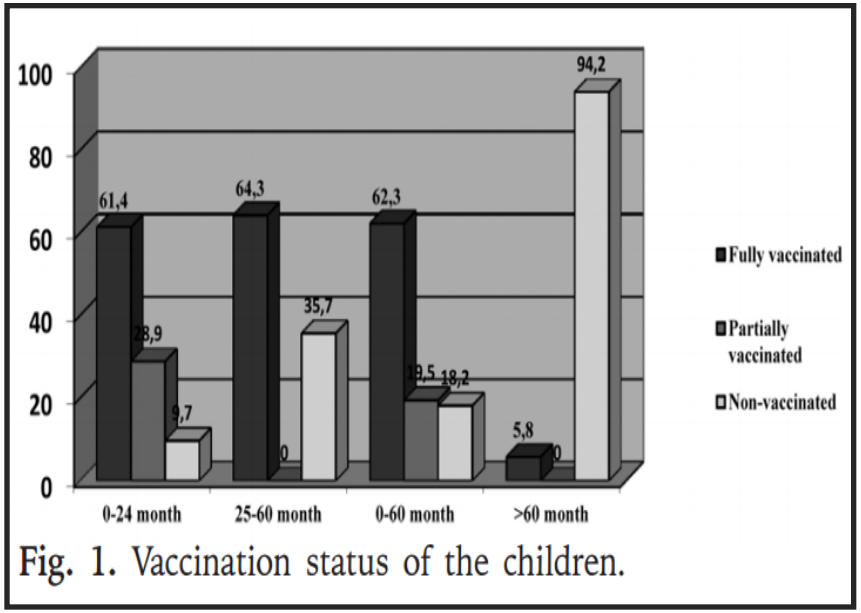


Fig. 1. Vaccination status of the children.

% 61.7: PCV7 aşılanmış

% 38.3: PCV7 aşılanmamış

PCV7 aşısı: Pnömokok taşıyıcılığına etkisi - Türkiye‡

- 138 PCV7 aşılanmış çocuk, 109 aşılanmamış toplam 247 çocuk
- Yaş grubu: 12-59 ay, Ekim 2007- Nisan 2008
- ***S. pneumoniae* izolasyonu: 32 (%12.9)**
- İki grup arasında anlamlı fark yok (10.1% vs 16.5%).
- **Aşı-tipi taşıyıcılık aşılanan grupta anlamlı daha düşük**
- Aşı-dışı serotip taşıyıcılığı benzer
- PRSP taşıyıcılığı: fark yok
- **"Türk çocuklarında 7 valanlı konjuge aşı, aşı-tipi *S. pneumoniae* taşıyıcılığına karşı koruma sağlar"**
- Uygunsuz antibiyotik kullanımı azaltılabilirse, konjuge aşı antibiyotik-dirençli *S. pneumoniae* bulaşını azaltabilir

Ercan TE, et al, Pediatr Int 2011 Apr;53(2):224-30

MALİYET- ETKİNLİK: Türkiye

‡

Bakır et al. BMC Health Services Research 2012, 12:386
http://www.biomedcentral.com/1472-6963/12/386

BMC Health Services Research

RESEARCH ARTICLE Open Access

Cost-effectiveness of new pneumococcal conjugate vaccines in Turkey: a decision analytical model

Mustafa Bakır[1*], Özden Türel[2] and Oleksandr Topachevskyi[3]

- **PCV-7**
- **PCV-13**
- **10-valanlı pnömokokal ve tiplendirilemeyen *Haemophilus influenzae* protein D konjuge aşısı (PHiD-CV)**

- **Türkiye'de çocuklarda pnömokokal hastalık insidansını azaltmada en maliyet etkin aşı: PHiD-CV**

MALİYET - ETKİNLİK: Türkiye

‡

RESEARCH PAPER

Human Vaccines 7:4, 441-450; April 2011; © 2011 Landes Bioscience

Cost of pneumococcal infections and cost-effectiveness analysis of pneumococcal vaccination in at risk adults and elderly in Turkey

Levent Akin,[1] Mehmet Kaya,[1] Serdar Altinel[2] and Laure Durand[3,*]

[1]Hacettepe University; Department of Public Health; Ankara, Turkey; [2]Sanofi Pasteur; Istanbul, Turkey; [3]Sanofi Pasteur; Lyon, France

- Yaşlılarda ve risk altındaki erişkinlerde pnömokok aşılaması sosyal güvenlik kurumları açısından pozitif geri-dönüş sağlar.
- Bu da, pnömokok aşılama önerilerinin devamını ve tamamıyla geri ödenmesini desteklemektedir.

Pnömokok Aşıları - YAN ETKİLER

PCV13:

- Lokal reaksiyonlar: ağrı, kızarıklık, şişlik; aşılanan kolda hareket kısıtlılığı
- Halsizlik, başağrısı, titreme, iştahsızlık, yaygın kas ağrısı, eklem ağrısı

PPSV23:

- Lokal reaksiyonlar: ağrı, kızarıklık, şişlik

KONTRAENDİKASYON:

- Ciddi allerjik reaksiyon (anaphylaxis)

Erişkinde Pnömokok Aşılaması

- Prospektif çalışma, **2383** kişiyle yüzyüze görüşme
- Akdeniz Üniversitesi, Tıp Fakültesi, Antalya

- Pnömokok aşısı farkındalığı: **%10.7**
- **Pnömokok aşısı yaptıranlar: % 0.9**

  - **Doktor önerisiyle aşılanan :% 68.2**
  - **Kendi isteği / çocuklarının önerisiyle aşılanan: % 31.8**
  - **Hastanede aşılanan: % 45.4**
  - **Aşıyı kendi cebinden karşılayan : % 45.4**

Turhan Ö, et al. Kuwait Medical Journal 2010, 42(2):135-138

Türkiye - Ege Bölgesi erişkin aşılanma durumu

TIHUD

Ege Bölgesi Çalışma Grubu

Türkiye'de Diyabetik Hastalardaki Aşılama Oranları

%0.1 pnömokok aşılama oranı

%9.1 influenza aşılama oranı

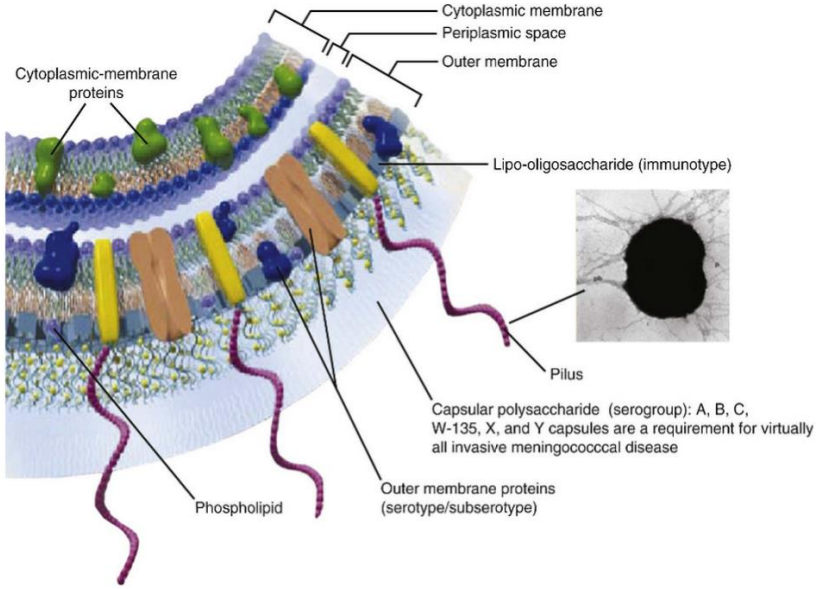
Pnömokok Aşıları - ÖZET

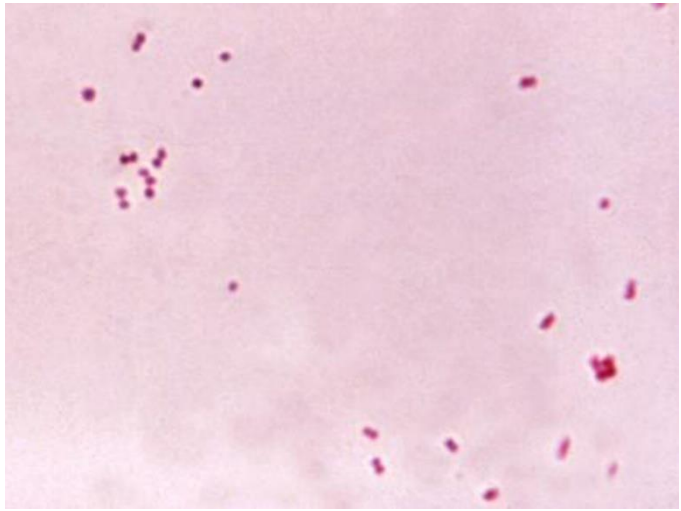
- **Yaşlı ve immunokompromize hastalarda immunojenite ve etkinlik daha düşük**
- **PPSV23: >50 yaş grubu aşılandığında antikorlar 1-2 yıl içinde hızla düşer, minimum 10 yıl boyunca düşük düzeyde kalır**
- **PCV7** : Erişkin ve çocuklarda aşı-serotipi İPH insidansında ve pnömoni nedeniyle hospitalizasyon sıklığında azalma
- **PCV13 : Öncül veriler yaygın kullanımla aşı-serotipi hastalıkta benzer azalmayı göstermekte**
- **<u>"Herd" Immunite</u>: Aşılanmamış çocuk ve erişkinlerde aşı serotipleriyle oluşan pnömokokal hastalıkda > %90 azalma**

WORLD MENINGITIS day

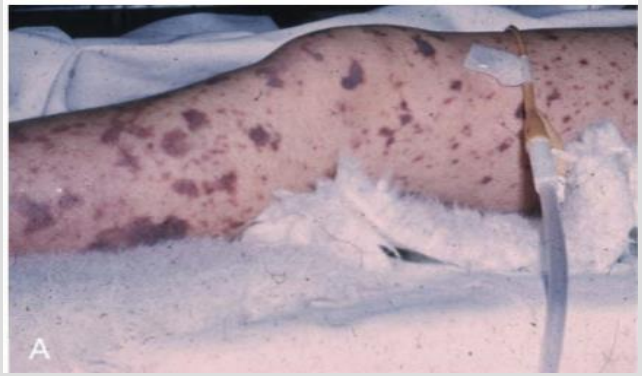
April 24

www.meningococcal-septicaemia.com





N. meningitidis AŞISI



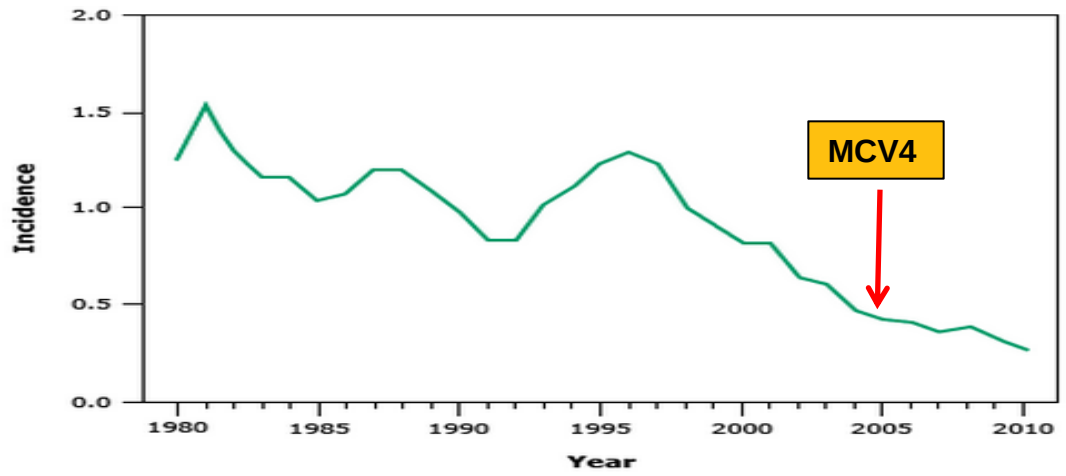
N. meningitidis

- **13 serogrup, 6 serogrup hastalık etkeni: A, B, C, W-135, X, Y**
- **İnsidans** (ABD) 2005-2011**: 0.3 /100,000**
- **1998 – 2007: İnsidans %64 ↓ (0.92 /100.000→ 0.33 /100.000)**
- **<2 yaş: hastalık 10 kat fazla, adölesanlarda 2. pik**
- Lise kampüslerinde salgın: 1.74/100.000
- Yatılı okul öğrencilerinde: 5.1/100,000 (3.6 kat fazla risk)
- Suudi Arabistan (Hac-Umre): salgın
- 2012 New York-Serogrup C İMH salgını (MSM),18-64 y: 12.6/100,000
- **İnvazif meningokokkal hastalık (İMH):**
  - Çoğunda etken **A,B,C,W-135, Y**
- **Aşının kapsadığı serogruplar: A,C,W-135, Y + B**

Cohn AC, et al. MMWR Recomm Rep 2013; 62:1
Harrison LH, et al. JAMA 1999; 281:1906

Meningokokal hastalık - EPİDEMİYOLOJİ

Meningococcal disease incidence*, by year – United States, 1980 to 2010



Meningococcal disease incidence remained low in 2010, but it continues to cause substantial morbidity and mortality in the United States. The highest incidence of meningococcal disease occurs among infants, with a second peak occurring in late adolescence. In 2005, a quadrivalent (A, C, Y, W-135) meningococcal conjugate vaccine was licensed and recommended for adolescents and others at increased risk for disease. In October 2010, a booster dose was added to recommendations for adolescents at age 16 years. In 2010, coverage with one dose of meningococcal conjugate vaccine was 62.7 percent among adolescents aged 13 to 17 years in the United States.

