

ける、免疫原性を向上させ、肺炎球菌ワクチン接種の防御効果を高めることである。多数の莢膜多糖体に対する免疫反応は、多糖体抗原がキャリア蛋白と共有結合することによって改善される(116,117)。今日の結合型ワクチン開発は、小児に感染症を最も高頻度で惹起する血清型に集中して行われている。開発および評価段階にあるワクチン製剤候補には、1種類以上のキャリア蛋白と結合する肺炎球菌多糖体の少なくとも7種類の血清型がカバーされている。7種類の最も一般的な血清型[4,6B,9V,14,18C,19F,23F]および血清学的交差反応性の血清型(例:6A)]に対して防御作用を発揮する有効な結合型ワクチンは、米国の6歳未満の小児に発生する菌血症の86%、髄膜炎の83%、中耳炎の65%を予防することが可能であると思われる(45)。6歳以上では、これらの血清型が脳脊髄液および血液からの分離株の50%を占めている(44)。第I相試験および第II相試験の中間結果では、これらのワクチンは概ね安全であり、2~5歳の幼児および生後2ヶ月の乳児において、一次抗体反応と既往抗体反応を惹起することが示唆されている(118-121)。小児における急性肺炎球菌性中耳炎と肺炎球菌による侵襲性疾患に対する結合型ワクチンの有効性を評価するための多施設共同試験が進行中である。

多糖体ワクチンには、小児の鼻咽頭における *S. pneumoniae* の保菌に対する抑制作用はない(122)。しかしながら、予備データによれば、結合型ワクチンの場合、ワクチンがカバーしている肺炎球菌血清型については、鼻咽頭保菌を抑制する可能性が示唆されている(123)。*S. pneumoniae* の保菌率を抑制することは、伝染を抑制して疾患発生率を低下させることにより、ワクチンの全体的な作用を強化する可能性がある。前向き無作為化試験を実施し、侵襲性肺炎球菌性感染症に対する結合型ワクチンの防御効果を証明する必要がある。これらのワクチンについては、現行の23価多糖体ワクチンが無効である成人の免疫不全患者において、肺炎球菌性疾患を予防する上で有用であるかどうかについても評価する必要がある。

#### 文献

- CDC. Pneumococcal polysaccharide vaccine usage, United States. MMWR 1984;33:273-6, 281.
- Williams WW, Hickson MA, Kane MA, Kendal AP, Spika JS, Hinman AR. Immunization policies and vaccine coverage among adults: the risk for missed opportunities. Ann Intern Med 1988; 108:616-25.
- Stool SE, Field MJ. The impact of otitis media. Pediatr Infect Dis J 1989;8(suppl):S11-S14.
- Jernigan DB, Cetron MS, Breiman RF. Minimizing the impact of drug-resistant *Streptococcus pneumoniae* (DRSP): a strategy from the DRSP working group. JAMA 1996;275:206-9.
- Istre GR, Tarpay M, Anderson M, Pryor A, Welch D, Pneumococcus Study Group. Invasive disease due to *Streptococcus pneumoniae* in an area with a high rate of relative penicillin resistance. J Infect Dis 1987;156:732-5.
- Breiman RF, Spika JS, Navarro VJ, Darden PM, Darby CP. Pneumococcal bacteremia in Charleston County, South Carolina: a decade later. Arch Intern Med 1990;150:1401-5.
- Bennett NM, Buffington J, LaForce FM. Pneumococcal bacteremia in Monroe County, New York. Am J Public Health 1992;82:1513-6.
- Vol. 46 / No. RR-8 MMWR 19
- Hofmann J, Cetron MS, Farley MM, et al. The prevalence of drug-resistant *Streptococcus pneumoniae* in Atlanta. N Engl J Med 1995;333:481-6.
- Plouffe JF, Breiman RF, Facklam RR, Franklin County Pneumonia Study Group. Bacteremia with *Streptococcus pneumoniae* in adults—implications for therapy and prevention. JAMA 1996;275:194-8.
