Splenektomili Hastada Aşılama

Dr. Özlem GÜZEL TUNÇCAN
Gazi Üniversitesi Tıp Fakültesi
Klinik Mikrobiyoloji ve Enfeksiyon Hastalıkları AD

İmmun yetmezlik > sağlıklı kişiler

- Enfeksiyonlara duyarlılık
- Enfeksiyonun şiddeti ve süresi
- Komplikasyonlar
- Mortalite

Bu nedenle özellikle aşı ile korunulabilen hastalıklara karşı korunma zorunludur

Uzun süreli korunma sağlanması açısından tekrar immünizasyon önerilmektedir

Ljungman P. Bone Marrow Transplant. 2009 ;44:521-6.

Splenektomi hastasında neden aşı gerekli

Splenektomi sonrası sepsis,

- Dalak fonksiyonları bozulan veya splenektomi yapılan hastalarda 24 saat içinde gelişen ve klinik olarak kötüleşen bir tablo olarak tanımlanır

- Yaygın damar içi pıhtılaşması nedeniyle birkaç saat içinde sepsise girmekte ve **mortalite hızları % 50'lere** kadar yükselebilmektedir

Korunma

- Aşılar,
- antibiyotik profilaksisi,
- eğitim ve
- erken empirik antibiyotik tedavileri ile ilgilidir.

Clinical Infectious Diseases

MAJOR ARTICLE

Overwhelming Postsplenectomy Infection: A Prospective Multicenter Cohort Study

Christian Theilacker,[1,2,a] Katrin Ludewig,[5] Annerose Serr,[3] Julia Schimpf,[3] Jürgen Held,[3,7] Martin Bögelein,[1,2,4] Viola Ba… Klaus Kogelmann,[8] Sigrun Frieseke,[9] Ralph Bogdanski,[10] Frank M. Brunkh…st,[5,6,b] and Winfried V. Kern[2,b]; for the S… Fulminant Infection (SPLEEN OFF) Study Group[c]

[1]Center for Chronic Immunodeficiency, [2]Division of Infectious Diseases, Department of Medici… Center, [5]Center for Sepsis Control and Care, and [6]Paul Martini Sepsis Research Group, Jena U… Universität Erlangen-Nürnberg, [8]Klinikum Emden, [9]University Medical Center, Greifswald, and

Almanya, prospektif, YBÜ
52 splenektomili ve 52 kontrol grubu hast
Toplum kökenli Sepsis ve septik şoklu hastalar
S.pneumoniae en sık etken ve sepsise neden olduğu saptanmış

Background. Recent population-based cohort studies have … causing severe infection in patients after splenectomy. The aim … sentation of patients with overwhelming postsplenectomy infec…

Methods. In a prospective cohort study in 173 German inte… and community-acquired severe sepsis/septic shock. Clinical a… were assessed.

Results. Fifty-two patients with severe sepsis or septic shock … were included. OPSI patients more often had a history of malignancy (38% vs 17%; $P = .016$) and … index (24 kg/m^2 vs 28 kg/m^2; $P = .004$). *Streptococcus pneumoniae* was detected more frequently in OPSI patients (42% vs 12% without asplenia; $P < .001$) and more frequently manifested as bloodstream infection (31% vs 6%; $P = .002$). Gram-negative infection was similar in both groups (12% vs 19%; $P = .157$). Pneumococcal vaccine coverage of OPSI patients was low overall (42% vs 8% among patients without asplenia; $P < .001$). Purpura fulminans was a frequent complication, developing in 19% of OPSI patients vs 5% of patients without asplenia ($P = .038$). The interval between splenectomy and OPSI was 6 years (range, 1 month–50 years). On multivariable Poisson regression, asplenia was the only predictive variable independently associated with pneumococcal sepsis (adjusted relative risk, 2.53 [95% confidence interval, 1.06–6.08]).

Aşılama

- Dalak esas görevi kapsüllü bakterilerin opsonizasyonu için gerekli olan IgM üretimi yapılan yerlerdir

- *Strep pneumoniae, Neisseria meningitidis, Haemophilus influenzae type b* gibi kapsüllü bakteriler asplenik hastalarda önemli enfeksiyon nedeni olmaktadır

Aşılama zamanı

Splenektomili hastada

- Elektif operasyondan; 14 gün önce
- Acil operasyondan; 14 gün sonra

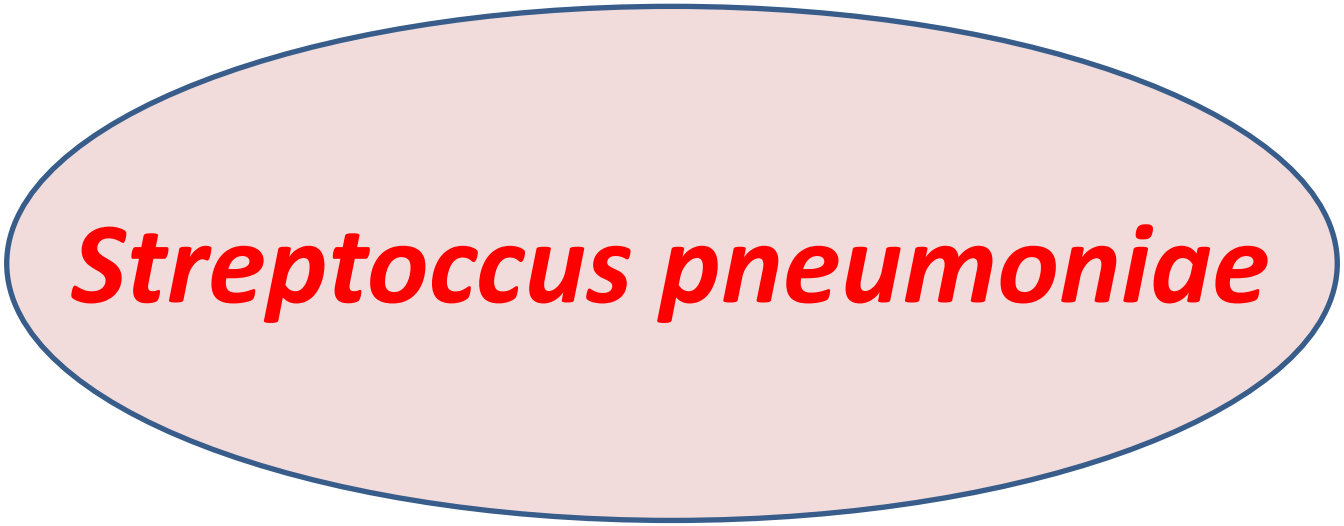
Splenektomili bir hasta yoğun kemoterapi veya immunsupresyon alacaksa aşıların 3 ay ertelenmesi önerilir

Aşılama zamanı

- CONCLUSIONS: Postvaccinatio… …m antibo… …t from norma… …ation (1, 7, … …rmal, functi… …er functi… …nd seroty… …y) vaccin…

Travma sonrası Splenektomize hastaların pnömokok aşısı (1.,7.,14. gün) yapıldıktan sonra, aşı sonrası serum antikor IgG konsantrasyonları kontrol grup ile arasında istatistiksel farklılık saptanmamış ve en iyi cevabın 14. günde belirlenmiş

Shatz DV Immune responses of splenectomized trauma patients to the 23-valent pneumococcal polysaccharide vaccine at 1 versus 7 versus 14 days after splenectomy. J Trauma. **1998**;44(5):760-5 [US,Florida]