* Per 100,000 population.

Reproduced from: Centers for Disease Control and Prevention. Summary of notifiable diseases - United States, 2010. MMWR Morb Mortal Wkly Rep 2012; 59:1.

- İnsidans azalıyor
- Morbidite yüksek
- Mortalite yüksek

Cohn AC, et al. Clin Infect Dis 2010; 50:184.

EPİDEMİ - “Menenjit kuşağı”

Areas of Africa with frequent epidemics of meningococcal meningitis

Reproduced from: Cohn A, MacNeil JR. Meningococcal Disease. In: The Yellow Book, CDC Health Information for International Travel, 2014. Available at: http://wwwnc.cdc.gov/travel/yellowbook/2014/chapter-3-infectious-diseases-related-to-travel/meningococcal-disease#3972 (Accessed on December 18, 2013).

İnsidans:

Toplam popülasyon: 1/1000

< 2 yaş: 1/100

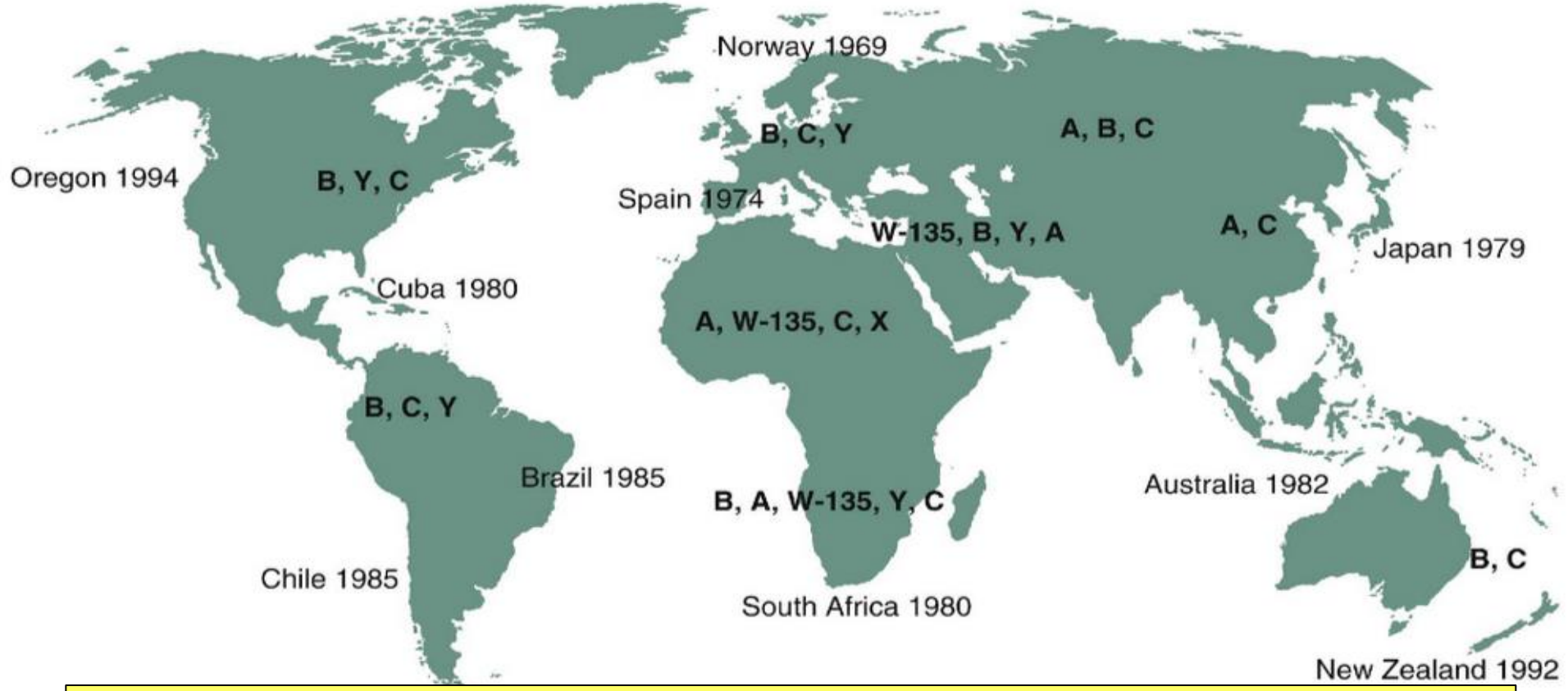
WHO sürveyans çalışmaları

1 haftada 5 olgu / 100.000

→ Epidemi→ aşılama

Hart CA, Cuevas LE. Meningococcal disease in Africa. Ann Trop Med Parasitol 1997; 91:777.

N. meningitidis - EPİDEMİOLOJİ



- **Dinamik epidemiyoloji (seyahat, sınırlarda göç vb)**
- **Ülkeye özgü aşılama (lokal atak hızı, kaynaklar, maliyet-etkinlik)**

Mandell, Douglas, Bennett's Principles and Practice of Infectious Diseases, 2015

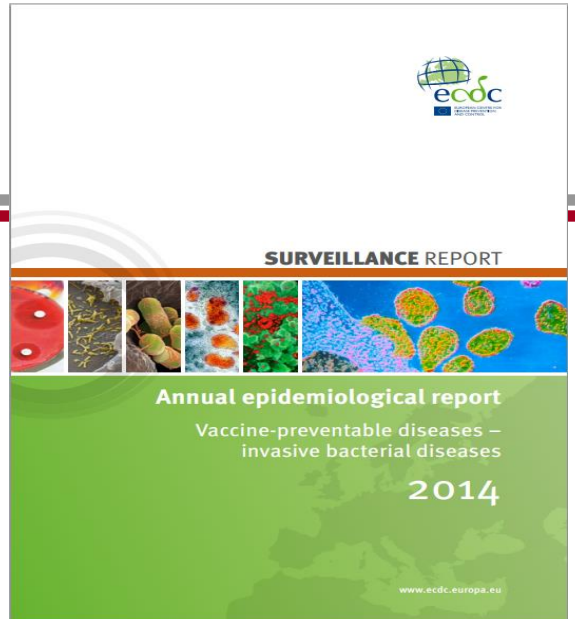


Figure 7. Rates of confirmed invasive meningococcal disease reported cases by age and gender, EU/EEA, 2012

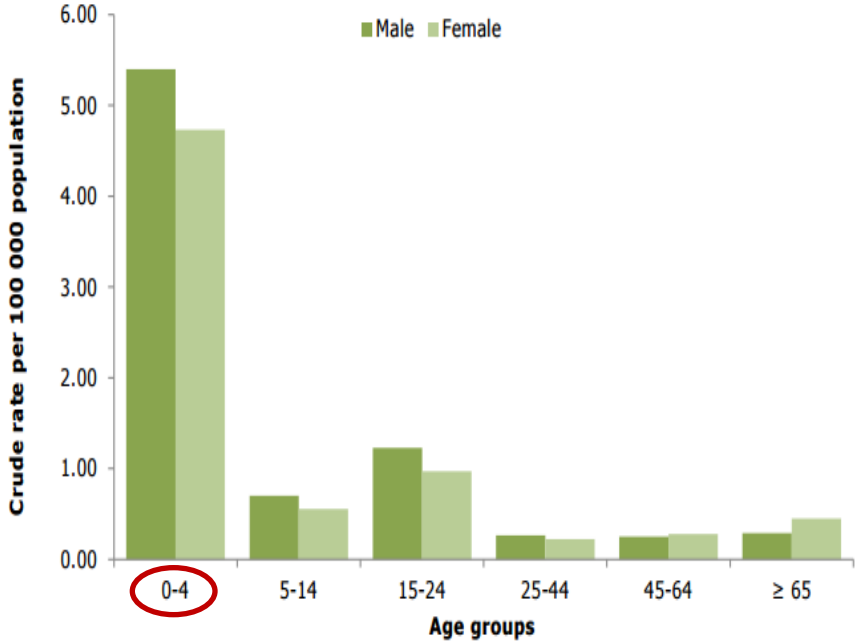
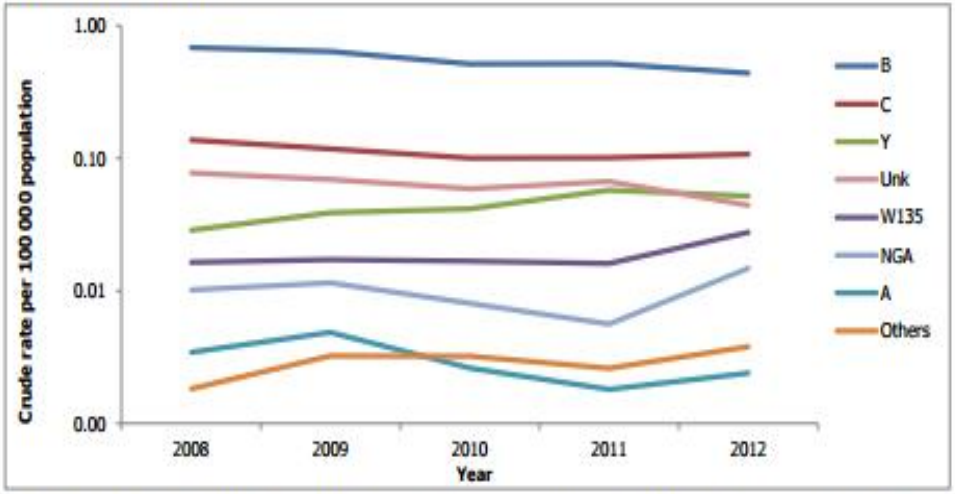
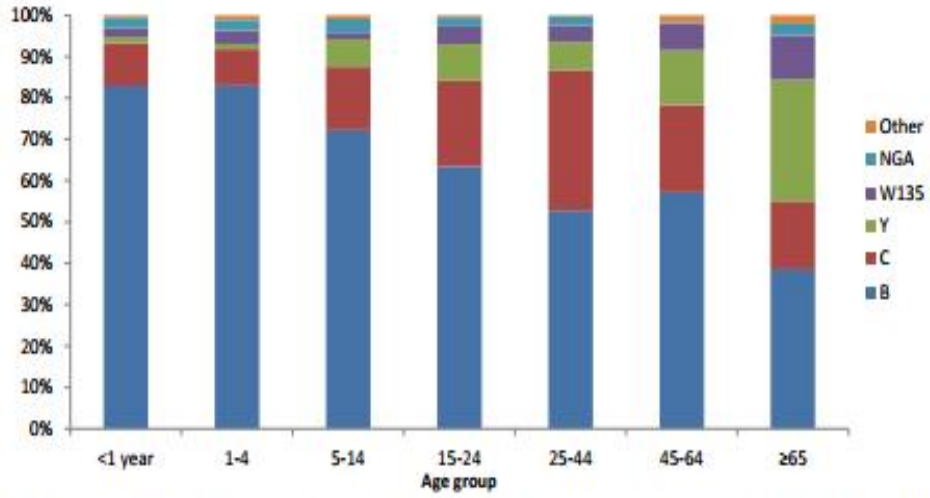


Figure 9. Rates of confirmed invasive meningococcal disease reported cases by serogroup, EU/EEA, 2008-2012 (n=20 161)



Source: Country reports; NGA: non-groupable; Unk: unknown. The specific codes are kept for the most common serogroups. Others are the remaining/other groupable serogroups that should be reported. Apart from serogroups reported as 'other' (n=42), it includes cases of serogroups 29E (13), X (n=13) and Z (n=5) reported during the period 2008–2012.

Figure 10. Rates of confirmed invasive meningococcal disease reported cases by age and serogroup, EU/EEA, 2012 (n=3 233)



Source: Country reports; NGA: non-groupable.; 'Other' includes confirmed cases reported as serogroup 'other' (n=15), as serogroup A (n=12), serogroup 29E (n=3) and serogroup Z (n=1). The specific codes are kept for the most common serogroups. Others are the remaining/other groupable serogroups that should be reported.