- Burman LA, Norrby R, Trollfors B. Invasive pneumococcal infections: incidence, predisposing factors, and prognosis. Rev Infect Dis 1985;7:133-42.
- Kuikka A, Syrjänen J, Renkonen O-V, Valtonen V. Pneumococcal bacteremia during a recent decade. J Infect 1992;24:157-68.
- Afessa B, Greaves WL, Frederick WR. Pneumococcal bacteremia in adults: a 14-year experience in an inner-city university hospital. Clin Infect Dis 1995;21:345-51.
- Davidson M, Parkinson AJ, Bulkow LR, Fitzgerald MA, Peters HV, Parks DJ. The epidemiology of invasive pneumococcal disease in Alaska, 1986-1990: ethnic differences and opportunities for prevention. J Infect Dis 1994;170:368-76.
- Cortese MM, Wolff M, Almeido-Hill J, Reid R, Ketcham J, Santosh M. High incidence rates of invasive pneumococcal disease in the White Mountain Apache population. Arch Intern Med 1995;155:103-7.

- 1992;152:2277-82.
15. Wenger JD, Hightower AW, Facklam RR, Gaventa S, Broome CV, Bacterial Meningitis Study Group. Bacterial meningitis in the United States, 1986: report of a multistate surveillance study. *J Infect Dis* 1990;162:1316-23.
  16. Marrie TJ, Durant H, Yates L. Community-acquired pneumonia requiring hospitalization: 5-year prospective study. *Rev Infect Dis* 1989;11:586-99.
  17. Research Committee of the British Thoracic Society. Community-acquired pneumonia in adults in British hospitals in 1982-1983: a survey of aetiology, mortality, prognostic factors and outcome. *Q J Med* 1987;62:195-220.
  18. Fang GD, Fine M, Orloff J, et al. New and emerging etiologies for community-acquired pneumonia with implications for therapy: a prospective multicenter study of 359 cases. *Medicine* 1990;69:307-16.
  19. Torres A, Serra-Batilles J, Ferrer A, et al. Severe community-acquired pneumonia: epidemiology and prognostic factors. *Am Rev Respir Dis* 1991;144:312-8.
  20. CDC. Recommendations of the Immunization Practices Advisory Committee: pneumococcal polysaccharide vaccine. *MMWR* 1989;38:64-8,73-6.
  21. Schappert SM. Office visits for otitis media: United States, 1975-90. Hyattsville, MD: United States Department of Health and Human Services, Public Health Service, Centers for Disease Control, 1992 (Advance data no. 214).
  22. Bluestone CD, ed. *Pediatric otolaryngology*. 3rd ed. Philadelphia, PA: WB Saunders Company, 1990.
  23. Teele DW, Klein JO, Rosner B, Greater Boston Otitis Media Study Group. Epidemiology of otitis media during the first seven years of life in children in Greater Boston: a prospective, cohort study. *J Infect Dis* 1989;160:83-94.
  24. Fedson DS, Musher DM. Pneumococcal vaccine. In: Plotkin SA, Mortimer EA Jr, eds. *Vaccines*. 2nd ed. Philadelphia, PA: WB Saunders, 1994:517-63.
  25. Gardner P, Schaffner W. Immunization of adults. *N Engl J Med* 1993;328:1252-8.
  26. Hook EW, Horton CA, Schaberg DR. Failure of intensive care unit support to influence mortality from pneumococcal bacteremia. *JAMA* 1983;249:1055-7.
  27. Mufson MA, Oley G, Hughey D. Pneumococcal disease in a medium-sized community in the United States. *JAMA* 1982;248:1486-9.
  28. Campbell JF, Donohue MA, Mochizuki RB, Nevin-Woods CL, Spika JS. Pneumococcal bacteremia in Hawaii: initial findings of a pneumococcal disease prevention project. *Hawaii Med J* 1989;48:513-8.