Streptoccus pneumoniae

Splenektomili hasta klavuz önerileri

- Fonksiyonel ve asplenik hastalara PCV13 yapılmışsa 8 hafta sonra ek doz olarak PPSV23 önerilmekte
- Eğer PPSV23 yapılmışsa 1 yıl sonra PCV 13 yapılması önerilmekte(19 yaş üzeri)
- ACIP splenektomili çocuk ve erişkinlere PPSV23 polisakkarit aşıyı 5 yılda bir önermekte
- 65 yaş üzerinde splenektomili kişilere bir doz PPSV23 reimmunizasyonda önerilmekte

Pasternack MS, Prevention of sepsis in the asplenic patient uptodate, April 2017
https://www.uptodate.com/contents/prevention-of-sepsis-in-the-asplenic-patient

Polisakkarit aşı (PPSV23)

- Polisakkarit aşı (PPSV23) 24 ay üzerindeki çocuklarda öneriliyor
- Çocukluk çağı aşı takviminde yer almaz
- Koruyuculuk süresi sınırlıdır (3-5 yıl) tekrarlayan dozlar ile uyarılabilir bir immün yanıt oluşmaz

Pasternack MS, Prevention of sepsis in the asplenic patient uptodate, April 2017
https://www.uptodate.com/contents/prevention-of-sepsis-in-the-asplenic-patient

Journal of Internal Medicine 2004; 255: 664–673

A prospective study on antibody response to repeated vaccinations with pneumococcal capsular polysaccharide in splenectomized individuals with special reference to Hodgkin's lymphoma

O. LANDGREN[1], M. BJÖRKHOLM[1], H. B. KONRADSEN[2], M. SÖDERQVIST[1], B. NILSSON[3], A. GUSTAVSSON[4], U. AXDORPH[1], M. KALIN[5] & G. GRIMFORS[1]

From the [1]Division of Hematology, Department of Medicine, Karolinska Hospital and Institutet, Stockholm, Sweden; [2]World Health Organization Collaborating Centre for Reference and Research on Pneumococci, Statens Seruminstitut, Copenhagen, Denmark; [3]Unit of Cancer Epidemiology, Karolinska Hospital and Institutet, Stockholm, Sweden; [4]Department of Oncology, University Hospital, Lund, Sweden; and [5]Division of Infectious Diseases, Department of Medicine, Karolinska Hospital and Institutet, Stockholm, Sweden

Abstract. Landgren O, Björkholm M, Konradsen HB, Söderqvist M, Nilsson B, Gustavsson A, Axdorph U, Kalin M, Grimfors G (Karolinska Hospital and Institutet, Stockholm, Sweden; World Health Organizatio... Centre for Reference and Resea... Statens Seruminstitut, C... Unit of Cancer Epidemiolo... and Institutet, Stockholm, ... Hospital, Lund, Sweden). ... antibody response to repe... pneumococcal capsular ... splenectomized individuals ... to Hodgkin's lymphoma. *J* ... 664–673.

Background. Splenectomy i... long risk of overwhelming p... (OPSI), mainly caused b... encapsulated bacteria s... *pneumoniae*. Despite extens... the mortality and morbidity ... present study was based ... predefined vaccination algor... 23-valent pneumococcal ... monitoring of pneumococcal antibody levels. ... antibody levels of splenectomized Hodgkin's lymphoma (HL) patients were compared with those patients splenectomized due to immune-mediated cytopenias [autoimmune haemolytic anaemia (AIHA) and immune thrombocytopenic purpura (ITP)] and also individuals who were splenectomized because of trauma (TRAUMA).

Methods. A total of 311 spl... were included in this ... AIHA; 60 ITP; 28 ... individual anti-PS... enzyme-li...

...low-up. No severe ... reported. Amongst 124 ... HL patients, 10 OPSI were ... patients during the study period. ... patients, a middle-aged female, died as a result of fulminant pneumococcal bacteraemia, which was her third OPSI during a 7-year period.

Conclusions. A significant response to pneumococcal PS vaccination was found in all three groups (HL, AIHA/ITP and TRAUMA) of splenectomized patients. Importantly, both primary and repeated vaccinations were safe. Until further

2004 yılı, isviçre, 311 splenektomi (208-Hodgkin lenfoma, 60-ITP, 15-otoimmun hemolitik ve 28- travma) nedeniyle splenektomize hastaların PPSV23 aşı sonrası
7 yıl takip, 10 Hodgkin hastasında OPSI bağlı fulminan bakteremi gelişmesi nedeniyle primer ve tekrar aşıların önemli olduğu vurgusu yapılmış

Administration of Protein-Conjugate Pneumococcal Vaccine to Patients Who Have Invasive Disease after Splenectomy Despite Their Having Received 23-Valent Pneumococcal Polysaccharide Vaccine

Daniel M. Musher,[1,3,4] Heather Ceasar,[1] Erna M. Kojic,[3] Benjamin L. Musher,[3] Joseph C. Gathe, Jr.,[3] Sandra Romero-Steiner,[5] and A. Clinton White, Jr.[2,3,4]

[1]Infectious Disease Section, Michael E. DeBakey Veterans Affairs Medical Center, [2]Ben Taub General Hospital, and Departments of [3]Medicine and [4]Molecular Virology and Microbiology, Baylor College of Medicine, Houston, Texas; [5]Centers for Disease Control and Prevention, Atlanta, Georgia

Patients who undergo splenectomy are at greatly increased risk for overwhelming pneumococcal bacteremia and death. Twenty-three–valent pneumococcal polysaccharide vaccine (PPV-23), which contains capsular polysaccharides (PSs) from 23 common serotypes of *Streptococcus pneumoniae*, is strongly recommended for such patients. The capacity to respond to PPV-23 by producing immun tically regulated. Some proportion of adults do not respond and, despite postsplene may remain susceptible to recurrent pneu ococcal sepsis. Here, we describ eumococcal bacteremia after undergoing s tomy despite having tavalent protein-conjugate pneumococcal va IgG to all 7 PSs; in one of the patients, fun itro and in vivo. Recurrent pneumococcal b ate a genetically regulated failure to respon ch patients.

PPV23 aşı sonrası splenektomili hastada pnömokokal bakteremi gelişen iki hasta PCV-7 konjugat aşı uygulaması sonrası yüksek seviyelerde Ig G saptanmış

Morbidity and Mortality Weekly Report

Use of 13-Valent Pneumococcal Conjugate Vaccine and 23-Valent Pneumococcal Polysaccharide Vaccine for Adults with Immunocompromising Conditions: Recommendations of the Advisory Committee on Immunization Practices (ACIP)

MMWR / October 12, 2012 / Vol. 61 / No. 40

PCV13 Vaccine in Adults

PCV13 was licensed by the Food and Drug Administration (FDA) for prevention of IPD and otitis media in infants and young children in February 2010, supplanting PCV7 (*6*). PCV13 is identical in formulation for the seven common serotypes in PCV7, but it includes six additional antigens. One dose of PCV13 is recommended by ACIP for children aged 6–18 years with high-risk conditions such as functional or anatomic asplenia, immunocompromising conditions, cochlear implants, or CSF leaks. In December 2011, FDA licensed PCV13 for prevention of pneumonia and IPD in adults aged ≥50 years (*7*). The license for adult use was granted under FDA's