N. meningitidis EPİDEMİYOLOJİ - Türkiye

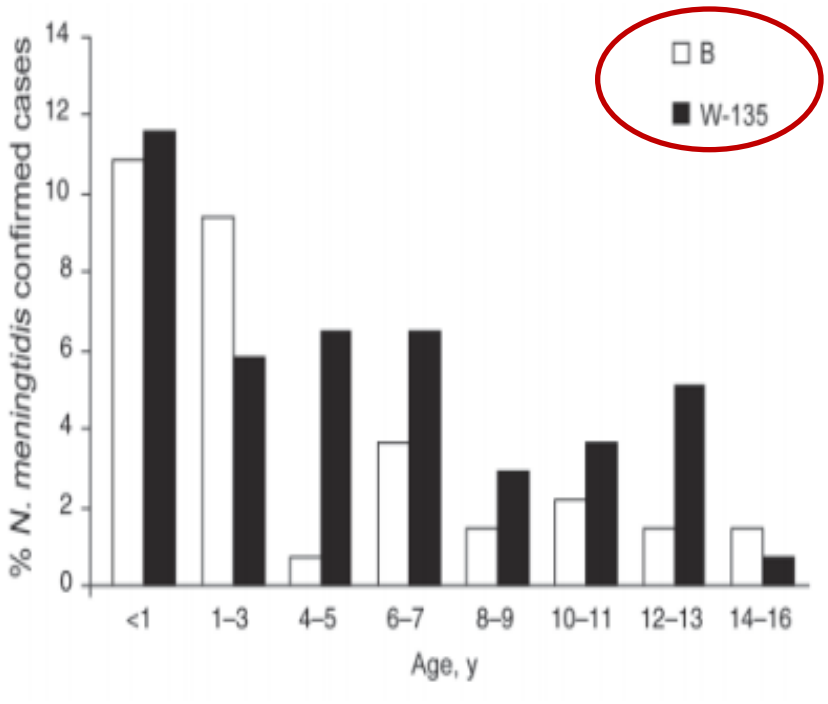


Figure 4. Distribution of predominant *Neisseria meningitidis* serogroups in different age groups. Serogroups W-135 and B caused 42.7% and 31.1% of all meningococcal infections, respectively. W-135 was the most common cause of meningococcal infection in all but 2 age groups analyzed.

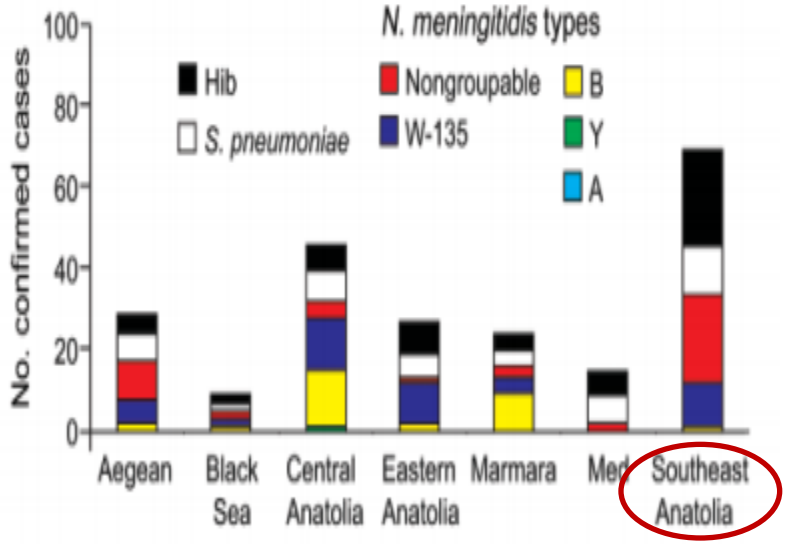


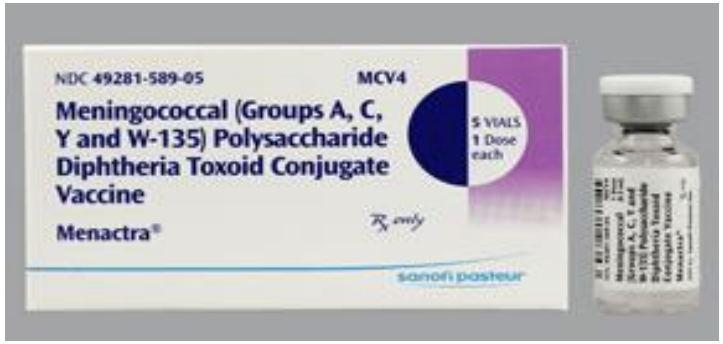
Figure 5. Etiology of confirmed cases of bacterial meningitis in different geographic regions. W-135 was the most prominent *Neisseria meningitidis* serogroup in the Southeast Anatolia, Aegean, Eastern Anatolia, and Black Sea regions. The percentages of cases caused by *Streptococcus pneumoniae* and *Haemophilus influenzae* type b (Hib) are also shown.

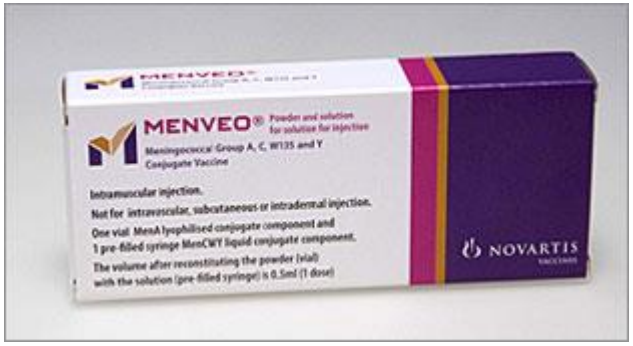
Ceyhan M, et al. Emerging Infectious Diseases • www.cdc.gov/eid • Vol. 14, No. 7, July 2008,1089-96

MENİNGOKOK AŞILARI

- **Tetravalan polisakkarit aşısı** (**Menomune, MPSV4**)
  - 0.5 mL SC
  - FDA onayı **≥56 yaş**
- **Tetravalan konjuge aşı** (**Menactra, MenACWY-D**)
  - difteri toksoidi - **(2-55 yaş)** 0.5 mL IM
  - **2005**
- **Tetravalan konjuge aşı** (**Menveo, MenACWY-CRM**)
  - mutant difteri toksini, CRM197 - **(2-55 yaş)** 0.5 mL IM
  - **2010**
- **Kombine konjuge aşı** (**MenHibrix, HibMenCY-TT**)
  - ***N. meningitidis*** **serogroups C and Y and** ***Haemophilus influenzae*** **type b**
  - **Haziran 2012: FDA onayı – (6 hafta-18 ay)**
  - **Ekim 2012: ACIP önerisi**

MENİNGOKOK AŞILARI





MENİNGOKOK AŞILARI – En yeniler

- **Serogroup B meningococcal vaccine** (**Trumenba**):
  - **Ekim 2014: FDA onayı (10-25 yaş)**

- **Serogroup B meningococcal vaccine** (**Bexsero**):
  - Ocak 2013: EC onayı (>2 yaş)
  - **Ocak 2015:** FDA onayı (**10-25 yaş)**
  - **Şubat 2015:** ACIP onayladı (≥10 yaş)

MENİNGOKOK AŞILARI

- Serogrup C konjuge aşı (Menjugate) UK
- Serogrup A konjuge aşı (Sahra-altı Afrika)
- Serogrup AC polisakkarit aşı
- Serogrup B aşısı

ACIP – Meningokok aşılaması

- **Menactra (MenACWY-D) :**
  - **FDA 2011: ≥9 ay**
  - **ACIP 2011: 9-23 ay risk grubu**
    - 11-12 yaş herkese, rapel 16 yaş
    - 2-10 yaş ve 19-55 yaş risk grubuna

- **Menveo (MenACWY-CRM):**
  - **FDA 2013: >2 ay**
  - **ACIP 2014: ≥2 ay risk grubu**
    - 11-12 yaş herkese, rapel 16 yaş
    - 2-10 yaş ve 19-55 yaş risk grubuna

- **Kombine konjuge aşı - MenHibrix (HibMenCY)**
  - ***N. meningitidis* serogrup C ve Y ve *Haemophilus influenzae* tip b**
  - **FDA 2012: 6 hafta-18 ay**
  - **ACIP 2013: risk grubu bebek ve çocuklar**

ACIP Erişkinde Meningokok Aşılama Önerileri – Risk grupları

‡

- **Askeri birlikler, yatılı okul öğrencileri**
- **Mikrobiyologlar** (*N. meningitidis'*e maruziyet)
- **Fonksiyonel / anatomik asplenia***
- **Kompleman eksikliği*** (properdin, Factor D, Factor H, C5-C9)
- **Hiperendemik veya epidemik bölgeye seyahat edecekler**
  - Sahra-altı Afrika- Menenjit kuşağı (Aralık-Haziran)
  - Hac ve umre döneminde Mekke ve Medine, Suudi Arabistan
    - Son 3 yıl içinde yapılmış olmalıdır
    - Tüm yenidoğan, çocuk ve erişkin hacı adayları 10 gün veya daha önceden kuadrivalan (A/C/Y/W-135) meningokok menenjiti aşısı ile aşılandıklarını belgelemelidir. Belge en fazla 3 yıl geçerlidir.
- **HIV infeksiyonu** *

➢ *:Başlangıçta 2 doz

➢ Risk grubuna 5 yılda bir booster, >55 yaş + 1 MCV4 (yoksa MPSV4)

Meningokok Aşılama - ACIP Önerileri

Meningococcal vaccination recommendations in the United States by age and/or risk factor*

Targeted group by age and/or risk factor	Primary dose(s)	Booster dose(s)
People ages 11 through 18 years	Give patients without HIV infection one dose of Menactra or Menveo, preferably at age 11 or 12 years; give HIV-infected patients two doses of Menactra or Menveo at least two months apart	Give booster at age 16 years if primary dose given at age 12 years or younger
		Give booster at age 16 through 18 years if primary dose given at age 13 through 15 years[¶]
People ages 19 through 21 years who are first year college students living in residence halls	Give patients without HIV infection one dose of Menactra or Menveo; give HIV-infected patients two doses of Menactra or Menveo at least two months apart	Give booster if previous dose given at age younger than 16 years
Travelers to or residents of countries where meningococcal disease is hyperendemic or epidemic[Δ], people present during outbreaks caused by a vaccine serogroup[◇§], and other people with prolonged increased risk for exposure (eg, microbiologists routinely working with *Neisseria meningitidis*)		
For children age 2 through 18 months	Give Menveo at ages 2, 4, 6, and 12 to 15 months[¥]	If risk continues, give initial booster after three years followed by boosters every five years
For children age 7 through 23 months who have not initiated a series of Menveo or MenHibrix	Give two doses, separated by three months[‡] of Menveo (if age 7 to 23 months)[†] or Menactra (if age 9 to 23 months)	
For age 2 through 55 years	Give patients without HIV infection one dose of Menactra or Menveo; give HIV-infected patients two doses of Menactra or Menveo at least two months apart	Boost every five years with Menactra or Menveo[**,¶¶]
For age 56 years and older	Give patients without HIV infection and no previous Menactra or Menveo dose and either short-term travel or outbreak-related one dose of Menomune; give HIV-infected patients two doses of Menactra or Menveo at least two months apart; all others, give one dose of Menactra or Menveo[ΔΔ]	Boost every five years with Menactra or Menveo[¶¶]
People with persistent complement component deficiencies[◇◇]		
For age 2 through 18 months	Give Menveo or MenHibrix at ages 2, 4, 6, and 12 to 15 months	Give Menactra or Menveo booster after three years followed by boosters every five years thereafter
For children age 7 through 23 months who have not initiated a series of Menveo or MenHibrix	Give two doses, separated by three months, of Menveo (if age 7 to 23 months)[†] or Menactra (if age 9 to 23 months)	
For age 2 through 55 years	Give two doses of Menactra or Menveo, two months apart	Boost every five years with Menactra or Menveo[**,§§]
For age 56 years and older	Give two doses of Menactra or Menveo, two months apart[ΔΔ]	Boost every five years with Menactra or Menveo[§§]
People with functional or anatomic asplenia, including sickle cell disease		
For age 2 through 18 months	Give Menveo at ages 2, 4, 6, and 12 months or MenHibrix at ages 2, 4, 6, and 12 to 15 months	Give Menactra or Menveo booster after three years followed by boosters every five years thereafter
For children age 19 through 23 months who have not initiated a series of Menveo or MenHibrix	Give two doses of Menveo, three months apart	
For age 2 through 55 years	Give two doses of Menactra or Menveo, two months apart[¥¥]	Boost every five years with Menactra or Menveo[**,§§]
For age 56 years and older	Give two doses of Menactra or Menveo, two months apart[ΔΔ]	Boost every five years with Menactra or Menveo[§§]

This table was adapted from the recommendations of the United States Centers for Disease Control and Prevention's (CDC's) Advisory Committee on Immunization Practices (ACIP) for the use of meningococcal vaccines[1-4].

The quadrivalent meningococcal conjugate vaccines (MenACWY) are Menactra (MenACWY-D) and Menveo (MenACWY-CRM). The quadrivalent meningococcal polysaccharide vaccine is Menomune (MPSV4). MenHibrix (HibMenCY) is a combination conjugate vaccine against meningococcus serogroups C and Y and *Haemophilus influenzae* type b.