  29. Lipsky BA, Boyko EJ, Inui TS, Koepsell TD. Risk factors for acquiring pneumococcal infections. *Arch Intern Med* 1986;146:2179-85.
  30. Musher DM. *Streptococcus pneumoniae*. In: Mandell GL, Bennett JE, Dolin R, eds. *Principles and Practice of Infectious Diseases*. 4th ed. Churchill Livingstone, 1994:1811-26.
  31. CDC. Recommendations of the Advisory Committee on Immunization Practices (ACIP): use of vaccines and immunoglobulins in persons with altered immunocompetence. *MMWR* 1993; 42(No. RR-4):1-18. 20 MMWR April 4, 1997
  32. Keller DW, Breiman RF. Preventing bacterial respiratory tract infections among persons infected with human immunodeficiency virus. *Clin Infect Dis* 1995;21(suppl 1):S77-S83.
  33. Redd SC, Rutherford GW, Sande MA, et al. The role of human immunodeficiency virus infection in pneumococcal bacteremia in San Francisco residents. *J Infect Dis* 1990;162:1012-7.
  34. Takala AK, Jero J, Kela E, Rönnberg P-R, Koskenniemi E, Eskola J. Risk factors for primary invasive pneumococcal disease among children in Finland. *JAMA* 1995;273:859-64.
  35. Gessner BD, Ussery XT, Parkinson AJ, Breiman RF. Risk factors for invasive disease caused by *Streptococcus pneumoniae* among Alaska native children younger than two years of age. *Pediatr Infect Dis J* 1995;14:123-8.
  36. Cherian T, Steinhoff MC, Harrison LH, Rohn D, McDougal L, Dick J. A cluster of invasive pneumococcal disease in young children in child care. *JAMA* 1994;271:695-8.
  37. CDC. Hemorrhage and shock associated with invasive pneumococcal infection in healthy infants and children—New Mexico, 1993-1994. *MMWR* 1995;43:949-52.
  38. Klugman KP. Pneumococcal resistance to antibiotics. *Clin Microbiol Rev* 1990;3:171-96.
  39. Butler JC, Hofmann J, Cetron MS, Elliott JA, Facklam RR, Breiman RF. The continued emergence of drug-resistant *Streptococcus pneumoniae* in the United States: an update from the Centers for Disease Control and Prevention's Pneumococcal Sentinel Surveillance System. *J Infect Dis* 1996;174:986-93.
  40. Arnold KE, Leggiadro RJ, Breiman RF, et al. Risk factors for carriage of drug-resistant *Streptococcus pneumoniae* among children in Memphis, Tennessee. *J Pediatr* 1996;128:757-64.

41. Duchin JS, Breiman RF, Diamond A, et al. High prevalence of multidrug-resistant *Streptococcus pneumoniae* among children in a rural Kentucky community. *Pediatr Infect Dis J* 1995;14:745-50.
42. American Academy of Pediatrics, Committee on Infectious Diseases. Therapy for children with invasive pneumococcal infections. *Pediatrics* 1997;99:289-99.
43. Robbins JB, Austrian R, Lee CJ, et al. Considerations for formulating the second-generation pneumococcal capsular polysaccharide vaccine with emphasis on the cross-reactive types within groups. *J Infect Dis* 1983;148:1136-59.
44. Butler JC, Breiman RF, Campbell JF, Lipman HB, Broome CV, Facklam RR. Pneumococcal polysaccharide vaccine efficacy: an evaluation of current recommendations. *JAMA* 1993;270:1826-31.
45. Butler JC, Breiman RF, Lipman HB, Hofmann J, Facklam RR. Serotype distribution of *Streptococcus pneumoniae* infections among preschool children in the United States, 1978-1994: Implications for development of a conjugate vaccine. *J Infect Dis* 1995;171:885-9.
46. Musher DM, Luchi M, Watson DA, Hamilton R, Baughn RE. Pneumococcal polysaccharide vaccine in young adults and older bronchitics: determination of IgG responses by ELISA and the effect of adsorption of serum with non-type-specific cell wall polysaccharide. *J Infect Dis* 1990;161:728-35.
