Two Doses of PCV7 Can't Do the Work of Three

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CHICAGO — Trimming the seven-valent pneumococcal conjugate vaccine schedule from three prebooster doses to two may leave children more vulnerable to infection, according to data presented at the annual Interscience Conference on Antimicrobial Agents and Chemotherapy.

"Our study demonstrates that the reduced two-dose schedule at age 4 and 6 months cannot be regarded as equivalent to the licensed three-dose schedule at 2, 4, and 6 months," said Dr. Ron Dagan, who presented the results of an ongoing, open-label randomized trial that was launched in 2005.

"The two-dose schedule resulted in significantly lower antibody concentrations to four vaccine serotypes compared with the three-dose licensed schedule, and the most impressive observed difference in immunogenicity was serotype 6B, which has cross-protection with 6A," said Dr. Dagan of the pediatric infectious disease unit at Soroka University Medical Center, Ben-Gurion University, Beer-Sheva, Israel.

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In its April 2007 meeting, the Immunization Strategic Advisory Group of Experts of the World Health Organization concluded that the number of doses required in primary vaccination schedules was not completely understood, though some evidence suggested that two doses in infancy were likely to be as good as three. They added that for pneumococcal conjugate vaccines, there may be differences in immunogenicity for some serotypes, Dr. Dagan explained.

"Despite the lack of knowledge, there is a tendency by some authorities to state that two and three doses of PCV7 in the primary immunization series—during the first year of life—are equivalent," he said at the conference, which was sponsored by the American Society for Microbiology.

This study included healthy children aged 2 months, plus or minus 3 weeks, with parental informed consent. Exclusion criteria included prematurity (less than 35 weeks), acute disease, any chronic condition not permitting evaluation of the vaccine, prior administration of pneumococcal vaccine, known allergies related to vaccine constituents, and any contraindication to concomitant vaccines.

The children were randomized 2:1:1 to three groups:

► **Group 1:** Licensed schedule of PCV7 at 2, 4, and 6 months.

► **Group 2:** Reduced-dose schedule of PCV7 at 4 and 6 months.

► **Group 3:** Unvaccinated (received the vaccine at 12 and 18 months).

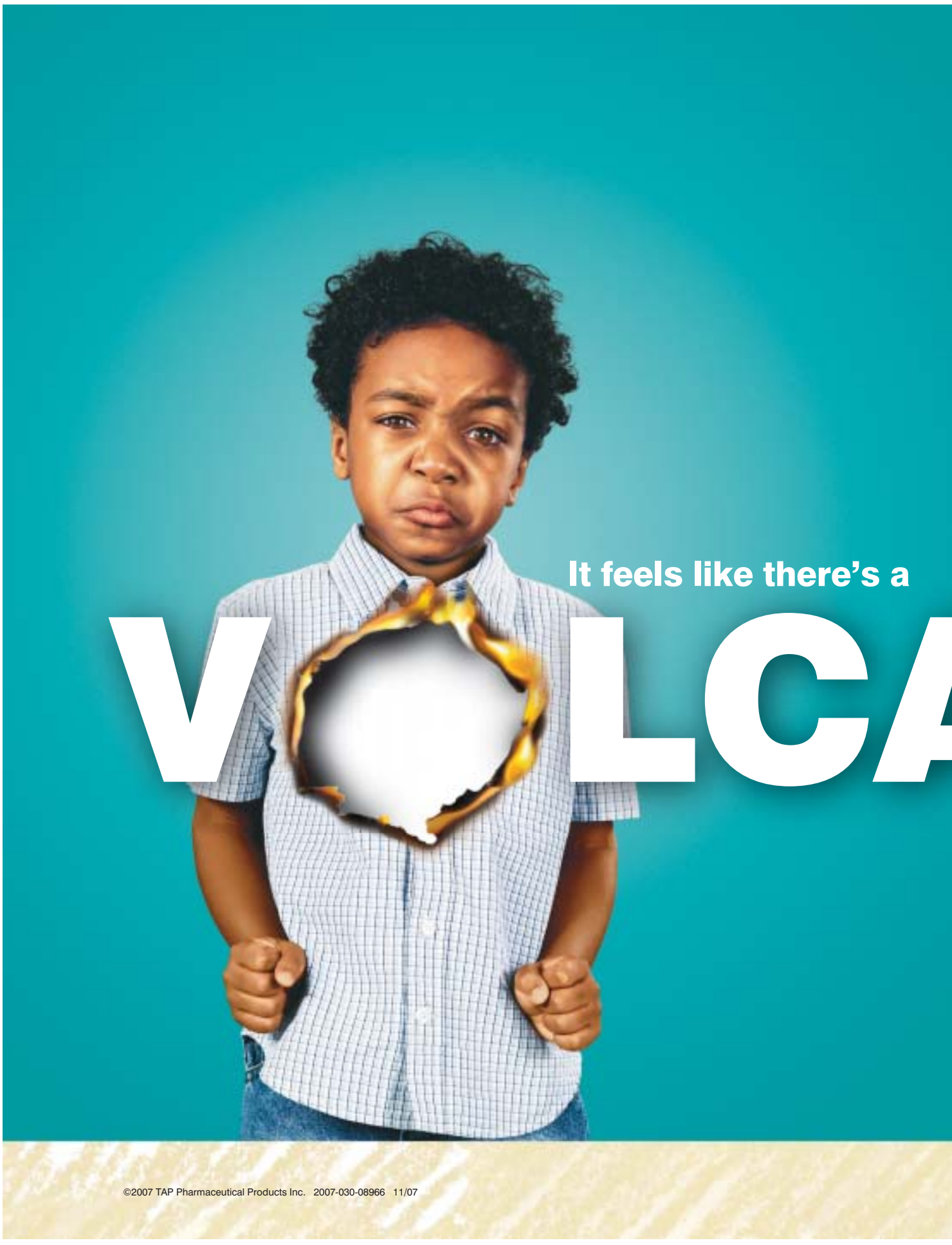
Blood samples were refrigerated up to 8 hours until processed and serum was kept at –70° C until tested. Serum serotype-specific pneumococcal anticapsular IgG concentrations were tested by enzyme-linked immunosorbent assay after double absorption with C-polysaccharide and 22F-polysaccharide. Nasopharyngeal (NP) and oropharyngeal (OP) specimens were obtained by transport swabs and cultured within 16 hours, and OP results were reported only if *Streptococcus pneumoniae* was not isolated from the NP, Dr. Dagan said.