* In late 2014 and early 2015, the US Food and Drug Administration approved two serogroup B meningococcal vaccines (Trumenba and Bexsero) for use in individuals 10 through 25 years of age. In February 2015, the ACIP voted

Meningokok Aşılama - ACIP Önerileri

‡

Yaş ve/veya risk faktörü	Primer Doz	Rapel Doz
11 - 18 yaş	1 doz Menactra / Menveo (11-12 y) HIV+'de 2 doz en az 2 ay arayla	İlk doz ≤12 yaş ise 16 y'da rapel İlk doz 13-15 y'da ise 16-18 y'da rapel
19 - 21 yaş (Yatılı okul)	1 doz Menactra / Menveo HIV+'de 2 doz en az 2 ay arayla	Önceki doz ≤16 yaş ise 1 doz rapel
Epidemik / hiperendemik bölgeye seyahat, salgın zamanı, mikrobiyologlar		
2 - 18 ay	2, 4, 6, 12-15. ayda Menveo	Risk devam ediyorsa ilk rapel 3 yıl, sonrakiler 5 yıl sonra
7 - 23 ay (Menveo / Menhibrix almamış)	3 ay arayla 2 doz Menveo (7-23 ay) / Menactra (9-23 ay)	
2- 55 yaş	1 doz Menactra / Menveo HIV+'de 2 doz en az 2 ay arayla	5 yılda bir rapel (Menactra / Menveo)
≥ 56 yaş	Önceden aşılanmamış, kısa süreli seyahat/salgın: 1 doz Menomune HIV+'de 2 doz en az 2 ay arayla Menactra / Menveo Diğer: 1 doz Menactra / Menveo	5 yılda bir rapel (Menactra / Menveo)

Meningokok Aşılama - ACIP Önerileri ‡

Yaş ve/veya risk faktörü	Primer Doz	Rapel Doz
Kalıcı kompleman eksikliği olanlar		
2 - 18 ay	2, 4, 6, 12-15. ayda Menveo / Menhibrix	Menactra /Menveo ile ilk rapel 3 yıl, sonrakiler 5 yıl sonra
7 - 23 ay (Menveo/Menhibrix almamış)	3 ay arayla 2 doz Menveo	
2 - 55 yaş	2 ay arayla 2 doz Menactra / Menveo	5 yılda bir rapel (Menactra / Menveo)
≥ 56 yaş	2 ay arayla 2 doz Menactra / Menveo	5 yılda bir rapel (Menactra / Menveo)
Fonksiyonel / anatomik aspleni		
2 - 18 ay	2, 4, 6, 12. ayda Menveo / 2, 4, 6, 12-15. ayda Menhibrix	
19 - 23 ay (Menveo/Menhibrix almamış)	3 ay arayla 2 doz Menveo	
2 - 55 yaş	2 ay arayla 2 doz Menactra / Menveo	5 yılda bir rapel (Menactra / Menveo)
≥ 56 yaş	2 ay arayla 2 doz Menactra / Menveo	5 yılda bir rapel (Menactra / Menveo)

‡

2 - 23 ay risk grubu çocuklarda Meningokok aşılama

TABLE. Summary of recommendations for meningococcal vaccination of children aged 2–23 months at increased risk for meningococcal disease — Advisory Committee on Immunization Practices, 2013

Vaccine	Age of primary vaccination	Booster doses*	Indicated for infants who:	Not indicated for:
MenACWY-CRM (Menveo)	2, 4, 6, and 12 months	• 1st booster 3 years after primary series • Additional boosters every 5 years	• Have complement component deficiencies • Have functional or anatomic asplenia (including sickle cell disease) • Are in the risk group for an outbreak for which vaccination is recommended • Are traveling to or residing in regions where meningitis is epidemic or hyperendemic	
MenACWY-D (Menactra)	9 and 12 months†	• 1st booster 3 years after primary series • Additional boosters every 5 years	• Have complement component deficiencies • Are in the risk group for an outbreak for which vaccination is recommended • Are traveling to or residing in regions where meningitis is epidemic or hyperendemic	• Infants with functional or anatomic asplenia (including sickle cell disease)§
Hib-MenCY-TT (MenHibrix)	2, 4, 6, and 12–15 months	• 1st booster (using MenACWY-CRM or MenACWY-D¶) 3 years after primary series	• Have complement component deficiencies	• Infants traveling internationally to regions where meningitis is epidemic or hyperendemic
		• Additional boosters (using MenACWY-CRM or MenACWY-D¶) every 5 years	• Have functional or anatomic asplenia (including sickle cell disease) • Are in the risk group for an outbreak for which vaccination is recommended	• Booster dose in children aged >18 months

* If the most recent dose was received before age 7 years, a booster dose should be administered 3 years later.
† For infants aged 9–23 months, 2 doses of MenACWY-D should be administered 12 weeks apart. For infants receiving the vaccine before travel, the second dose may be administered as soon as 8 weeks after the first dose (additional information at http://www.cdc.gov/mmwr/preview/mmwrhtml/rr6202a1.htm).
§ Because of high risk for invasive pneumococcal disease, children with functional or anatomic asplenia should not be immunized with MenACWY-D before age 2 years to prevent immune interference with 13-valent pneumococcal conjugate vaccine (PCV13).
¶ Hib-MenCY-TT should not be used for booster doses. A quadrivalent meningococcal vaccine (MenACWY-CRM or MenACWY-D) should be used for booster doses.

ACIP - 2-13 ay risk grubuna aşılama

‡

AŞI	Primer aşılama	Rapel doz	Endikasyonlar	Endikasyon yok
MenACWY-CRM (Menveo)	2, 4, 6 ve 12 ay	**Primer aşılamadan 3 yıl sonra 1 rapel**	**Kompleman eksikliği**	
		Her 5 yılda bir rapel	**Fonksiyonel / anatomik aspleni**	
			Aşı önerilen salgın riski	
			Epidemik / hiperendemik bölgeye seyahat	
MenACWY-D (Menactra)	9 ve 12 ay	**Primer aşılamadan 3 yıl sonra 1 rapel**	**Kompleman eksikliği**	**Fonksiyonel/ anatomik aspleni**
		Her 5 yılda bir rapel	**Aşı önerilen salgın riski**	
			Epidemik / hiperendemik bölgeye seyahat	
HibMenCY-TT (MenHibrix)	2, 4, 6, ve 12-15 ay	**Primer aşılamadan 3 yıl sonra ilk rapel (Menveo / Menactra)**	**Kompleman eksikliği**	**Epidemik / hiperendemik bölgeye seyahat**
		Her 5 yılda bir rapel (Menveo / Menactra)	**Fonksiyonel / anatomik aspleni**	**<18 ay rapel dozu**
			Aşı önerilen salgın riski	

Meningokokal Polisakkarit Aşısı (MPV4, Menomune) ‡

- Serogrup A, C, Y, W-135
- >%85 etkinlik, <2 yaş ve 2-10 yaş: zayıf immunojenik
- **11-55 yaş arası Menactra kadar immunojenik**
- **3-5 yılda koruyuculuk azalır**
- **Menomune** (**MPSV4**): Konjuge meningokok aşısı için kontraendikasyonu olan >2 yaş çocuklarda kullanılabilir
- **≥ 55 yaş tekrar aşılama gerekmiyorsa** (immunolojik yanıtsızlık!)

Etkinlik

- **Serogrup A ve C: ≥85** (salgın sırasında erişkinler ve okul çocukları)
- **Serogrup Y ve W135:** Bakterisidal antikor oluşturur. Klinik korunma ?

- **Yanetkiler:** Menactra'ya göre lokal yanetkiler daha az

Pichichero M, Casey J, Blatter M, et al. Pediatr Infect Dis J 2005; 24:57.

Meningokokal Konjuge Aşısı (MCV)

- T hücre bağımlı yüksek immunite, bellek yanıt
- Tekrarlanan dozlarda amnestik antikor düzeyleri
- İlk MCV serogrup C, UK, <19 yaş (en yüksek taşıyıcılık)
- **Serogrup C nazofaringeal taşıyıcılığı >%75 azaltmış**

- **Serogrup B polisakkariti:**
  - insan nöral hücre adhezyon molekülüne benzer
  - zayıf immunojenik, otoimmünite?
  - OM vezikül proteinleri-yarı-korunmuş yüzey protein antijenleri

- **≥ 56 yaş tekrar aşılama gerekliyse**

Cohn AC, et al. (ACIP). MMWR Recomm Rep 2013; 62:1

Menactra – Dikkat edilecekler

- Etkinlik adölesanlarda %80-85 (zamanla azalır), herd immünite oluşturmaz
- Tek doz Menactra ile aşılanan adölesanlarda immunojenisite verileri: koruyuculuk maksimum 5 yıl → 16 yaşında rapel aşılama gerekli

- Birlikte uygulandığında Menactra, **pnömokokal konjuge aşıyla sağlanacak koruyuculuğu azaltır.**
- **Tüm pnömokokal konjuge aşı dozların tamamlanmasından sonra en az 4 hafta boyunca veya 2 yaşına kadar Menactra uygulanmamalı!**

- Fonksiyonel ya da anatomik asplenisi olan çocuklarda pnömokokal hastalık, meningokokal hastalıktan daha ciddi bir tehdit oluşturur. **ACIP 9-23 ay arasında bu çocuklara Menactra uygulanmasını önermiyor!**

YAN ETKİLER

- **Menactra:**
  - eritem, şişlik, ağrı, dizziness
  - Ciddi YE: ateş, başağrısı, bulantı, kusma, GBS?
  - Adölesanlarda senkop: %10

- **Menveo:**
  - Enjeksiyon bölgesinde eritem ve şişlik
  - Adölesanlarda senkop: %10

Macneil JR, Cohn AC, Zell ER, et al. Pediatr Infect Dis J 2011; 30:451.

BEXSERO ve TRUMENBA

- **2013 – 2014 -** Princeton University, New Jersey'de kampüste serogrup B menenjit salgınında kullanıldı

- **2014** - University of California, Santa Barbara, salgın nedeniyle benzer bir aşı kampanyası

- **Temmuz 2013 - United Kingdom Joint Committee on Vaccination and Immunisation (JCVI):**
  - **"routine infant or toddler immunization using Bexsero is highly unlikely to be cost-effective, not recommended"**

- **Mart 2014 - a new cost-effectiveness analysis, JCVI recommended the routine use of the meningococcal serogroup B vaccine in infants at 2, 4, and 12 months of age**

Christensen H, et al. BMJ 2014 Oct 9;349:g5725.

Serogrup B Meningokok - Türkiye

REVIEW

Human Vaccines & Immunotherapeutics 10:6, 1721–1724; June 2014; © 2014 Landes Bioscience

Meningococcal serogroup B disease in Turkey

A guess or reality?

Mustafa Bakir[1,*]

[1]Professor of Pediatrics; Division of Pediatric Infectious Diseases; Department of Pediatrics; Marmara University School of Medicine; Istanbul, Turkey

- Zamanla ve coğrafik bölgeye göre serogrupların etken sıklığı değişir
- **Avrupa'da serogrup B ve C İMH: %85**
- Türkiye'de gerçek prevalans bilinmiyor
- Son çalışmalardan birinde aşı olmamasına rağmen serogrup B IMH: % 35 → % 2.5 ?
- Avrupa – Türkiye arasında milyonlarca kişinin seyahati - Taşıyıcılık
- Gerçek epidemiyolojiyi ve İMH yükünü belirlemek için **ulusal aktif sürveyans çok önemli**

Eş zamanlı uygulama

- **TDaP ve Menactra**, aşılar eş zamanlı vaya 30 gün arayla uygulandığında güvenlik ve immun yanıt benzer

- **2-55 yaş**: MCV4 ve MPSV4 diğer aşılarla eş zamanlı farklı bölgeden

- **Tüm pnömokokal konjuge aşı dozların tamamlanmasından sonra en az 4 hafta boyunca veya 2 yaşına kadar Menactra uygulanmamalı!**

Weston WM, Friedland LR, Wu X, Howe B. Vaccine 2011; 29:1017.

