The Immune Response to Pneumococcal Polysaccharides 14 and 23F Among Elderly Individuals Consists Predominantly of Switched Memory B Cells

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The phenotype of B cells that respond to vaccination with the purified pneumococcal polysaccharide (PPS) has been a topic of debate. We have recently identified the phenotype of cells from healthy young volunteers as CD27+IgM+ B cells. However, the PPS-responding B-cell population has not yet been identified in high-risk populations, such as elderly individuals. Previous studies have shown that elderly individuals have a lower percentage of immunoglobulin M memory B cells than healthy young adults. In this study, we directly characterized the phenotype of PPS-specific B cells before and after vaccination with PPS vaccine (PPV) in elderly adults, using fluorescently labeled PPS14 and PPS23F. In contrast to our observations in healthy young volunteers, the PPS-responding B-cell population consisted primarily of switched memory (CD27+IgM−) B cells. In concurrence with these findings, postvaccination immunoglobulin M concentrations were not significantly increased in this population, and the opsonophagocytic response was decreased, compared with that in young adults. These findings identify a significant shift in the phenotype of the B-cell population in response to PPV among elderly individuals.

Keywords. Streptococcus pneumoniae; Pneumococcus; elderly; vaccine; polysaccharide; B cell; CD27; flow cytometry; human; 23F.

Streptococcus pneumoniae is a major cause of morbidity and mortality worldwide. The groups at highest risk are young children, elderly adults (age, >65 years), and immunocompromised individuals. Despite the high efficacy of the pneumococcal polysaccharide vaccine (PPV) in young adults, it is less protective in populations at highest risk for invasive pneumococcal disease, including elderly individuals [1–4].

After vaccination with PPV, elderly individuals produce anti-PPS immunoglobulin G (IgG) antibodies (Abs) in concentrations similar to those produced by young adults [5, 6]. However, decreased opsonophagocytic activity (OPA), restricted variable gene use, and lower immunoglobulin M (IgM) concentrations may all play a role in the vaccine’s decreased efficacy [7–9]. The underlying cause of these differences remains to be elucidated.

The phenotype of the B-lymphocyte population responsible for the immune response to PPV has been controversial. After stimulation in vitro, anti-PPS Abs are secreted mainly by switched memory cells (CD27+IgM−) and are predominantly IgG and immunoglobulin A (IgA) [10–12]. However, individuals with reduced numbers of or no CD27+IgM+ B cells respond poorly to PPV and are more vulnerable to infections caused by encapsulated bacteria [7, 9, 13–16].

We recently described a highly significant increase in the CD27+IgM− PPS-specific B-cell population 7 days after vaccination in healthy young adults [17]. The specific aim of this study was to identify the phenotype, using CD19, CD27, and IgM markers, and to enumerate PPS-specific B cells in elderly individuals.
Our study demonstrates a significant change in the phenotype of PPS-responding B cells, PPS-specific IgM, and OPA after vaccination in elderly individuals as compared to young adults. These findings may help explain the decreased efficacy of the purified PPV in individuals older than 65 years.

**METHODS**

**Human Volunteers**

Fourteen elderly volunteers (mean age, 72 years; range, 64–88 years) participated in this University of Toledo Institutional Review Board committee–approved study (protocol 105137). Individuals were questioned about medications, previous illnesses, and present health. Informed consent was obtained from all participants. Ten volunteers (mean age, 71 years; range, 64–88 years) were PPV naive, and 4 (mean age, 78 years; range, 70–84 years) had been vaccinated with PPV >5 years prior. Volunteers were vaccinated with PPV (Pneumovax 23; Merck). Blood samples were collected before vaccination and on days 7 and 30 after vaccination.

**Labeling of PPS14 and PPS23F**

Conjugation of PPS14 to cascade blue (CB) ethylenediamine (Invitrogen, catalog no. C-621) or of PPS23F to 5-(4,6-dichloro-1H-triazinyl) amino fluorescein (5-DTAF; Sigma-Aldrich, catalog no. 36565) was carried out as previously described [17].