The postprimary serum analysis of geometric mean concentrations included 259 infants in the three-dose group and 133 infants in the two-dose group.

The three-dose group had four times more antibodies to serotype 6b (2.05 mcg/mL versus 0.55 mcg/mL) than was seen in the two-dose group. For serotype 14 the difference was 5.16 mcg/mL versus 3.54 mcg/mL; for 18C, 1.65 mcg/mL versus 1.23 mcg/mL and 23F levels were twice as high in the three-dose group at 1.08 mcg/mL versus 0.64 mcg/mL.

The Israeli scientists also found that a significantly higher proportion of three-dose subjects vs. two-dose subjects reached the cutoff serum anticapsular IgG concentration of 0.35 mcg/mL for serotypes 6B (87% versus 61%), 18C (96% versus 90%), and 23F (83% versus 70%).

In this analysis, they also used a cutoff of 1.0 mg/mL, which is favored by some physicians. Here again, the values were significantly higher in the three-dose



group for 6B (71% versus 35%), 18C (75% versus 65%), and 23F (54% versus 33%).

The prevalence of 7-valent pneumococcal serotypes carriage remained unchanged for the first 6 months, but at 1 year, nearly one-third of the unimmunized children were carrying the serotypes, whereas about one-fifth of both vaccinated groups had carriage.

In the primary intervention schedules, there was a clear and significant reduction of new NP acquisition of both serotypes 6A and 6B in the three-dose cohort at 12 months, whereas no such reduction could be demonstrated in the two-dose group.

Serotype 6B was acquired by 9% of unvaccinated children, 7% of those who received two doses, and 4% of those in the three-dose group, with the *P* value reaching significance between the three-dose and no-vaccine groups. Serotype 6A was a different story, showing up in about 9% of both the unvaccinated and two-dose children, but only 4% of the three-dose group. More than 15% of unvaccinated children acquired either 6A or 6B.

"Serotype 6A acquisition is influenced by 6B antibody concentration, but you need more antibodies of anti-6B to influence 6A, so we speculated that 6A may be even more affected and this is exactly what happened," Dr. Dagan said. ■

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Dr. Charles A. Scott, p. 38

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Please see adjacent page for brief summary of prescribing information.

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References **1.** Data on file, TAP Pharmaceutical Products Inc. **2.** PREVACID Complete Prescribing Information.

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