Polisakkarit konjuge aşılar (PCV)

- 2000; PCV7, 60 ay altı çocuklarda
- 2010; PCV13, 71. aya kadar
- 2011; PCV13, 50 yaş ve üzeri
  - invaziv pnömokok infeksiyonlar ve pnömoni için kullanımı onaylamıştır

- ✓ 2 yaş altında kullanılabilir
- ✓ Mukozal koruma sağlar,
- ✓ aşı içeriğinde yer alan serotiplerin nazofaringeal taşıyıcılığı azalır
- ✓ Antibiyotik direnci ile ilişkisi bilinen serotiplere bağlı infeksiyonlarda azalma

Pnömokok aşı

- İnvaziv pnömokok hastalığını yapan serotipleri önlemede pnömokok aşı (özellikle konjugat aşı) %80 oranında etkilidir
- **Polisakkarit konjuge aşılar (PCV);** 2 aydan büyük tüm bebeklere standart aşılama protokolünde
- Rutin şemada 4 doz PCV13 (2, 4, 6, 12 veya 15 ay) ek olarak asplenik çocuklarda 24 ay üzerinde PPSV23 verilmesi önerilmekte

✓ iki aşı arası en az 8 hafta olmalıdır.

- Eğer PVC13 verilirse 8 hafta sonra PPSV23 yapılmasını önermekte

- İkinci doz aşı ilk dozdan 5 yıl sonra önerilmekte

Pasternack MS, Prevention of sepsis in the asplenic patient uptodate, April 2017
https://www.uptodate.com/contents/prevention-of-sepsis-in-the-asplenic-patient

Summary of recommended intervals, by risk and age groups, for persons with indications to receive PCV13 and PPSV23 sequence — Advisory Committee on Immunization Practices, United States

Risk group/underlying medical condition	Intervals for PCV13-PPSV23 sequence, by age group				Intervals for PPSV23-PCV13 sequence, by age group			
	24 to 71 months	6 to 18 years	19 to 64 years	≥65 years	24 to 71 months	6 to 18 years	19 to 64 years	≥65 years
Persons with functional or anatomic asplenia ▪ Sickle cell disease/other hemoglobinopathy ▪ Congenital or acquired asplenia	≥8 weeks	≥8 weeks	≥8 weeks	≥8 weeks	≥8 weeks	≥8 weeks	≥1 year	≥1 year

Pasternack MS, Prevention of sepsis in the asplenic patient uptodate, April 2017
https://www.uptodate.com/contents/prevention-of-sepsis-in-the-asplenic-patient

Yakalama şeması

- 24-71 ay asplenik çocuklarda
  - 24 aydan önce eksik aşılama (0,1 veya iki doz PCV 7/13) yapılmış çocuklar için 2 doz PCV13 en az 8 hafta arayla önerilir
  - 3 doz PCV(7/13) yapılmış çocuklara ise son dozda en az 8 hafta ara olmak şartı ile tek doz PCV13 önerilmekte (primer şemayı yakalamak için)
- 6-18 yaş önceden aşılı değilse tek doz PCV13 ile aşıladıktan sonra 8 hafta sonra tek doz PPSV23 önerilmekte
- Pnömokok aşı serisi tamamlanan; PPSV23 öncelikle tercih edilmemeli, eğer PCV13 verilirse 8 hafta sonra PPSV23 yapılmalı sonra 5 yılda bir PPSV23 yapılmalı

Pasternack MS, Prevention of sepsis in the asplenic patient uptodate, April 2017
https://www.uptodate.com/contents/prevention-of-sepsis-in-the-asplenic-patient

Schedule for vaccination using 23-valent polysaccharide vaccine (PPSV23) after 13-valent pneumococcal conjugate vaccine (PCV13) for children aged ≥2 years with underlying medical conditions

Group	Schedule for PPSV23	Revaccination with PPSV23
Children who have sickle cell disease	1 dose of PPSV23 administered at age ≥2 years and ≥8 weeks after last indicated dose of PCV13	1 dose 3 or 5 years after the first dose of PPSV23*
Children who have other types of functional or anatomic asplenia or are immunocompromised	1 dose of PPSV23 administered at age ≥2 years and ≥8 weeks after last indicated dose of PCV13	1 dose 5 years after the first dose of PPSV23

* For patients with sickle cell disease, some experts recommend an interval of three years between the first and second dose of PPSV23[1,2], whereas others recommend an interval of five years[3-6].

Chronic heart disease, chronic lung disease, diabetes mellitus, cerebrospinal fluid leaks, or cochlear implant.

Pasternack MS, Prevention of sepsis in the asplenic patient uptodate, April 2017
https://www.uptodate.com/contents/prevention-of-sepsis-in-the-asplenic-patient

Ek doz

- Asplenik çocuklarda 4 doz PCV 7 ile tamamlanmış ise, ek doz PCV13, 5 yaşa kadar önerilmekte
- Asplenik 6-18 yaş; PCV7 veya PPSV23 verilmişse 8 hafta sonra PCV13 önerilmekte
- Asplenik 19-64 yaş; PPSV23aşıdan 1 yıl sonra PCV13
- Asplenik 6-18 yaş arasındakiler en azından tek doz PCV13 tek doz, ek olarak verilmelidir.

Çocuk ve erişkin tekrar aşılaması

- Avrupa da çoğunlukla asplenik bireylere 5 yılda bir PPSV23 ile tekrar aşılamaları önerilmektedir. (antikor seviyelerini korumak için)
- Bunun tersine Amerika da çocuk ve erişkinde farklı aşı önerileri bulunmakta
- Başlangıç aşılama ACIP önerileri ile yapıldıysa sadece bir kez 5yıl sonra PPSV23 ile tekrar aşılama (65 yaş üstü splenektomili bireylere)
- 65 yaş altında 5 yıldan daha uzun sürelerde de aşı önerilmektedir

İnvaziv hastalık sonrası aşılama

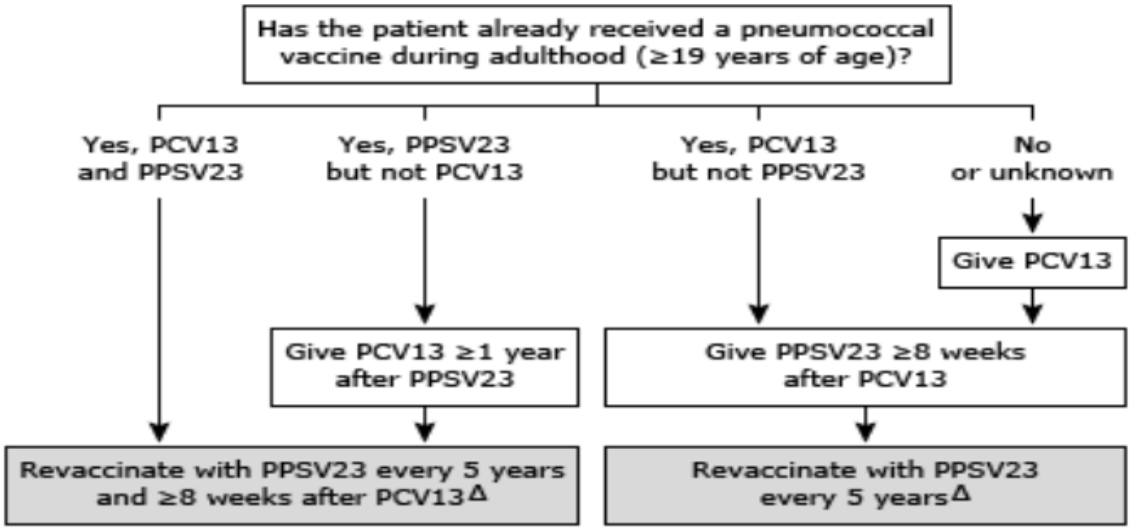
- Çocuklarda tam doz aşılamasına rağmen invaziv hastalık olabilmekte
- İnvaziv hastalıkta, aşı serotiplerine karşı yeterli koruma sağlanamamakta
- Bu bireylerde pnömokoklara serotiplerine karşı IgG saptanamamış
- Konjugat aşıdan verildikten sonra PPSV 23 ile aşılananlarda tüm polisakkarit aşı türlerine karşı yüksek seviyede T hücre bağımlı hafıza cevabı oluşmakta