‡

CVI
JournalsASM.org

Acquisition of Meningococcal Serogroup W-135 Carriage in Turkish Hajj Pilgrims Who Had Received the Quadrivalent Meningococcal Polysaccharide Vaccine

M. Ceyhan,[a] M. Celik,[a] E. T. Demir,[a] V. Gurbuz,[a] A. E. Aycan,[a] S. Unal[b]
Hacettepe University Department of Pediatric Infectious Diseases, Ankara, Turkey[a]; Hacettepe University Department of Infectious Diseases, Ankara, Turkey[b]

- **Türkiye'de serogrup B**'den sonra **ikinci en sık** patojen meningokok serogrubu: **W-135** (2005 epidemisi – hacılar)
- Hac öncesi MPV4 (serogrups A, C, W-135, Y)
- Hac sonrası kendilerinde ve ev temaslılarında meningokok taşıyıcılığı

- 472 Hacı, **Hac öncesi**: 63 (**%13**) kişi: **meningokok taşıyıcılığı**
  - 52 (**%83**) kişi: **serogrup W-135**
- 296 Hacı, **Hac sonrası**: 81 (**%27**) kişi: **meningokok taşıyıcılığı**
  - 74 (**%91**) kişi: **serogrup W-135**

Clinical and Vaccine Immunology p. 66–68 January 2013 Volume 20 Number 1

ABD- Meningokok Aşılama

2 ay - 10 yaş	• Risk grubu • Menactra : ≥ 9 ay • Menveo: ≥ 2 ay
11 - 18 yaş	• Tüm adölesanlar • Menactra veya Menveo
19 - 55 yaş	• Risk grubu • Menactra veya Menveo
> 55 yaş	• Risk grubu • Tek doz: Menomune • >1 doz: Menactra veya Menveo

MENİNGOKOK AŞISI - ÖZET

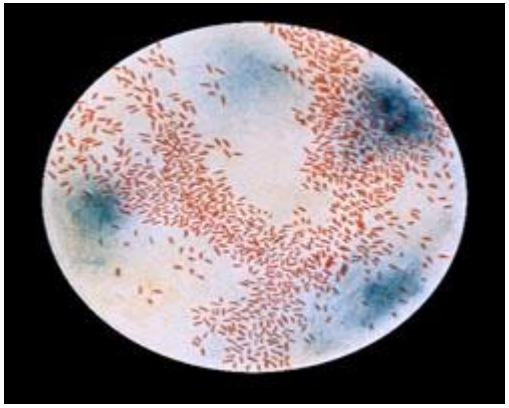
- **Yüksek risk grubu**
  - Seyahat öncesi
  - <5 yaş ve adölesanlar

- **Kalıcı bağışıklık için risk gruplarına 5 yılda bir rapel**

- ACIP: < 55 yaş: Konjuge meningokok aşısı
  ≥ 56 yaş: Polisakkarit meningokok aşısı

- **Sürekli ulusal sürveyans gerekli** (meningokok sero-epidemiyolojisinde dinamik değişiklikler)


Take Action
AGAINST MENINGITIS



H. influenzae Tip b AŞISI

H. influenzae Tip b

- **Polisakkarit kapsülüne göre 6 serotipi var: a→f**
- Tip b kapsül polisakkariti: **PRP (**polyribosylribitol phosphate)
- **Aşı öncesi: < 5 yaş çocuklarda akut bakteriyel menenjitin %85 etkeni**

- İlk polisakkarit aşı (PRP) -**1985**: ≥ 8 ay
- Opsonofagositik bakterisidal antikorlar
- **"Herd immunite"**
- 1989–2000: < 5 yaş çocuklarda **yıllık invazif Hib hastalığı insidansında % 99 azalma** (< 1/ 100,000)
- **Aşılama sonrası nazofaringeal taşıyıcılık: < %1**

Tiplendirilemeyen (nontypeable) *H. influenzae*

- **Polisakkarit kapsülü yok**

- **Mukozal ve solunumsal infeksiyonlar**:
  - Akut otitis media
  - Akut sinüzit
  - Bronşit
  - Toplum kökenli pnömoni
  - Endometrit, amnionit, Bartholin gland abscess (+/- bakteremi)

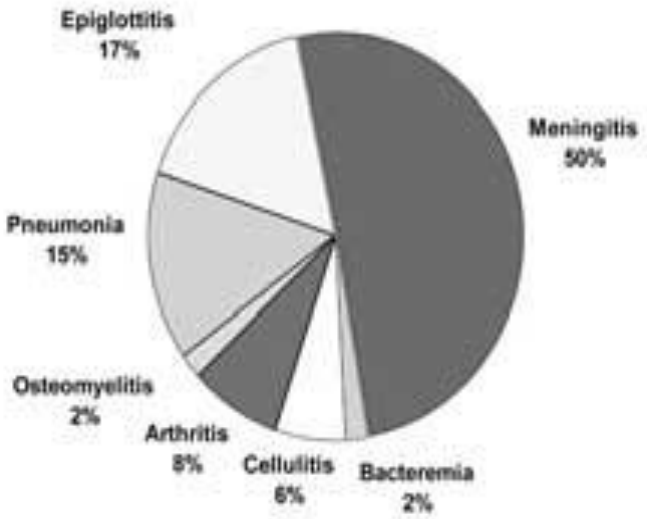
- Yenidoğan ve immunokompromize hastalar dışında yaygın sistemik infeksiyon nadir

- Hücre duvarı proteini immunojen
- İmmunokompromize hastalara IVIG

H. influenzae Tip b infeksiyonu - Risk grupları

- **< 5 yaş**
- **Immun baskılanma durumları**
  - Kompleman eksikliği
  - Hipogammaglobulinemi
  - Orak hücreli anemi
  - Anatomik aspleni
  - Malignite
- **HIV**
- **Erişkinlerde**:
  - Kardiyopulmoner hastalık
  - Malignite
  - Sigara tüketimi
  - Alkolizm
  - Gebelik

- **Sosyoekonomik risk faktörleri**
  - Kalabalık yaşam
  - Zayıf immunizasyon
  - Kreş/yuvaya gitmek



H. influenzae Tip b

‡

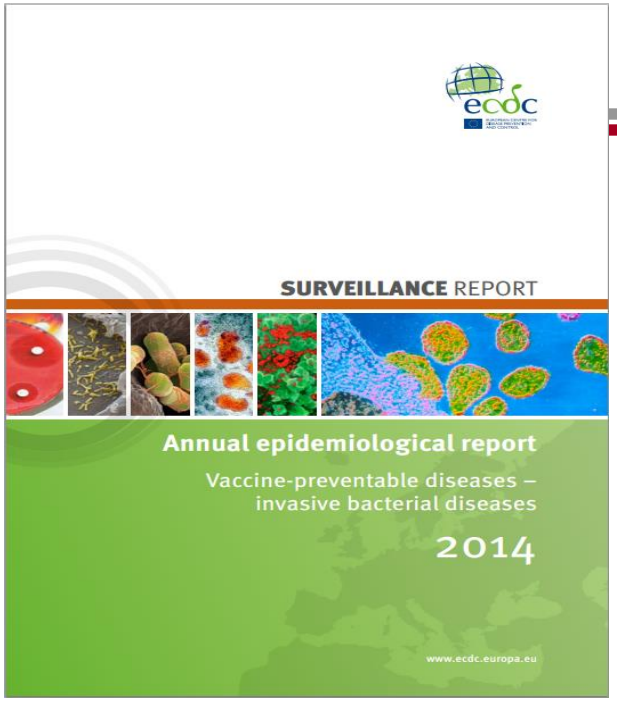


Figure 2. Rates of confirmed invasive *Haemophilus influenzae* disease reported cases by age and gender, EU/EEA, 2012

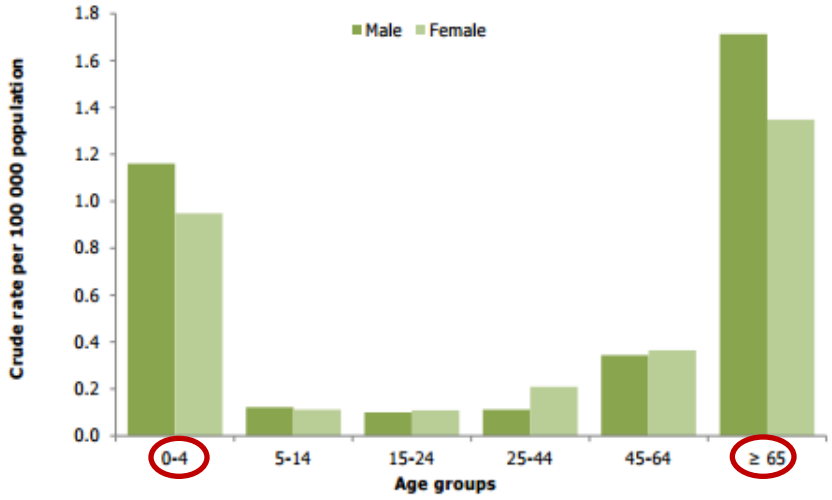


Figure 4. Rates of confirmed invasive *Haemophilus influenzae* disease reported cases by serotype, EU/EEA, 2008–2012 (n=1 352)

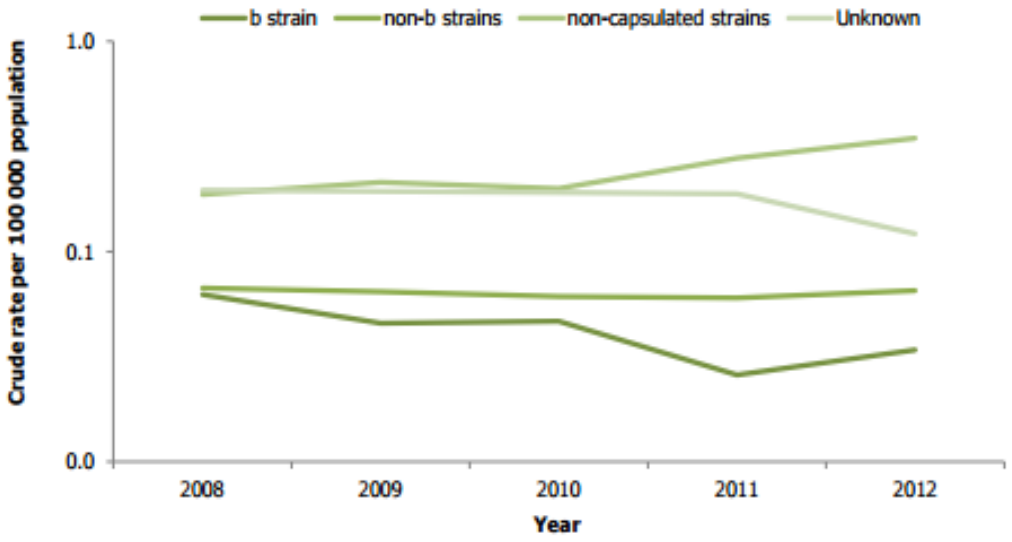
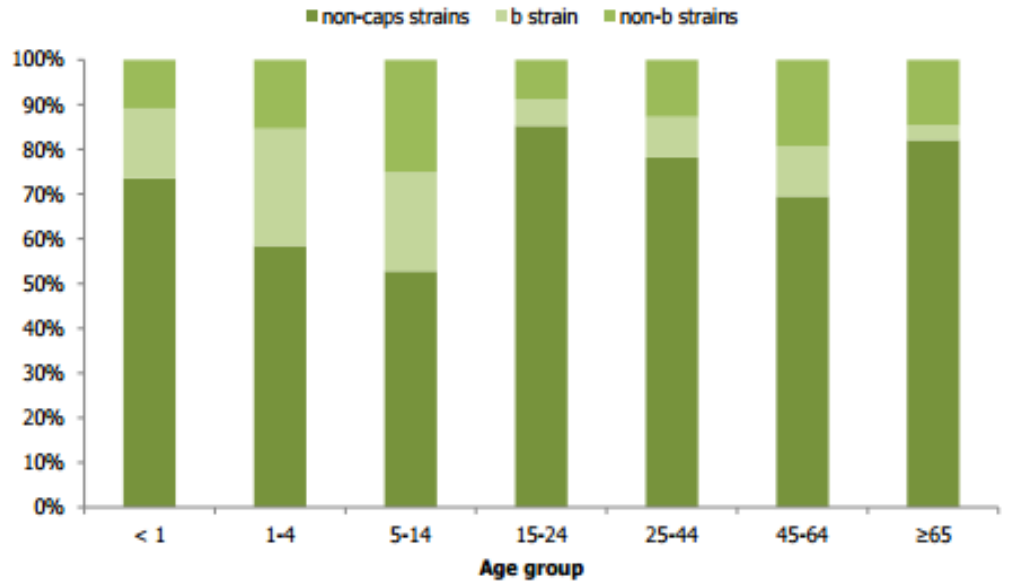
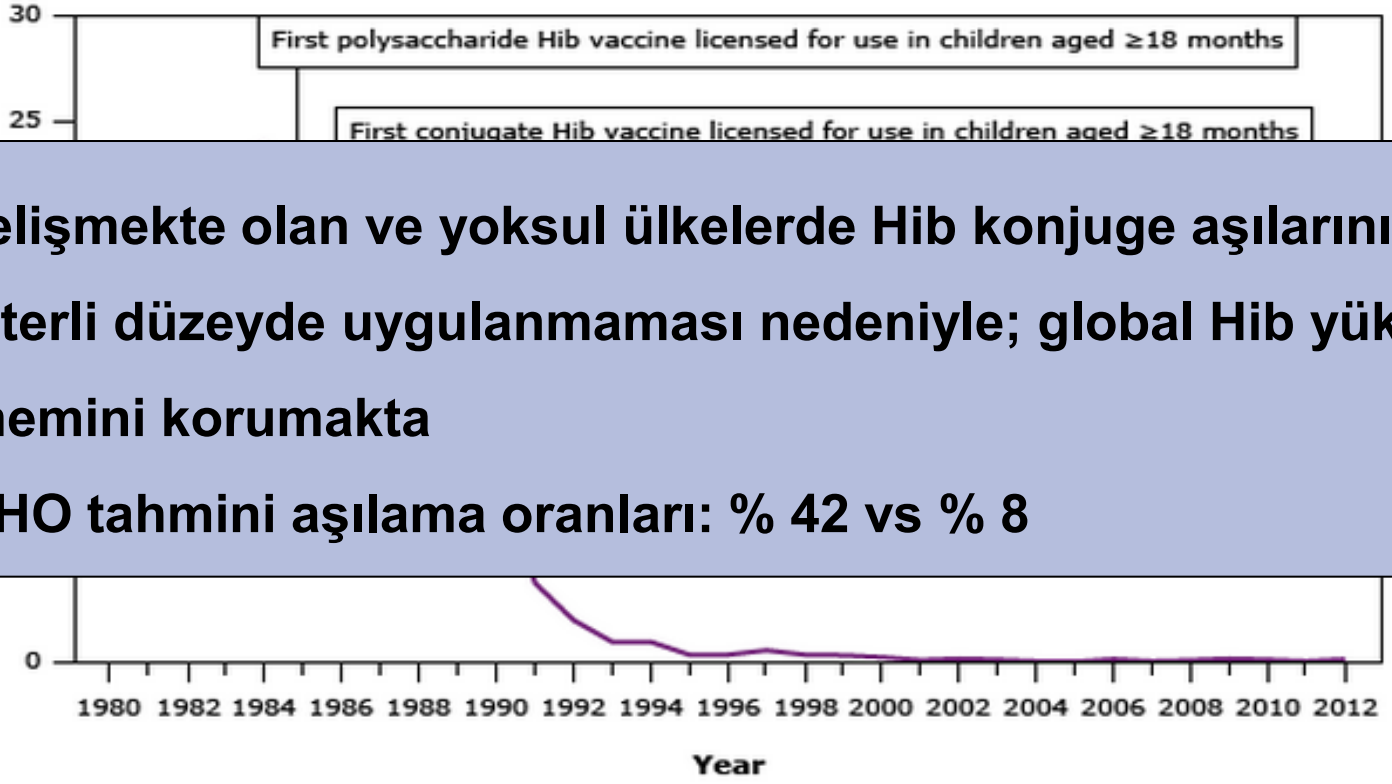