47. Ammann AJ, Addiego K, Wara DW, Lubin D, Smith WB, Mentzer WC. Polyvalent pneumococcal-polysaccharide immunization of patients with sickle cell anemia and patients with splenectomy. *N Engl J Med* 1977;297:897-900.
48. Siber GR, Gorham C, Martin P, Corkey JC, Schiffman G. Antibody response to pretreatment immunization and post-treatment boosting with bacterial polysaccharide vaccines in patients with Hodgkin's disease. *Ann Intern Med* 1986;104:467-75.
49. Ammann AJ, Schiffman G, Abrams D, Volberding P, Ziegler J, Conant M. B-cell immunodeficiency in acquired immune deficiency syndrome. *JAMA* 1984;251:1447-9.
50. Ballet J-J, Sulcebe G, Couderc L-J, et al. Impaired anti-pneumococcal antibody response in patients with AIDS-related persistent generalized lymphadenopathy. *Clin Exp Immunol* 1987;68:479-87.
51. Huang K-L, Ruben FL, Rinaldo CR Jr, Kingsley L, Lyter DW, Ho M. Antibody responses after influenza and pneumococcal immunization in HIV infected homosexual men. *JAMA* 1987;257:2047-50.
52. Rodriguez-Barradas MC, Musher DM, Lahart C, et al. Antibody to capsular polysaccharides of *Streptococcus pneumoniae* after vaccination of human immunodeficiency virus-infected subjects with 23-valent pneumococcal vaccine. *J Infect Dis* 1992;165:553-6.
53. Koskela M, Leinonen M, Häivä V-M, Timonen M, Mäkelä PH. First and second dose antibody responses to pneumococcal polysaccharide vaccine in infants. *Pediatr Infect Dis* 1986;5:45-50. Vol. 46 / No. RR-8 MMWR 21
54. Leinonen M, Säkkinen A, Kallikoski R, Luotonen J, Timonen M, Mäkelä PH. Antibody response to 14-valent pneumococcal capsular polysaccharide vaccine in pre-school age children. *Pediatr Infect Dis* 1986;5:39-44.
55. Douglas RM, Paton JC, Duncan SJ, Hansman DJ. Antibody response to pneumococcal vaccination in children younger than five years of age. *J Infect Dis* 1983;148:131-7.
56. Mufson MA, Krause HE, Schiffman G. Long-term persistence of antibody following immunization with pneumococcal polysaccharide vaccine. *Proc Soc Exp Biol Med* 1983;173:270-5.
57. Mufson MA, Krause HE, Schiffman G, Hughey DF. Pneumococcal antibody levels one decade after immunization of healthy adults. *Am J Med Sci* 1987;293:279-89.
58. Giebink GS, Le CT, Schiffman G. Decline of serum antibody in splenectomized children after vaccination with pneumococcal capsular polysaccharides. *J Pediatr* 1984;105:576-84.
59. Weinrub PS, Schiffman G, Addiego JE Jr., et al. Long-term follow-up and booster immunization with polyvalent pneumococcal polysaccharide in patients with sickle cell anemia. *J Pediatr* 1984;105:261-3.
60. Spika JS, Halsey NA, Le CT, et al. Decline of vaccine-induced antipneumococcal antibody in children with nephrotic syndrome. *Am J Kidney Dis* 1986;7:466-70.
61. Vella PP, McLean AA, Woodhour AF, Weibel RE, Hilleman MR. Persistence of pneumococcal antibodies in human subjects following vaccination. *Proc Soc Exp Biol Med* 1980;164:435-8.
62. Hilleman MR, Carlson AJ, McLean AA, Vella PP, Weibel RE, Woodhour AF. *Streptococcus pneumoniae* polysaccharide vaccine: age and dose responses, safety, persistence of antibody, revaccination, and simultaneous administration of pneumococcal and influenza vaccines. *Rev*