Pasternack MS, Prevention of sepsis in the asplenic patient uptodate, April 2017
https://www.uptodate.com/contents/prevention-of-sepsis-in-the-asplenic-patient

conjugate vaccine (PCV13) and 23-valent pneumococcal polysaccharide vaccine (PPSV23) for children at high risk* of pneumococcal disease

Age	Previous doses	Recommendations
Anatomic or functional asplenia (including sickle cell disease), immunocompromising condition (including HIV, chronic renal failure, nephrotic syndrome), cochlear implant, or cerebrospinal fluid leak		
6 through 18 years	No doses of PPSV23 or PCV13 (0 to 4 doses of PCV7)	1 dose of PCV13
		1 dose of PPSV23, at least 8 weeks after PCV13
		Second dose¶ of PPSV23, 3 or 5 years$^{\Delta}$ after the first dose for children with sickle cell disease, 5 years after the first dose for children who have other types of functional or anatomic asplenia or are immunocompromised$^{\diamond}$
	1 dose of PCV13 and no doses of PPSV23	1 dose of PPSV23, at least 8 weeks after PCV13
		Second dose¶ of PPSV23, 3 or 5 years$^{\Delta}$ after the first dose for children with sickle cell disease, 5 years after the first dose for children who have other types of functional or anatomic asplenia or are immunocompromised$^{\diamond}$
	1 dose of PPSV23 and no doses of PCV13 (0 to 4 doses of PCV7)	1 dose of PCV13, at least 8 weeks after first dose of PPSV23
		Second dose¶ of PPSV23, 3 or 5 years$^{\Delta}$ after the first dose for children with sickle cell disease, 5 years after the first dose for children who have other types of functional or anatomic asplenia or are immunocompromised$^{\diamond}$

UpToDate recommendations* for pneumococcal vaccination in asplenic¶ adults (≥19 years) in the United States



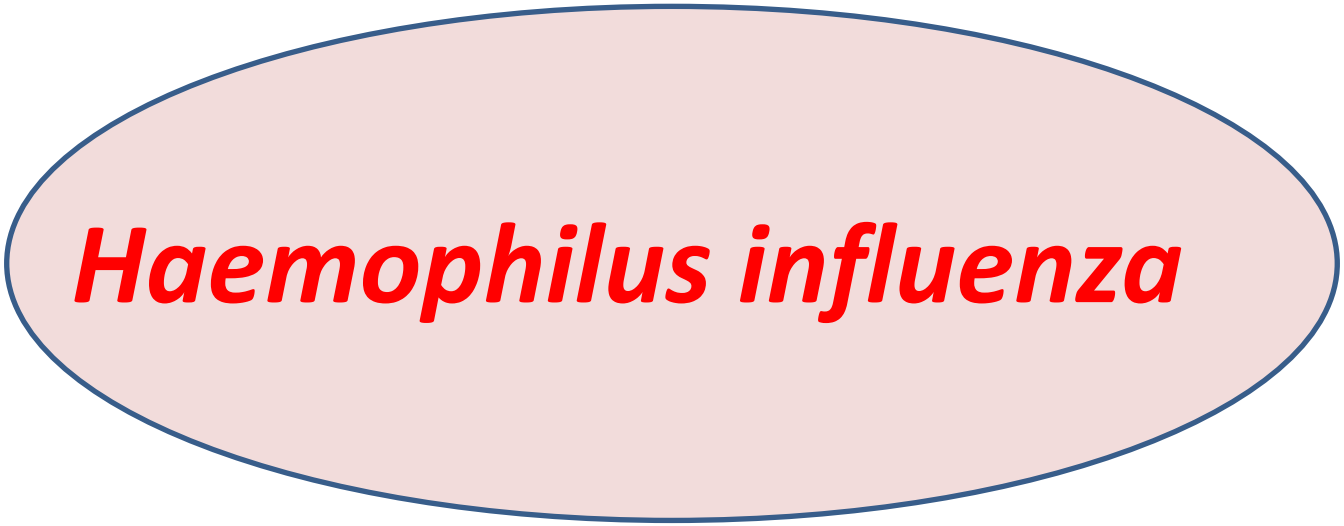
PCV13: 13-valent pneumococcal conjugate vaccine (Prevnar); PPSV23: 23-valent pneumococcal polysaccharide vaccine (Pneumovax).

* UpToDate's recommendations differ from those of the United States Advisory Committee on Immunization Practices (ACIP). Refer to the relevant UpToDate topics for additional information.

¶ Anatomic or functional asplenia that are indications for pneumococcal vaccination are:

- Sickle cell disease, other hemoglobinopathies
- Congenital or acquired asplenia
- Splenic dysfunction
- Splenectomy

Δ For asplenic patients, UpToDate recommends revaccination with PPSV23 every 5 years. This differs from the ACIP guidelines, which recommend that patients <65 years of age receive 2 doses of PPSV given at least 5 years apart; if both doses were given before age 65, the ACIP recommends an additional dose of PPSV23 at or after age 65 and at least 5 years after the previous dose.


Haemophilus influenza

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)