Figure 5. Rates of confirmed invasive *Haemophilus influenzae* disease reported cases by age and serotype, EU/EEA, 2012 (n=1 348)



H. influenzae Tip b

Estimated annual incidence* of invasive *Haemophilus influenzae* type b (Hib) disease in children aged <5 years - United States 1980 to 2012



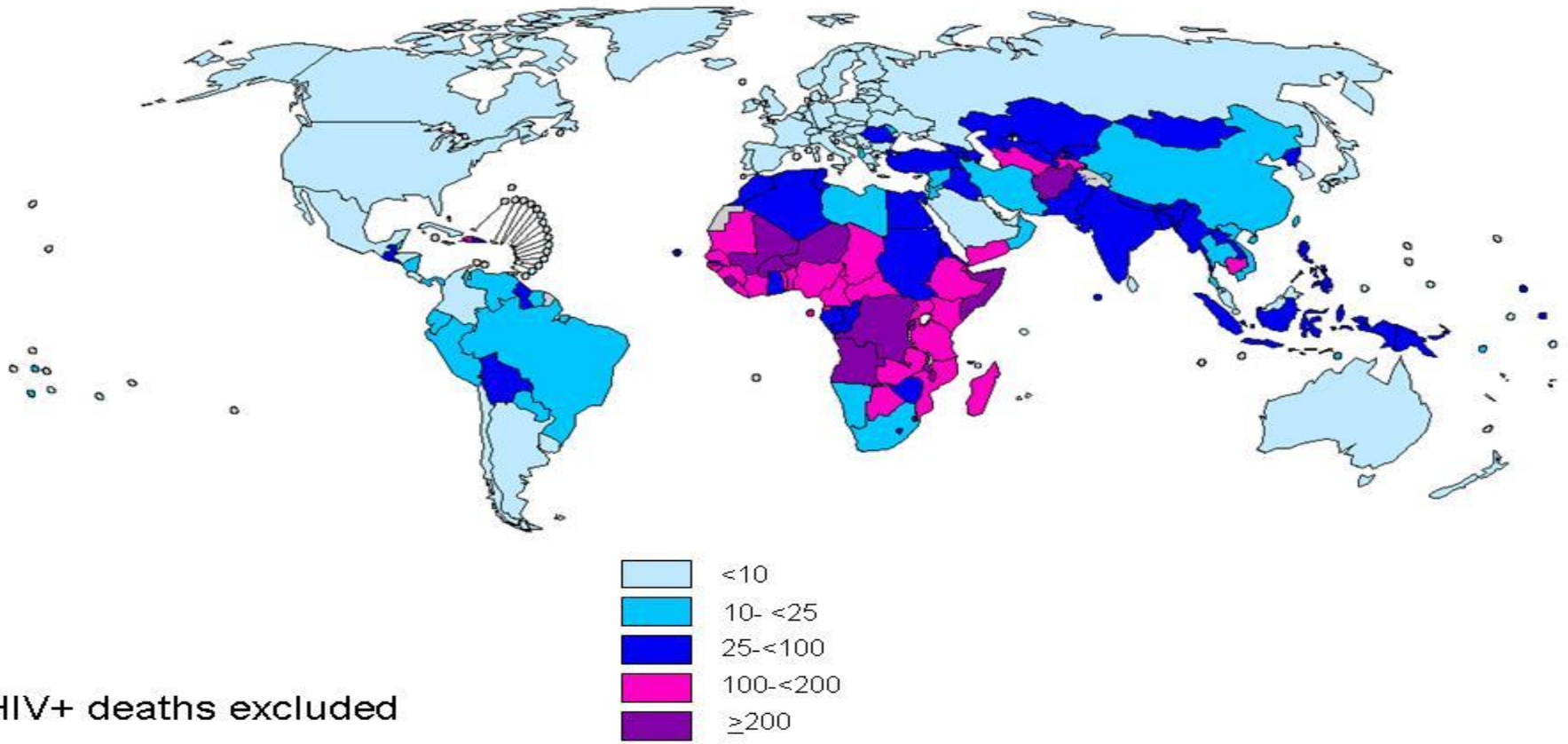
Gelişmekte olan ve yoksul ülkelerde Hib konjuge aşılarının yeterli düzeyde uygulanmaması nedeniyle; global Hib yükü önemini korumakta

WHO tahmini aşılama oranları: % 42 vs % 8

* Per 100,000 population.

http://www.cdc.gov/mmwr/PDF/rr/rr6301.pdf

Hib death* rate
(per 100000 children under age 5)



* HIV+ deaths excluded

Date of slide: 03 August 2009

http://www.who.int/immunization/monitoring_surveillance/burden/estimates/pneumo_hib/Hib_deaths_map.JPG?ua=1

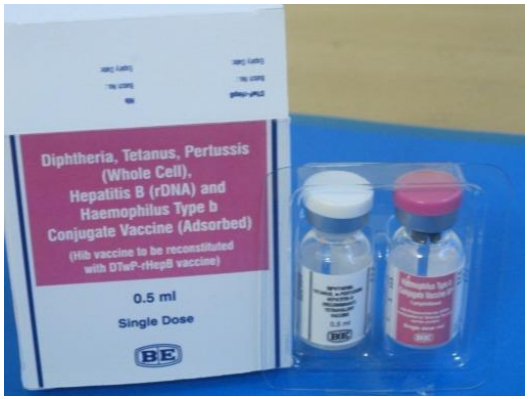
H. influenzae Tip b - Konjuge Aşılar

- **PRP - OMP** – dış membran proteiniyle konjuge aşı (**PedvaxHIB**)
  - *Neisseria* meningitis serogrup B suşunun dış membran veziküllerinin protein bileşenleri
  - **2., 4., 12-15. ay**

- **PRP-T** – (**PRP-tetanoz toksoidiyle konjuge aşı (PRP-T)**
  - **ActHIB: 2., 4., 6., 12-15. ay**
  - **Hiberix :**
    - 2-3 doz primer seriyle aşılanan 15 ay-4 yaş çocuklarda **rapel** doz
    - Primer seri aşılama için onaylı değil

- **DTaP-IPV/Hib (Pentacel, Pentaxim)**:
  - Beşli karma: **2, 4, 6, 15-18. ay**

H. influenzae Tip b AŞILARI



H. influenzae Tip b - Kombine konjuge aşı

- **Hib-MenCY (MenHibrix): Kombine konjuge aşı**
  - Hib ve meningokok serogrup C - Y
  - **Haziran 2012**'de onay, **6 hafta - 18 ay**
  - **Ocak 2013: ACIP** önerisi

  - **Meningokokal hastalık riski olan bebeklere**
    - Kompleman eksikliği
    - Anatomik veya fonksiyonel aspleni [sickle cell disease]
    - Serogrup C veya Y meningokokal hastalık salgınları olan bölgede yaşayanlar

Centers for Disease Control and Prevention
MMWR
Morbidity and Mortality Weekly Report
Recommendations and Reports / Vol. 63 / No. 1
February 28, 2014

Prevention and Control of *Haemophilus influenzae* Type b Disease

Recommendations of the Advisory Committee on Immunization Practices (ACIP)

H. influenzae Tip b - Aşılama

Guidance for Haemophilus influenzae type b (Hib) vaccination in high-risk groups

High-risk group*	Hib vaccine guidance
Patients aged <12 months	Follow routine Hib vaccination recommendations
Patients aged 12 to 59 months	If unimmunized or received 0 or 1 dose before age 12 months: 2 doses, 8 weeks apart
	If received ≥2 doses before age 12 months: 1 dose 8 weeks after last dose
	If completed a primary series and received a booster dose at age ≥12 months: No additional doses
Patients aged <60 months undergoing chemotherapy or radiation therapy•	If routine Hib doses administered ≥14 days before starting therapy: Revaccination not required
	If dose administered within 14 days of starting therapy or given during therapy: Repeat doses starting at least 3 months following therapy completion
Patients aged ≥15 months undergoing elective splenectomy	If unimmunized:Δ 1 dose prior to procedure◊
Asplenic patients aged >59 months and adults	If unimmunized:Δ 1 dose
HIV-infected children aged ≥60 months	If unimmunized:Δ 1 dose
HIV-infected adults	Hib vaccination is not recommended
Recipients of hematopoietic stem cell transplant, all ages	Regardless of Hib vaccination history: 3 doses (at least 4 weeks apart) beginning 6 to 12 months after transplant

HIV: human immunodeficiency virus.

* Persons with functional or anatomic asplenia, HIV infection, immunoglobulin deficiency including immunoglobulin G2 subclass deficiency, or early component complement deficiency, recipients of a hematopoietic stem cell transplant, and those receiving chemotherapy or radiation therapy for malignant neoplasms.

• Some experts suggest conducting serologic testing for these patients.

Δ Patients who have not received a primary series and booster dose or at least 1 dose of Hib vaccine after 14 months are considered unimmunized.

◊ Some experts suggest vaccination at least 14 days before the procedure. Some experts suggest administering a dose prior to elective splenectomy regardless of prior vaccination history.

Reproduced from: Briere EC, Rubin L, Moro PL, et al. Prevention and Control of Haemophilus influenzae Type b Disease: Recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR Recomm Rep 2014; 63:1.

H. influenzae Tip b - Aşılama ‡

Yüksek risk grubu	Hib aşılaması
< 12 ay	Rutin Hib aşılama önerileri
12 - 59 ay	Aşılanmamışsa, < 12 ay 1 doz aşılıysa, 8 hafta arayla 2 doz
	≥ 2 doz <12 ay, son dozdan 8 hft sonra 1 doz
	Primer seri tamamlanmış, <12 ay rapel yapılmışsa gerek yok
< 60 ay, Kemoterapi / Radyoterapi alacak	Tedaviden ≥ 14 gün önce rutin aşılama yapıldıysa, tekrar aşılama gereksiz Son 14 gün içinde / tedavi sırasında 1 doz aldıysa, tedaviden 3 ay sonra tekrar doz
≥ 15 ay, elektif splenektomi yapılacak	Aşılanmamışsa, işlem öncesi 1 doz
>59 ay ve erişkinler, asplenik	Aşılanmamışsa, 1 doz
≥ 60 ay HIV pozitif	Aşılanmamışsa, 1 doz
HIV pozitif erişkinler	Hib aşılaması gereksiz
HKHA, tüm yaşlar	Aşı öyküsü ne olursa olsun, Tx sonrası 6-12 ay sonra en az 4 hft arayla 3 doz

‡

H. influenzae Tip b - Aşılama

Comparison of conjugate vaccines against *Haemophilus influenzae* type b licensed in the United States

Vaccine (commercial name)	Carrier protein	Recommended age of administration	Allergy considerations
Monovalent Hib vaccines			
PRP-OMP* (PedVaxHIB)	Outer membrane protein complex of *Neisseria meningitidis*	2, 4, and 12 through 15 months	Vial stoppers contain natural rubber latex
PRP-T (ActHIB)	Tetanus toxoid	2, 4, 6, and 12 through 15 months	Vial stoppers contain natural rubber latex
PRP-T (Hiberix)	Tetanus toxoid	12 through 15 months (following primary series with PRP-OMP or ActHIB)	Tip caps of prefilled syringes may contain natural rubber latex
Combination Hib vaccines			
DTaP-IPV/PRP-T (Pentacel)	Tetanus toxoid	2, 4, 6, and 15 through 18 months•	Vial stoppers do not contain natural rubber latex
Hib-MenCYΔ (Menhibrix)	Tetanus toxoid	2, 4, 6, and 12 through 15 months	Vial stoppers do not contain natural rubber latex

Hib: *Haemophilus influenzae* type b; PRP-OMP: polyribosylribitol phosphate conjugated to outer membrane protein complex of *N. meningitidis*; PRP-T: polyribosylribitol phosphate conjugated to tetanus toxoid; DTaP: diphtheria toxoid-tetanus toxoid-acellular pertussis vaccine; IPV: inactivated polio vaccine; Hib-MenCY: combination Hib and meningococcus serogroups C and Y conjugate vaccine.