**PPS Enzyme-Linked Immunosorbent Assay (ELISA)**

ELISA was performed to examine anti-PPS–specific human Abs in all volunteers. The PPS ELISA used in this study is modified version of the World Health Organization assay [18]. All steps were performed as reported previously [17].

**OPA Assay**

The OPA assay was performed as previously described [19, 20]. Briefly, *S. pneumoniae* serotypes 14 and 23F were incubated with serially diluted heat-inactivated sera. Newborn rabbit serum (Pel-Freez, Brown Deer, WI) was added as a source of complement. Differentiated HL-60 cells were added at an E:T ratio of 400:1. Sera were tested in duplicate. Results were obtained using the Opsotiter1 software program (University of Alabama–Birmingham).

**Flow Cytometry**

To determine the phenotype of B cells responding to vaccination, peripheral blood mononuclear cells (PBMCs) were collected from immunized volunteers 0, 7, and 30 days after vaccination. After Ficoll-gradient centrifugation and washing, cells were resuspended in FACS buffer (phosphate-buffered saline, 0.1% fetal calf serum, and 2 mM ethylenediaminetetraacetic acid). Before staining, cells were absorbed with 10 µg/mL cell wall polysaccharide (Statens Serum Institute; MiraVista Diagnostics, Indianapolis, IN) and PPS2F (American Type Culture Collection) to reduce nonspecific binding [21]. B lymphocytes were labeled with 10 µg/mL of either PPS14-CB or PPS23F-5-DTAF. Fluorochrome-conjugated monoclonals Abs (BD Bioscience or eBioscience) to the following anti-human antigens were used: CD19 (APC-Cy7), CD27 (PerCP-Cy5.5), IgM (APC), and immunoglobulin D (AlexaFluor 700). Cells were washed, resuspended in FACS buffer, and analyzed with FACSaria, using FACSdiva software (BD Biosciences). FCS files were analyzed using FlowJo software (Tree Star, Ashland, OR). Singlet lymphocytes were plotted on a histogram to gate on B lymphocytes (APC-Cy7:CD19). B-lymphocyte data were plotted using either CB:PPS14 or 5-DTAF:PPS23F to identify PPS-selected cells. B-cell populations were divided into 4 subpopulations: naive (CD27 IgM+), class switched (CD27“IgM+”), CD27“IgM+”, and switched memory (CD27“IgM+”).

**Statistical Analysis**

Geometric mean concentrations of IgG, IgM, and IgA and flow cell numbers specific to PPS14 and PPS23F were calculated for each group. Correlation between 2 groups was examined using the Pearson correlation coefficient. Comparison between 2-group values was performed using an unpaired t test. *P* values of <.05 were considered to be significant.

**RESULTS**

**Serum Ab Titers in Elderly Individuals Increased After Vaccination**

To study the PPS-specific immune response to PPV in elderly individuals, we obtained sera before and 30 days after vaccination and measured Ab responses to pneumococcal serotypes 14 and 23F. Elderly donors had a significant rise in the concentration of PPS14-specific IgG, from 0–16.2 µg/mL before vaccination to 14.8–86.9 µg/mL after vaccination (*P* < .001). There was no significant increase in the PPS14-specific IgM or IgA Ab concentrations after vaccination. Similarly, postvaccination IgG responses to PPS23F were significantly increased as compared to those in prevaccination sera (range, 0–2.2 µg/mL vs 0.5–15 µg/mL; *P* < .004). There was a significant increase in PPS23F-specific IgM (*P* < .03) but not in PPS23F-specific IgA after vaccination (data not shown). In our sample population, there was an increase in IgG concentration for both PPS14 and PPS23F and an increase in IgM concentration for PPS23F only after vaccination, compared with before vaccination. All donors but 1 displayed an increase in the serotype-specific IgG Ab response for PPS14.