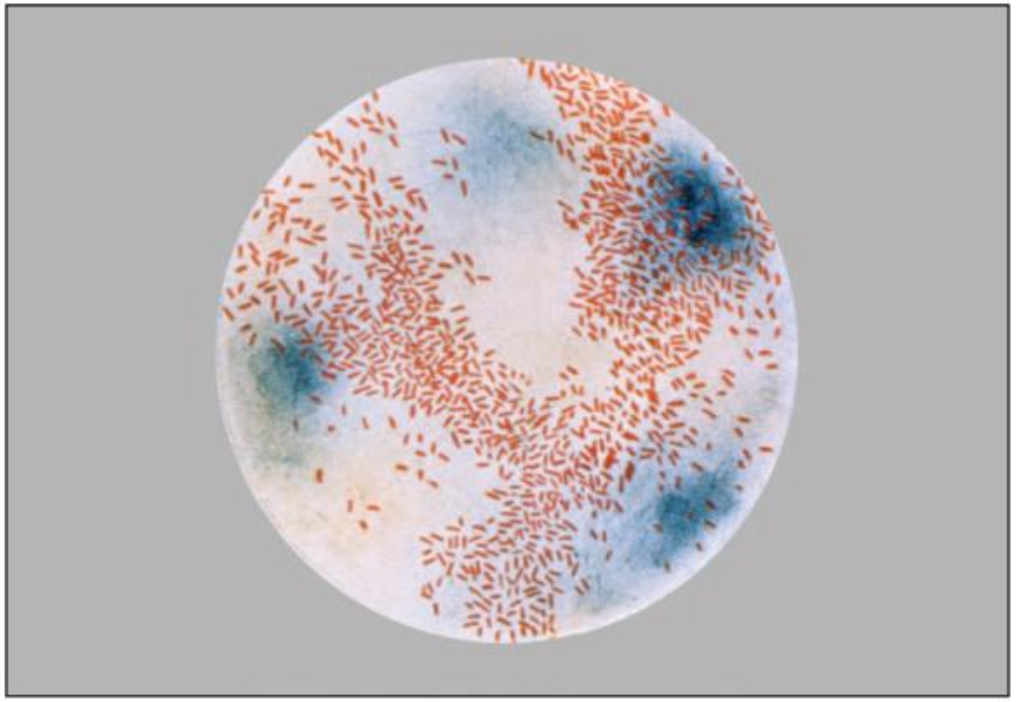
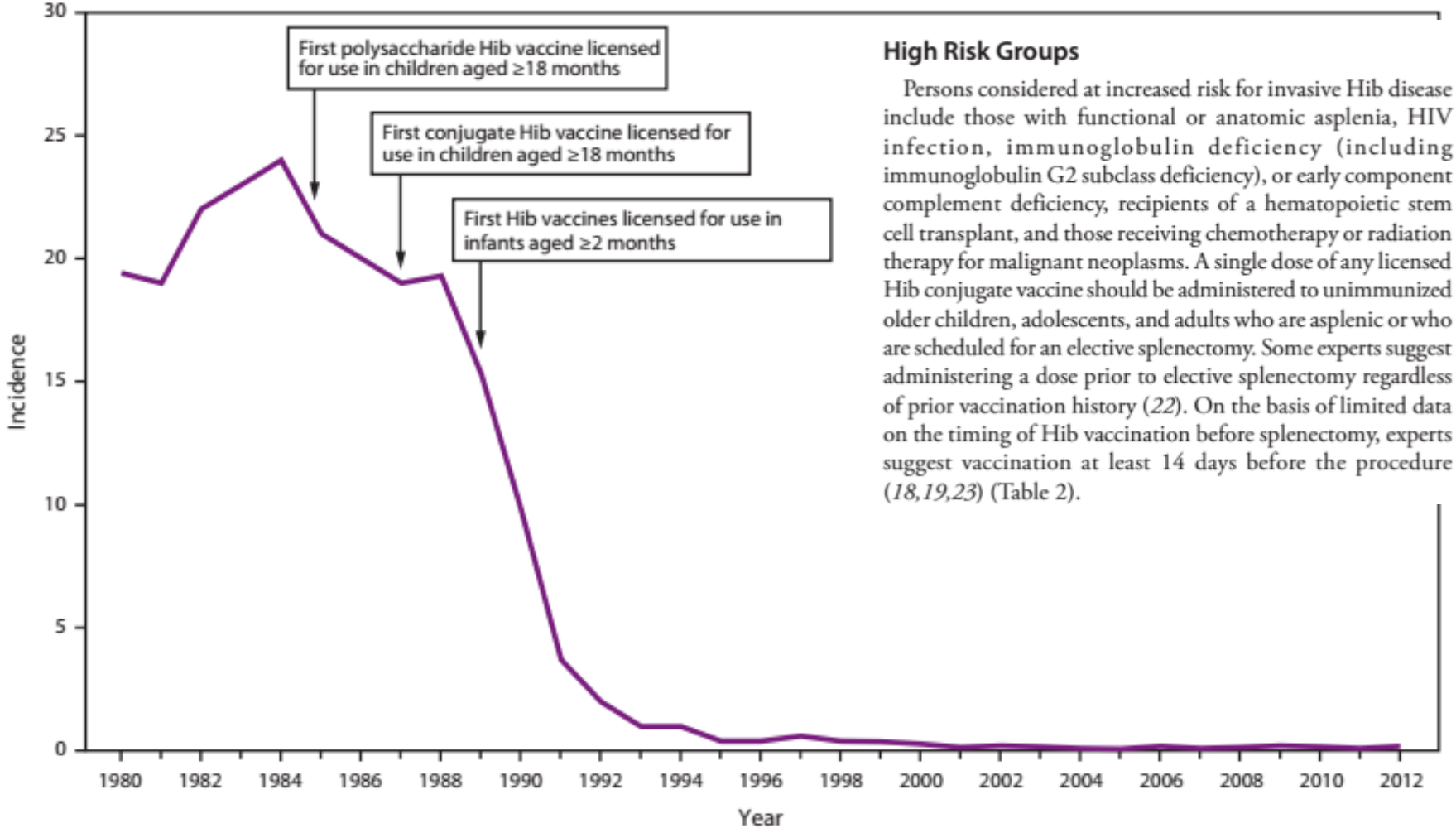


FIGURE 1. Estimated annual incidence* of invasive *Haemophilus influenzae* type b (Hib) disease in children aged <5 years — United States, 1980–2012



High Risk Groups

Persons considered at increased risk for invasive Hib disease include those 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. A single dose of any licensed Hib conjugate vaccine should be administered to unimmunized older children, adolescents, and adults who are asplenic or who are scheduled for an elective splenectomy. Some experts suggest administering a dose prior to elective splenectomy regardless of prior vaccination history (*22*). On the basis of limited data on the timing of Hib vaccination before splenectomy, experts suggest vaccination at least 14 days before the procedure (*18,19,23*) (Table 2).

Sources: 1980–1997: National Bacterial Meningitis Reporting System and National Notifiable Diseases Surveillance (NNDSS) data; Adams WG, Deaver KA, Cochi SL, et al. Decline of childhood *Haemophilus influenzae* Type b (Hib) disease in the Hib vaccine era. JAMA 1993;269:221–6; CDC. Progress toward elimination of *Haemophilus influenzae* type b disease among infants and children—United States, 1987–1995. MMWR 1996;45:901–6; CDC. Progress toward elimination of *Haemophilus influenzae* type b disease among infants and children—United States, 1987–1997. MMWR 1998;47:993–8. 1998–2009: NNDSS and Active Bacterial Core Surveillance (ABCs) data. 2010–2012: ABCs cases estimated to the U.S. population.

* Per 100,000 population.

TABLE 2. Guidance for *Haemophilus influenzae* type b (Hib) vaccination in high-risk groups

High-risk group*	Hib vaccine guidance
Patients aged <12 mos	Follow routine Hib vaccination recommendations
Patients aged 12–59 mos	If unimmunized or received 0 or 1 dose before age 12 mos: 2 doses, 8 wks apart If received ≥2 doses before age 12 mos: 1 dose 8 wks after last dose If completed a primary series and received a booster dose at age ≥12 mos: 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 mos following therapy completion
Patients aged ≥15 mos undergoing elective splenectomy	If unimmunized:§ 1 dose prior to procedure¶
Asplenic patients aged >59 mos and adults	If unimmunized:§ 1 dose
HIV-infected children aged ≥60 mos	If unimmunized:§ 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 wks apart) beginning 6–12 mos after transplant

* 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 (**Source:** Rubin LG, Levin MJ, Ljungman P, et al. 2013 IDSA clinical practice guideline for vaccination of the immunocompromised host. Clin Infect Dis 2013;[Epub ahead of print] doi: 10.1093/cid/cit684).