* Preferred for Native Americans and Alaskan natives.

• May be given as early as age 12 months of age, provided at least six months have elapsed since the third dose of DTaP.

Δ Recommended for use in infants at increased risk for meningococcal disease (ie, those with persistent complement pathway deficiencies or anatomic or functional asplenia [including sickle cell disease]).

Data from: Briere EC, Rubin L, Moro PL, et al. Prevention and control of Haemophilus influenzae type b disease: Recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR Recomm Rep 2014; 63:1.

H. influenzae Tip b – Aşılama

‡

AŞI	Taşıyıcı Protein	Önerilen yaş
Monovalan Hib aşıları		
PRP-OMP (PedVaxHIB)	N.meningitidisin dış membran protein komleksi	2, 4, ve 12-15 ay
PRP-T (ActHIB)	Tetanoz toksoidi	2, 4, 6, ve 12-15 ay
PRP-T (Hiberix)	Tetanoz toksoidi	12-15 ay (PedVaxHIB / ActHIB ile primer aşılamayı takiben)
Kombine Hib aşıları		
TDaP-IPV/PRP-T (Pentacel, Pentaxim)	Tetanoz toksoidi	2, 4, 6, ve 15-18 ay
Hib-Men CY (Menhibrix)	Tetanoz toksoidi	2, 4, 6, ve 12-15 ay

KOMBİNE AŞILAR

PENTACEL

PENTAXIM

MENHIBRIX

‡

H. influenzae Tip b – Rutin ve "Catch-up" Aşılama

Recommended routine schedule of administration of conjugate *Haemophilus influenzae* type b vaccine for children in the United States

Primary series (<12 months of age)	Booster (≥12 months of age)
2, 4, and 6 months for ActHIB, DTaP-IPV/PRP-T, or HibMenCY*	12 through 15 months for PRP-OMP, PRP-T (ActHIB or Hiberix), PRP-OMP-HepB, and HibMenCY*
2 and 4 months for PRP-OMP or PRP-OMP-HepB	15 through 18 months for DTaP-IPV/PRP-T•

Catch-up schedule for *Haemophilus influenzae* type b (Hib) immunization for children (<5 years) in the United States who are not at high-risk of invasive Hib disease

Current age	Catch-up regimen
<6 months	Up to three doses of PRP-T* or two doses of PRP-OMP ≥4 weeks apart before age 12 months and one dose of Hib conjugate vaccine at 12 through 15 months of age at least 8 weeks after the previous dose
7 through 11 months	Up to two doses of PRP-T* or PRP-OMP ≥4 weeks apart before age 12 months and one dose of Hib conjugate vaccine at 12 through 60 months of age• at least 8 weeks after the previous dose
12 through 14 months	Two doses of Hib conjugate vaccine ≥8 weeks apart, up to 60 months of age•
15 months through 5 years	Single dose of Hib conjugate vaccine$^{\Delta}$ up to 60 months of age•

H. influenzae Tip b – Konjuge Aşılar

‡

- **24 haftalıktan sonra invazif Hib hastalığı geçiren tüm çocuklar koruyucu immun yanıt oluştururlar ve bunları aşılamak gerekmez.**

Kontra-endikasyon:

- **<6 hafta, ciddi alerji**

Yanetkiler:

- **Lokal reaksiyonlar: ağrı, kızarıklık şişlik (%25)**
- Sistemik reaksiyonlar nadir (ateş, huzursuzluk)

Vaccine Adverse Events Reporting System (VAERS) (available at http:// www.vaers.hhs.gov)

Erişkinde geri ödemesi yapılan aşılar (SUT 22.10.2014)

- 4.5.3. Finansmanı Sağlanan Kişiye Yönelik Koruyucu Sağlık Hizmetleri
- 4.5.3-A- **Sağlık Bakanlığı Genişletilmiş Bağışıklama Programı kapsamına dahil olmayan aşı bedelleri**, kronik böbrek yetmezliği, kistik fibroz, KOAH, kanser, HIV/AIDS infeksiyonu, splenektomi olanlar ve immünosüpresif tedaviye bağlı olarak bağışıklık durumu olumsuz etkilendiği için infeksiyon hastalıklarının daha ağır seyrettiği yüksek riskli kişilerin bu durumlarını belgeleyen **sağlık raporuna istinaden ödenir.**

Erişkinde geri ödemesi yapılan aşılar (SUT 22.10.2014)

- 4.5.3-C- **Pnömokok aşısı bedeli (polisakkarit)**; **iki yaş üstü çocuklarda ve erişkinlerde**, aspleni, dalak disfonksiyonu, splenektomi (medikal, cerrahi ve otosplenektomi) yapılan veya planlanan olgular, orak hücre hastalığı, çölyak sendromu, immünosüpresif tedavi, radyasyon tedavisi, organ transplantasyonu ve HIV tüm evreleri dahil tedaviye veya hastalıklara bağlı immün yetmezlik ve immün baskılanma durumları, kronik renal hastalık ve nefrotik sendrom, kronik kalp hastalıkları, astım dahil kronik akciğer hastalıkları, siroz dahil kronik karaciğer hastalıkları, diabetes mellitus dahil herhangi bir kronik metabolik hastalığı, hemoglobinopati, doğuştan ve edinilmiş kraniyal defektler ve dermal sinüsler dahil beyin omurilik sıvısı sızıntısına sebep olan durumlarda, **hastalıklarını belirten sağlık raporuna dayanılarak** tüm hekimlerce reçete edilmesi halinde **5 yılda bir ödenir. 65 yaş ve üzerindeki kişilere rapor aranmaksızın beş yılda bir defa olmak üzere bedelleri ödenir**.

SONUÇLAR

- Bakteriyel menenjit etiyolojisinin sürekli sürveyansı
- Her ülkenin kendi sürveyans sistemi güçlendirilmeli, düzenli raporlama, insidans, taşıyıcılık, hastalığa bağlı ölüm verileri
- Aşı uygulamaları doğru bakteriyel serogrup /serotip hedeflendiğinde menenjit insidansını dramatik azaltır
- Aşı-dışı serotiplerle hastalıkda artma olsa da, bu artış, toplam İPH insidansında azalmayla kıyaslandığında küçüktür.

Her Şeyin Başı Sağlık, Sağlığın Başı Aşı

Aileniz ve kendiniz sağlığınız için aşılanın

Aşılar sadece çocuklar için değildir.

MUTLULUĞUMU ANNE VE BABAMIN AŞILARIMI TAM VE ZAMANINDA YAPTIRMASINA BORÇLUYUM

Aşılanma her çocuğun hakkıdır.

Onu Sevin, Koruyun, Aşılayın

21 -27 NİSAN AŞI HAFTASI

Sağlık Bakanlığı
Türkiye Halk Sağlığı Kurumu

her şeyin başı sağlık
sağlığın başı aşı

Aşı ile hem çocuklar hem yetişkinler hastalıklardan korunabilir.
Kendinizin ve sevdiklerinizin aşı ihtiyacı için doktorunuza danışın,
sağlığınızı koruma altına alın.

aşı çalışma grubu
turkish vaccination board

https://www.facebook.com/saglikbakanligi https://twitter.com/saglikbakanligi

T.C. Sağlık Bakanlığı

♦ TEŞEKKÜR EDERİM...

MAJOR ARTICLE

CID 2013:57 (15 December)

Effects of Immunocompromise and Comorbidities on Pneumococcal Serotypes Causing Invasive Respiratory Infection in Adults: Implications for Vaccine Strategies

Manel Luján,[1,3] Joaquín Burgos,[4] Miguel Gallego,[1,3] Vicenç Falcó,[4] Guadalupe Bermudo,[1] Anna Planes,[5] Dionisia Fontanals,[2] Maddalena Peghin,[4] Eduard Monsó,[1,3] and Jordi Rello[3,6]

- (PCV13) has recently been approved for use in immunocompromised adults. The objective was to determine the prevalence of serotypes covered by PCV13 in patients with IPD of respiratory origin
- 1094 adult patients hospitalized with IPD in 2 Spanish hospitals, 1996–2011
- the infecting serotype was determined in 993.
- In immunocompromised patients, 64% of infecting serotypes were covered by PCV13. After adjusting for age, smoking, alcohol abuse, and nonimmunocompromising comorbidities, the group of serotypes not included in either PCV13 or PPV23 were more frequently isolated in patients with immunocompromising conditions and cardiopulmonary co-morbidities.
- Serotypes 6A, 23F, 11A, and 33F were isolated more frequently in patients with immunocompromise. The subgroup analysis showed that serotype10A was also associated with HIV infection.
- Although the coverage of serotypes in the PCV13 was high, some non-PCV13-emergent serotypes are more prevalent in immunocompromised patients

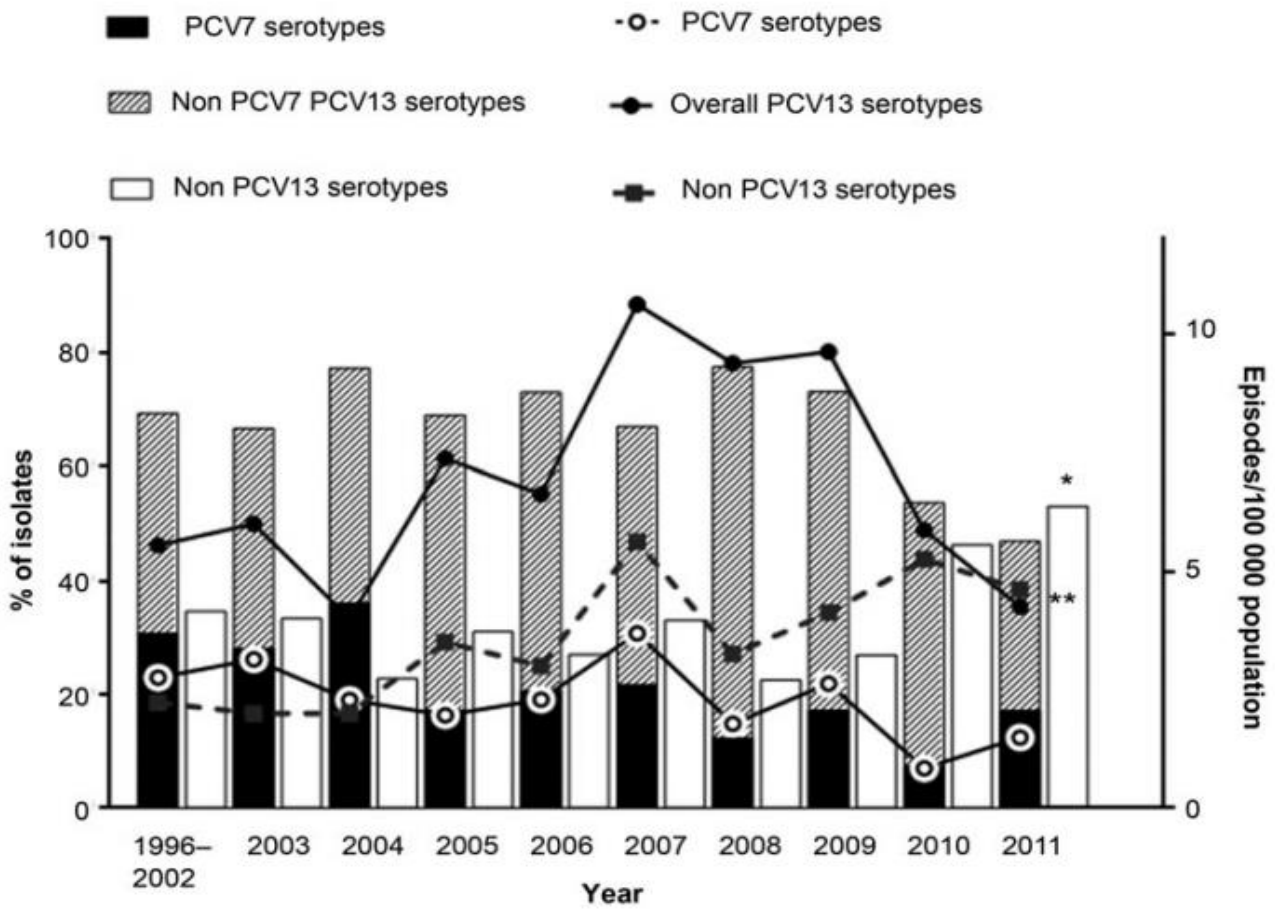


Table 3. Associations Between Individual Serotypes With >10 Isolates and Subgroups of Immunocompromised Patients[a]

Condition	Associated Serotypes	OR (95% CI)
Hematologic cancer	6A	64.47 (10.4–396)
HIV infection	10A	14.62 (3.06–69.84)
	23F	15.04 (3–75.24)
Solid tumors	11A	11.16 (2.56–48.65)
	23F	7.09 (1.52–32.94)
	33F	9.55 (2.01–45.39)

♦ Figure 1. Proportion distribution of 7-valent pneumococcal conjugate vaccine (PCV7), overall 13-valent pneumococcal conjugate vaccine (PCV13), and non-PCV13 serotypes during the 16 years of the study (bars, left axis) and incidence of infection by PCV7, overall PCV13 serotypes, and non-PCV13 sero-types (lines, right axis). *P< .05 for the proportion of non-PCV13 serotypes (2011); **P< .05 for the incidence of PCV13 serotypes (2010–2011). Abbrevia-tions: PCV7, 7-valent pneumococcal conjugate vaccine; PCV13, 13-valent pneumococcal conjugate vaccine.

‡

Comparing Haemophilus influenzae type b conjugate vaccine schedules: a systematic review and meta-analysis of vaccine trials.

- Optimum aşılama şeması ve rapel gereksinimi
- 21 veritabanı, Mayıs 2010-Haziran 2012, RKÇ, Yarı-RKÇ
- 3 primer doz rapelsiz [**3p+0], 3p+1 ve 2p+1**
- Primer aşılar ve rapeller arasında farklı intervaller
- Klinik etkinlik, nazofarengeal taşıyıcılık, immunolojik yanıt ve immun yanıt?
- 15 ülkeden 20 çalışma; 16 PRP-T
- **3 farklı aşılama şeması arasında koruyuculuk açısından fark yok**
- Aşı şemaları epidemiyolojik verilere göre programlanabilir

Low N, et al. Pediatr Infect Dis J, 2013 Nov;32(11):1245-56.

‡

- Clin Transplant. 2000 Feb;14(1):61-5.
- **Immunization of renal transplant recipients with pneumococcal polysaccharide vaccine.**
- Kazancioğlu R[1], Sever MS, Yüksel-Onel D, Eraksoy H, Yildiz A, Celik AV, Kayacan SM, Badur S.
- chronic renal failure, nephrotic syndrome and renal transplant recipients;
- however, a diminished immune response and loss of protective antibodies have been observed.
- In our prospective study, the efficacy and side effects of polyvalent pneumococcal vaccination were investigated in renal transplant recipients. A total of 21 patients (6 female, 15 male) with well-functioning renal allografts, who had transplant surgery at least 2 months before, were included in the study. The patients were stratified according to the immunosuppressive protocol and 8 received double, while 13 received triple, immunosuppressive agents. After obtaining basal serum samples, all cases were vaccinated with the 0.5 mL intramuscular administration of polyvalent polysaccharide pneumococcal vaccine (Pneumo 23 Pasteur Merieux, lot No: K 1131).
- Following a mean of 6 wk in all patients and also a mean of 12 wk in 12 patients, serum samples were again obtained to measurepneumococcal antibodies. Antibody titers following 6 and 12 wk of vaccination were significantly higher, as compared with basal values in all patients, except one. These titers did not show any statistically significant difference between double and triple therapies. There was no significant difference between the 12th and 6th wk postvaccination antibody titers. No systemic or local adverse effects were observed.
- Pneumococcal vaccination is safe and effective in patients with well-functioning renal allografts, at least in the short term. This vaccination policy may be useful for preventing invasive pneumococcal disease in immunosuppressed patients.

A. Pneumococcal Conjugate Vaccine to Prevent Pneumococcal Disease

Eligible groups

- *All children at least six weeks through 59 months of age and children 60 through 71 months with certain underlying medical conditions listed in the table below.*
- *Children 6 through 18 years of age who are at increased risk for invasive pneumococcoal disease because of anatomic or functional asplenia, including sickle cell disease, HIV-infection or other immunocompromising condition, cochlear implant, or cerebrospinal fluid leak.*

Table 1. Underlying medical conditions that are indications for pneumococcal vaccination among children

Immunocompetent persons	Chronic heart disease*
	Chronic lung disease**
	Diabetes mellitus
	Cerebrospinal fluid leaks
	Cochlear implant
Functional or anatomic asplenia	Sickle cell disease (SCD) and other hemoglobinopathies Congenital or acquired asplenia, or splenic dysfunction
Immunocompromised persons	HIV infection
	Chronic renal failure and nephrotic syndrome
	Diseases associated with immunosuppressive chemotherapy, 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 ** Including asthma if treated with high-dose oral corticosteroid therapy	
*** Includes B- (humoral) or T-lymphocyte deficiency; complement deficiencies, particularly C1, C2, C3, and C4 deficiency; and phagocytic disorders (excluding chronic granulomatous disease)	

Recommended Pneumococcal Conjugate Vaccine Schedule and Dosage Intervals

Table 2. Recommended schedules for administering doses of PCV13 among children who have not previously received PCV7 or PCV13, those incompletely vaccinated with PCV7 or PCV13 for age, and supplemental PCV13 immunization

Age	Vaccination history: total number of PCV7 and/or PCV13 doses received previously	Recommended PCV13 Regimen[1]
2–6 mo	0 doses	3 doses, 8 weeks apart; fourth dose at age 12–15 mos
	1 dose	2 doses, 8 weeks apart; fourth dose at age 12–15 mos
	2 doses	1 dose, 8 weeks after the most recent dose; fourth dose at age 12-15 mos
7–11mo	0 doses	2 doses, 8 weeks apart; third dose at 12-15 mos
	1 or 2 doses before age 7 mo	1 dose at age 7–11 mos, with a second dose at 12–15 mos (≥ 8 weeks later)
12–23 mo	0 doses	2 doses, ≥ 8 weeks apart
	1 dose before age 12 mo	2 doses, ≥ 8 weeks apart
	1 dose at ≥12 mo	1 dose, ≥ 8 weeks after the most recent dose[2]
	2 or 3 doses before age 12 mo	1 dose, ≥ 8 weeks after the most recent dose[2]
	4 doses of PCV7 or other age-appropriate complete PCV7 schedule	1 supplemental dose, ≥ 8 weeks after the most recent dose*
24–59 mo		
Healthy children	Any incomplete schedule	1 dose, ≥ 8 weeks after the most recent dose[2]
	4 doses of PCV7 or other age-appropriate complete PCV7 schedule	1 supplemental dose, ≥ 8 weeks after the most recent dose*

‡

24– 71 mo		
Children with underlying medical conditions as defined in Table 1[3]	Any incomplete schedule of ≤2 doses	2 doses, one ≥ 8 weeks after the most recent dose and another dose ≥ 8 weeks later
	Any incomplete schedule of 3 doses	1 dose, ≥ 8 weeks after the most recent dose
	4 doses of PCV7 or other age-appropriate complete PCV7 schedule	1 supplemental dose, ≥ 8 weeks after the most recent dose*
6–18 years		
Children who are at increased risk for invasive pneumococcoal disease as defined in footnote 4.	Not previously vaccinated with PCV 13	1 dose

Footnotes:

1) Minimum interval between doses is 8 weeks except for children vaccinated at age <1 year, for whom minimum interval between doses is 4 weeks.

2) No additional PCV13 doses are indicated for children 12 through 23 months of age who have received 2 or 3 doses of PCV7 before age 12 months and at least 1 dose of PCV13 at age 12 months or older.

3) For children with underlying medical conditions (see Table 1), PCV13 is indicated through 71 months of age.

4) Includes children with anatomic or functional asplenia, including sickle cell disease, HIV-infection or other immunocompromising condition, cochlear implant, or cerebrospinal fluid leak.

* A single supplemental dose of PCV13 given at least 8 weeks after the last dose of PCV7 is recommended for all children 14 through 59 months of age who have received 4 doses of PCV7 or other age-appropriate, complete PCV7 schedule (fully vaccinated with PCV7). For children who have underlying medical conditions, a supplemental dose is recommended through 71 months of age.

‡

B. 23-valent Pneumococcal Polysaccharide Vaccine (PPSV23) after PCV7 or PCV13 to Prevent Pneumococcal Disease

Eligible groups

Children and adolescents 2 through 18 years with certain underlying medical conditions listed in Table 1 above or children 2 through 18 years who are Alaska Native or American Indian.

Recommended Pneumococcal Polysaccharide Vaccine Schedule and Dosage Intervals

Table 3. Schedule for vaccination with PPSV23 after PCV13 for children ≥2 years of age with underlying medical conditions*

Group	Schedule for PPSV23	Revaccination with PPSV23
Children who are immunocompromised,** have sickle cell disease, or functional or anatomic asplenia	1 dose of PPSV23 administered at age ≥2 yrs and ≥ 8 weeks after last indicated dose of PCV13	1 dose 5 years after the first dose of PPSV23
Immunocompetent** children with chronic illness	1 dose of PPSV23 administered at age ≥2 yrs and ≥ 8 weeks after last indicated dose of PCV13	Not recommended

*Doses of PCV13 should be completed before PPSV23 is given. No more than two PPSV23 doses are recommended.

**See Table 1 for definitions of immunoncompromised and immunocompetent with chronic illness.

Clinical Infectious Diseases Advance Access published February 13, 2014

MAJOR ARTICLE

Effectiveness of the 23-Valent Pneumococcal Polysaccharide Vaccine Against Community-Acquired Pneumonia in the General Population Aged ≥60 Years: 3 Years of Follow-up in the CAPAMIS Study

Olga Ochoa-Gondar,[1] Angel Vila-Corcoles,[1] Teresa Rodriguez-Blanco,[2] Frederic Gomez-Bertomeu,[3] Enric Figuerola-Massana,[4] Xavier Raga-Luria,[5] and Imma Hospital-Guardiola[1]

[1]Primary Care Service Camp de Tarragona, Institut Catala de la Salut, Tarragona; [2]Primary Care Research Institute (IDIAP Jordi Gol) and Autonomous University of Barcelona; [3]Department of Microbiology and [4]Department of Otolaryngology, Hospital Joan XXIII, and [5]Department of Laboratory and Microbiology, Hospital Santa Tecla, Tarragona, Spain

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Polysaccharide Conjugate Vaccine against Pneumococcal Pneumonia in Adults

M.J.M. Bonten, S.M. Huijts, M. Bolkenbaas, C. Webber, S. Patterson, S. Gault, C.H. van Werkhoven, A.M.M. van Deursen, E.A.M. Sanders, T.J.M. Verheij, M. Patton, A. McDonough, A. Moradoghli-Haftvani, H. Smith, T. Mellelieu, M.W. Pride, G. Crowther, B. Schmoele-Thoma, D.A. Scott, K.U. Jansen, R. Lobatto, B. Oosterman, N. Visser, E. Caspers, A. Smorenburg, E.A. Emini, W.C. Gruber, and D.E. Grobbee

N ENGL J MED 372;12 NEJM.ORG MARCH 19, 2015

- Aşı-tipi İPH önlemede %75 etkili

- Studies have reported contrasting results, noting either a reduction or no effect on all-cause pneumonia hospitalizations.
- a study recently completed in the US suggests that the PCV7 serotypes remain a notable cause of CAP in US adults 10 to 12 y post-introduction of PCV7.
- even in settings of high uptake of conjugate vaccine in the pediatric population there remains a need to offer direct protection to prevent pneumococcal CAP.
- adult age- and risk-based recommendations for PCV13 are still expected to be cost-effective

- HOLLINGSWORTH

- **Koruyucu antikor düzeyi:** net bilinmiyor (≥0.35 mcg/mL one month after primary immunization)
- PCV13 serotypes currently account for approximately one third of IPD among adults aged 65 years and older
- In addition, 11 serotypes that account for 25% of IPD in adults aged 65 years and older are included in PPSV23 but not in PCV13.
- **widespread use of pneumococcal conjugate vaccines** → emergence of "replacement strains (nonvaccine pneumococcal serotypes that have appeared as colonizers of the nasopharynx)"

Comparison of properties of the pneumococcal polysaccharide and conjugate vaccines

	Polysaccharide vaccine	Conjugate polysaccharide vaccine
Stimulates antibodies in infants and toddlers	No	Yes
Stimulates antibodies in healthy adults	Yes	Yes
Stimulates antibodies in immunocompromised adults	+/-	+/-
Antibodies are long-lasting	+/-	+/-
Primes immunologically for enhanced responses	No	Possibly
Stimulates mucosal immunity, resulting in decreased colonization	No	Yes
Exhibits herd effect (secondary protection of unvaccinated individuals)	No	Yes
Use is associated with replacement strains	No	Yes

- PPSV23 provides protection against IPD but for which no consensus exists regarding protection against nonbacteremic pneumococcal pneumonia*
- In two randomized, multicenter, immunogenicity studies conducted in the United States and Europe, adults aged 50 years and older received a single dose of PCV13 or PPSV23** Functional antibody responses were measured 1 month after vaccination using an opsonophagocytic activity (OPA) assay.
- Safety of PCV13: in PPSV23-naïve and PPSV23-experienced adults aged 50 years and older (3). Overall incidence of serious adverse events reported within 1 month of an initial study dose of PCV13 or PPSV23 ranged from 0.2% to 1.7%. From 1 month to 6 months after an initial study dose, the overall incidence of serious adverse events ranged from 1.2% to 5.8% among persons vaccinated with PCV13 and 2.4% to 5.5% among persons vaccinated with PPSV23.

***CDC. Updated recommendations for prevention of invasive pneumococcal disease among adults using the 23-valent pneumococcal polysaccharide vaccine (PPSV23). MMWR 2010;59:1102–6.**