§ 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 (**Sources:** CDC. General recommendations on immunization: recommendations of the Advisory Committee on Immunization Practices [ACIP]. MMWR 2011;60[No. RR-2]; CDC. Recommendations of the Advisory Committee on Immunization Practices (ACIP): use of vaccines and immune globulins in persons with altered immunocompetence. MMWR 1993;42[No. RR-4]; Rubin LG, Levin MJ, Ljungman P, et al. 2013 IDSA clinical practice guideline for vaccination of the immunocompromised host. Clin Infect Dis 2013;[Epub ahead of print] doi: 10.1093/cid/cit684.) Some experts suggest administering a dose prior to elective splenectomy regardless of prior vaccination history (**Source:** American Academy of Pediatrics. *Haemophilus influenzae* infections. In: Pickering L, Baker C, Kimberlin D, Long S, eds. Red book: 2012 report of the Committee on Infectious Diseases. Elk Grove Village, IL: American Academy of Pediatrics; 2012:345–52).

Haemophilus influenza konjugat aşı tip B

- *Haemophilus influenza* konjugat aşı tip B (HIB)
- Primer aşı şemasında bulunmakta 12 -15 ay booster dozu takiben
- Tam aşılı çocuklarda elektif splenektomi öncesinde ek doz önerilmektedir
- Yakalama aşıları 12-59 ay asplenik çocuklarda aşısı eksikse 12 aydan önce tek doz aşılı ise 2 ay arayla iki doz aşı
- 12-59 ay asplenik çocuklarda 2 doz aşılı ise ek bir doz HIB aşısı
- 5 yaş üzerinde asplenik bireylerde bir doz HIB önerilmektedir

Pasternack MS, Prevention of sepsis in the asplenic patient uptodate, April 2017
https://www.uptodate.com/contents/prevention-of-sepsis-in-the-asplenic-patient

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, Hiberix, DTaP-IPV/PRP-T, or HibMenCY*	12 through 15 months for PRP-OMP, ActHIB, Hiberix, and HibMenCY*
2 and 4 months for PRP-OMP	15 through 18 months for DTaP-IPV/PRP-T¶

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

* The Advisory Committee on Immunization Practices recommends HibMenCY for infants at increased risk for meningococcal disease (ie, those with persistent complement pathway deficiencies or anatomic or functional asplenia [including sickle cell disease]).

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


Neisseria meningitidis

Meningokok aşısı

- Splenektomili hastaya meningokok aşısı önerilmektedir
- 2013 ACIP önerisi;
- Yaş grubuna göre konjuge meningokok (6 hf -18 ay) infant ve bebeklere önerilmekte
- 2014 ACIP önerisi;
- Quadrivalan konjuge aşı **meningokok A,C,Y, W135(menveo) 2 ay** üzerindeki bebeklere önerilmekte
- Quadrivalan olan diğer aşı; **Menectra 9 ay üzeri** bebekler önerilmemektedir

Meningokok aşısı

- 2-55 yaş arası asplenik bireylere quadrivalan meningokok polisakkarit aşı (menectra veya menveo) önerilmektedir
- MPSV4 FDA tarafından 56 yaş ve üzerinde asplenik bireylerde ACIP tarafından önerilmektedir
- Tekrar aşılama ilgili olarak başlangıç immunolojik cevapta azalmaya neden olabilmektedir
- 2015 ACIP meningokok serogrup B aşı 10 yaş üzerinde asplenik bireylere önerilmektedir

ELSEVIER

Vaccine 19 (2001) 1129–1132

Vaccine

www.elsevier.com/locate/vaccine

Reduced antibody response to revaccination with meningococcal serogroup A polysaccharide vaccine in adults

Ray Borrow [a,*], Helen Joseph [a], Nick Andrews [b], Marisa Acuna [a], Emma Longworth [a], Sarah Martin [a], Nicholas Peake [a], Rukhsana Rahim [a], Peter Richmond [c], Edward Kaczmarski [a], Elizabeth Miller [c]

[a] *Meningococcal Reference Unit, Manchester Public Health Laboratory, Withington Hospital, Nell Lane, West Didsbury, Manchester M20 2LR, UK*

[b] *Statistics Unit, PHLS HQ, 61 Colindale Avenue, London NW 9 5DF, UK*

[c] *Immunisation Division, PHLS CDSC, 61, Colindale Avenue, London NW 9 5EQ, UK*

Received 21 June 2000; received in revised form 7 August 2000; accepted 15 August 2000

Abstract

Widespread use of meningococcal A and C polysaccharide (MACP) vaccines has raised concerns about induction of hyporesponsiveness to these polysaccharides. Immunological hyporesponsiveness to C polysaccharide has been clearly documented in infants, children and adults but only limited data from Gambian children are available for A polysaccharide. We investigated whether a second dose of MACP, given 6 months after an initial dose affected the immunological response as measured by the serum bactericidal assay (SBA) and enzyme-linked immunosorbent assay (ELISA), to serogroup A meningococci in young adults (university students, $n = 36$). Serogroup A SBA responses 1 month following the second dose of MACP (geometric mean titre (GMT) 103.6, 95% CI 45.6–235.1) were approximately one third of the levels observed 1 month post first dose (GMT 281.9, 95% CI 134.9–581.4). The serogroup A-specific IgG levels post second dose (GMC 21.2, 95% CI 15.3–29.4) were also significantly lower at an average of three-quarters the level post first dose (GMC 28.7, 95% CI 20.8–39.7). This confirms that revaccination with MACP vaccine, 6 months following the initial dose, results in a reduced immunological response to A polysaccharide in adults. Repeated vaccination with MACP vaccine may be ineffective and development and use of meningococcal serogroup A conjugate vaccines should be encouraged.

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 3 years followed by boosters every 5 years thereafter.
For children age 19 through 23 months who have not initiated a series of Menveo or MenHibrix	Give two doses of Menveo 3 months apart.	
For age 2 through 9 years	Give two doses of Menactra or Menveo 2 months apart[‡‡].	Boost every 5 years with Menactra or Menveo[†,¥¥].
For age 10 through 55 years	Give two doses of Menactra or Menveo 2 months apart[‡‡] **and either** Trumenba (3 doses administered at 0, 1 to 2, and 6 months) or Bexsero (2 doses administered at least one month apart)[ΔΔ].	Boost every 5 years with Menactra or Menveo[†,¥¥].
For age 56 years and older	Give two doses of Menactra or Menveo 2 months apart[¶¶] **and either** Trumenba (3 doses administered at 0, 1 to 2, and 6 months) or Bexsero (2 doses administered at least one month apart)[ΔΔ].	Boost every 5 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[1-7].

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. Trumenba (MenB-FHbp) and Bexsero (MenB-4C) are meningococcus serogroup B vaccines.

Annals of Pharmacotherapy
2014, Vol. 48(3) 404–411

DOI: 10.1177/1060028013514375
aop.sagepub.com
SAGE

MenHibrix: A New Combination Meningococcal Vaccine for Infants and Toddlers

Sarah F. Hale, PharmD[1], Lauren Camaione, and Ben M. Lomaestro, BS, PharmD[3]

N.meningitidis serogrup C ve Y+HIB+tetanoz toxoid

Abstract

Objective: To review the immunogenicity and safety of the *Haemophilus influenzae* type b-*Neisseria meningitidis* serogroups C and Y tetanus toxoid conjugate vaccine (Hib-MenCY-TT) for infants and toddlers. **Data Sources:** Studies conducted in humans and limited to publication in English were identified through a MEDLINE (January 2000 to September 2013) search using the terms *Hib-MenCY-TT, MenHibrix*, and *Haemophilus influenzae type b-Neisseria meningitidis serogroups C and Y tetanus toxoid conjugate vaccine*. Clinical trial registries, Web sites, and reference citations from publications identified were reviewed for additional sources. **Study Selection and Data Extraction:** Randomized controlled trials were included to evaluate the safety and immunogenicity of Hib-MenCY-TT. Epidemiological data and recommendations from the Advisory Committee on Immunization Practices (ACIP) were also reviewed. **Data Synthesis:** Hib-MenCY-TT is available for primary vaccination of infants as a 4-dose series at 2, 4, 6, and 12 to 15 months of age. Hib-MenCY-TT has comparable immunogenicity to licensed Hib vaccines and produces high levels of *N meningitidis* antibodies against serogroups C and Y. The most common adverse events were pain and redness at the injection site, drowsiness, and irritability. **Conclusions:** Hib-MenCY-TT has been demonstrated to be a safe and immunogenic vaccination for prevention of disease caused by *N meningitidis* serogroups C and Y and *H influenzae* type b in healthy infants and toddlers. Currently, the ACIP recommends the use of Hib-MenCY-TT specifically in high-risk infants aged 6 weeks to 18 months. Hib-MenCY-TT provides the first therapeutic option for vaccination of infants as young as 6 weeks of age who are at increased risk for meningococcal disease.

İnfluenza aşısı

- 6 ay üzerindeki tüm bireylere önerilmektedir
- influenzanın aspleniklerde ciddi veya şiddetli olabileceğine dair veri olmamasına rağmen

- sekonder bakteriyel enfeksiyon
  - örneğin şiddetli pnömokok infeksiyonu

Tablo 3. Özel riski olan erişkinde aşılama

Özel risk durumu	Önerilen aşılar
İmmünyetmezlik (HIV dışı)*	Pnömokok, influenza
HIV infekte CD4-T-lenfosit < 200 hücre/µL CD4-T-lenfosit > 200 hücre/µL	 Canlı aşılar kontrendike, pnömokok,influenza, hepatit B Pnömokok, influenza, hepatit B, suçiçeği ve MMR yapılabilir
Diyabet, kronik kardiyovasküler ve akciğer hastalığı, kronik alkolizm, siroz	Pnömokok, influenza
Aspleni; fonksiyonel veya anatomik	Pnömokok, influenza, Hib, meningokok
Kronik karaciğer hastalığı	Pnömokok, influenza, hepatit A
Renal yetmezlik,diyaliz	Pnömokok, influenza, hepatit B
Sağlık personeli	Hepatit B,suçiçeği, MMR, influenza,Tdap

* Kanser, 2 haftadan uzun, 2 mg/kg, sistemik kortikosteroid kullanımı, son 3 ay içinde kemoterapi almış olmak.

HIV: İnsan immünyetmezlik virüsü, MMR: Kızamık, kızamıkçık, kabakulak aşısı, Hib: *Haemohilus influenzae* tip b aşısı.

Vaccination of persons with asplenia or sickle cell disease

Vaccine	Asplenia or sickle cell disease	
	Recommendation	Strength, evidence quality
Haemophilus influenzae b conjugate	U: age <5 years	Strong, moderate
	R: age ≥5 years	Weak, low
Hepatitis A	U	Strong, moderate
Hepatitis B	U	Strong, moderate
Diphtheria toxoid, tetanus toxoid, acellular pertussis; tetanus toxoid, reduced diphtheria toxoid; tetanus toxoid, reduced diphtheria toxoid, and reduced acellular pertussis	U	Strong, moderate
Human papillomavirus	U	Strong, moderate
Influenza-inactivated (inactivated influenza vaccine)	U	Strong, moderate
Influenza-live attenuated (live attenuated influenza vaccine)	X	Weak, very low
Measles, mumps, and rubella-live	U	Strong, moderate
Measles, mumps, and rubella-varicella-live	U	Strong, moderate
Meningococcal conjugate*	R¶	Strong, low
Meningococcal serogroup B	R if age ≥10 years△	Strong, low
Pneumococcal conjugate (PCV13)	U: age <6 years◇	Strong, moderate
	R: age ≥6 years§	Strong, very low
Pneumococcal polysaccharide (PPSV23)	R: age ≥2 years¥	Strong, low
Polio-inactivated (inactivated poliovirus vaccine)	U	Strong, moderate
Rotavirus-live	U	Strong, moderate
Varicella-live	U	Strong, moderate
Zoster-live	U	Strong, moderate

R: recommended—administer if not previously administered or not current; such patients may be at increased risk for this vaccine-preventable infection; U: usual—administer if patient not current with recommendations for dose(s) of vaccine for immunocompetent persons in risk and age categories; X: contraindicated.

* Only the quadrivalent meningococcal polysaccharide vaccine (Menomune, MPSV4) has been approved by the US Food and Drug Administration for individuals ≥56 years of age. However, a quadrivalent meningococcal conjugate vaccine (Menactra or Menveo) is preferred by the United States Advisory Committee on Immunization Practices (ACIP) for individuals in this age group who are expected to require revaccination since limited data demonstrate a higher antibody response after a subsequent dose of a quadrivalent meningococcal conjugate vaccine compared with a subsequent dose of the quadrivalent meningococcal polysaccharide vaccine.

¶ A two-dose primary series should be administered with an additional dose every five years.

Δ A meningococcal serogroup B vaccine should be administered as either a two-dose series of Bexsero or a three-dose series of Trumenba.

◇ Two doses of PCV13 for children aged two to five years who have not received doses of PCV or received <3 doses of PCV7.

§ If PCV13 has not been administered. For patients aged ≥19 years who have received PPSV23, PCV13 should be administered after an interval of ≥1 year after the last PPSV23 dose (weak, low).

¥ Administer eight or more weeks after indicated dose(s) of PCV13 with a single revaccination with PPSV23 five years after the initial dose (strong, moderate).

References:

1. *Cohn AC, MacNeil JR, Clark TA, et al. Prevention and control of meningococcal disease: recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR Recomm Rep 2013; 62:1.*
2. *Rubin LG, Levin MJ, Ljungman P, et al. 2013 IDSA Clinical Practice Guideline for Vaccination of the Immunocompromised Host. Clin Infect Dis 2013; 58:e44.*
3. *Folaranmi T, Rubin L, Martin SW, et al. Use of serogroup B meningococcal vaccines in persons aged ≥10 years at increased risk for serogroup B meningococcal disease: Recommendations of the Advisory Committee on Immunization Practices, 2015. MMWR Morb Mortal Wkly Rep 2015; 64:608.*
4. *Kim DK, Riley LE, Harriman KH, et al. Recommended Immunization schedule for adults aged 19 years or older, United States, 2017. Ann Intern Med 2017; 166:209.*

Table 7. Vaccination of Persons With Asplenia or a Sickle Cell Disease, Cochlear Implants, or Cerebrospinal Fluid Leak

	Asplenia or a Sickle Cell Disease		Cochlear Implants[a] or Cerebrospinal Fluid Leak	
Vaccine	Recommendation	Strength, Evidence Quality	Recommendation	Strength, Evidence Quality
Haemophilus influenzae b conjugate	U: age <5 y R: age ≥5 y	Strong, moderate weak, low	U	Strong, moderate
Hepatitis A	U	Strong, moderate	U	Strong, moderate
Hepatitis B	U	Strong, moderate	U	Strong, moderate
Diphtheria toxoid, tetanus toxoid, acellular pertussis; tetanus toxoid, reduced diphtheria toxoid; tetanus toxoid, reduced diphtheria toxoid, and reduced acellular pertussis	U	Strong, moderate	U	Strong, moderate
Human papillomavirus	U	Strong, moderate	U	Strong, moderate
Influenza-inactivated (inactivated influenza vaccine)	U	Strong, moderate	U	Strong, moderate
Influenza-live attenuated (live attenuated influenza vaccine)	X	Weak, very low	U	Strong, moderate
Measles, mumps, and rubella–live	U	Strong, moderate	U	Strong, moderate
Measles, mumps, and rubella–varicella–live	U	Strong, moderate	U	Strong, moderate
Meningococcal conjugate	R: age 2–55 y[b]	Strong, low	U	Strong, moderate
Meningococcal polysaccharide	R: age >55 y[b]	Strong, low	U	Strong, moderate
Pneumococcal conjugate (PCV13)	U: age <6 y[c] R: age ≥6 y[d]	Strong, moderate Strong, very low	U: age <6 y[c] R: age ≥6 y[d]	Strong, moderate strong, low
Pneumococcal polysaccharide (PPSV23)	R: age ≥2 y[e]	Strong, low	R: age ≥2 y[e]	Strong, moderate
Polio-inactivated (inactivated poliovirus vaccine)	U	Strong, moderate	U	Strong, moderate
Rotavirus–live	U	Strong, moderate	U	Strong, moderate
Varicella–live	U	Strong, moderate	U	Strong, moderate
Zoster–live	U	Strong, moderate	U	Strong, moderate

Sağlık Bakanlığı "Genişletilmiş Bağışıklama Programı

- *2.4.3-A - Sağlık Bakanlığı "Genişletilmiş Bağışıklama Programı" kapsamına dahil olmayan aşı bedelleri; kronik böbrek yetmezliği, kistik fibrozis, KOAH, kanser, HIV/AIDS enfeksiyonu, splenektomi olanlar ve immünsupresif tedaviye bağlı olarak bağışıklık durumu olumsuz etkilendiği için enfeksiyon hastalıklarının daha ağır seyrettiği yüksek riskli kişilerin bu durumlarını belgeleyen sağlık raporuna istinaden karşılanır.*
- *2.4.3-B - Grip aşısı bedeli; 65 yaş ve üzerindeki kişiler ile yaşlı bakımevi ve huzurevinde kalan kişilerin bu durumlarını belgelendirmeleri halinde sağlık raporu aranmaksızın; astım dâhil kronik pulmoner ve kardiyovasküler sistem hastalığı olan erişkin ve çocuklar, diyabet dâhil herhangi bir kronik metabolik hastalığı, kronik renal disfonksiyonu, hemoglobinopatisi veya immün yetmezliği olan veya immünsupresif tedavi alan erişkin ve çocuklar ile 6 ay - 18 yaş arasında olan ve uzun süreli asetil salisilik asit tedavisi alan çocuk ve adolesanların hastalıklarını belirten sağlık raporuna dayanılarak tüm hekimlerce reçete edildiğinde yılda bir defaya mahsus olmak üzere karşılanır.*
- *2.4.3-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, immünsupresif 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, diyabet 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 karşılanır. 65 yaş ve üzerindeki kişilere rapor aranmaksızın beş yılda bir defa olmak üzere bedelleri ödenir.*

Aşı formları

Pnömokok aşı

- Pneumo 23 Aşısı 0.5 ml 1 Enjektör (Polisakkarit)
- Pneumovax 23 Aşısı 0.5 ml 1 Flakon (Polisakkarit 44TL)
- Synflorix 0.5 ml Enjektör (Polisakkarit Serotip 1 + Serotip 4)
- PCV13
- Prevenar 13/0.5 ml IM 1 Enjektör (164 TL)

Haemophilus influenza tip B

- Hiberix
  (HIB Polısakkaridin , 40,46 TL)
- ACT-HİB
  (Hemofilus İnfluenza Tip B aşı, 21 TL)

Meningokok aşı

- **Menactra Meningokok Aşısı**
  0.5 ml 1 Flakon (Meningokok A, C, Y ve W135 Polisakkariti, 182 TL
- **Menveo Aşı**
  0.5 ml 1 Flakon (Meningokok A, C, Y ve W135 Oligosakkariti, 185 TL
- **Nimenrix Meningokok Aşısı**
  0.5 ml 1 Flakon (Meningokok A, C, Y ve W135 Polisakkariti-Tetanoz Toksoid, 177 TL

Kombine aşılar

Haemophilus influenza tip B+ meningokok

HibMenYC

Recommended Adult Immunization Schedule

United States - 2017

Figure 2. Recommended immunization schedule for adults aged 19 years or older by medical condition and other indications, United States, 2017

Vaccine	Pregnancy[1-6,9]	Immuno-compromised (excluding HIV infection)[3-7,11]	HIV infection CD4+ count (cells/µL)[3-7,9-11]		Asplenia, persistent complement deficiencies[7,10,11]	Kidney failure, end-stage renal disease, on hemodialysis[7,9]	Heart or lung disease, chronic alcoholism[7]	Chronic liver disease[7-9]	Diabetes[7,9]	Healthcare personnel[3,4,9]	Men who have sex with men[6,8,9]
			< 200	≥ 200							
Influenza[1]	1 dose annually										
Td/Tdap[2]	1 dose Tdap each pregnancy	Substitute Tdap for Td once, then Td booster every 10 yrs									
MMR[3]	contraindicated	1 or 2 doses depending on indication									
VAR[4]	contraindicated	2 doses									
HZV[5]	contraindicated			1 dose							
HPV–Female[6]		3 doses through age 26 yrs									
HPV–Male[6]		3 doses through age 26 yrs			3 doses through age 21 yrs						3 doses through age 26 yrs
PCV13[7]		1 dose									
PPSV23[7]		1, 2, or 3 doses depending on indication									
HepA[8]	2 or 3 doses depending on vaccine										
HepB[9]	3 doses										
MenACWY or MPSV4[10]	1 or more doses depending on indication										
MenB[10]	2 or 3 doses depending on vaccine										
Hib[11]	3 doses post-HSCT recipients only	1 dose									

Recommended for adults who meet the age requirement, lack documentation of vaccination, or lack evidence of past infection

Recommended for adults with additional medical conditions or other indications

Contraindicated

No recommendation

Sonuç

- Asplenik hastalarda pnömokok, meningokok, *Haemophilus influenzae* tip B
- Elektif splenektomide aşılar 14 gün önce
- En az 2 hafta öncesinde PCV13 ve PPSV23 uygulamalarının (önce PCV13 en az 8 hafta sonra PPSV23 tamamlanması önerilir.
- Eğer yapılmamışsa splenektomiden sonra en az 14 gün geçmesi önerilmekte

IDSA Clinical Practice Guideline for Vaccination of the Immunocompromised Host. Clin Infect Dis. 2013


Teşekkür ederim