**Serum Opsonophagocytic Ab Titers in Elderly Individuals Increased After Vaccination**

The functional or opsonophagocytic response of serum Ab obtained before and 30 days after vaccination against both serotype 14 and 23F PPS was determined for all donors. Data are
reported as opsonophagocytic Ab titers, defined as the Ab dilution required to obtain 50% opsonophagocytic killing by differentiated HL-60 cells. Overall, postvaccination sera showed a significant increase in opsonophagocytic Ab titers against both serotype 14 and serotype 23F as compared to prevaccination sera ($P < .01$). All donors except 3 demonstrated an increase of ≥2-fold in opsonophagocytic Ab titers after vaccination. There was good correlation between the anti-PPS IgG concentration and the opsonophagocytic Ab titer ($r^2 = 0.8$ and $P = .0025$ for PPS14; $r^2 = 0.863$ and $P = .0008$ for PPS23F) but not between the IgM concentration and the opsonophagocytic Ab titer (data not shown).

Unselected B-Lymphocyte Counts Are Decreased in Peripheral Blood From Elderly Individuals

Peripheral blood lymphocytes (PBLs) were isolated, and the percentage and absolute number of B cells were determined for elderly individuals and compared to data we obtained from our previous study involving young adults (Table 1). The percentage of B cells in elderly individuals was 7.84%, with a mean absolute B cell count (±standard error of the mean [SEM]) of 149 300±40 950 cells/mL. These values were significantly lower than those for young adults (18.67% and 368 100±65 400 cells/mL, respectively; $P < .01$ for both comparisons).

Phenotype of PPS-Specific B Lymphocytes Isolated From PBMCs From Elderly Individuals

Before vaccination and on day 7 after vaccination, PBMCs were isolated, labeled, and subjected to flow cytometry. The phenotype of pre- and postvaccination PPS-specific B cells was compared to the phenotypes of unselected B cells and of B cells from our historical young adult controls [17]. B lymphocytes (CD19$^+$) were subdivided into 4 categories: naive (CD27$^{-}$IgM$^+$), class-switched (CD27$^{-}$IgM$^-$), CD27$^+$IgM$^+$, and switched memory (CD27$^+$IgM$^-$).

Analysis of unselected B cells obtained before vaccination from elderly individuals showed that a large proportion (68.5%) were CD27$^{-}$. The majority (mean, 57.8%; range, 24.9%–84.3%) of CD27$^-$ B cells expressed the naive phenotype, whereas a minority (10.7%; 6.7%–28%) represented class-switched B cells. The memory B-cell population represented 33.6% of B cells, with 17.7% (4.2%–36.3%) expressing the IgM$^+$CD27$^+$ phenotype and 15.9% (3.5%–29.9%) expressing the switched memory phenotype (Figure 1).

Before vaccination, a mean percentage (±SEM) of 1.85% ±0.21% and 2.01%±0.38% of B cells stained with fluorescently

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<th>Young Adults</th>
<th>Elderly Individuals</th>
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<tr>
<td>CD19$^+$ B cells, %</td>
<td>18.67 ± 1.74</td>
<td>7.84 ± 1.89</td>
<td>.008</td>
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<tr>
<td>CD19$^+$ B-cell count</td>
<td>368 100 ± 65 400</td>
<td>149 300 ± 40 950</td>
<td>.01</td>
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Data are mean ± standard error of the mean.

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**Figure 1.** Pre- and postimmunization pneumococcal polysaccharide (PPS)–selected B-cell phenotypes in elderly individuals. The phenotypes of B lymphocytes that respond to vaccination with PPS vaccine were determined by flow cytometry. Before and 7 days after vaccination, circulating peripheral blood mononuclear cells were isolated and labeled fluorescently with different anti-surface marker antibodies. The phenotype of unselected and PPS14- and PPS23F-selected B cells were compared in elderly individuals. In each sample, 100 000 events were recorded. Abbreviation: IgM, immunoglobulin M.
B cells were equally divided between IgM+CD27+ and switched-memory B cells. The IgM+CD27+ population represented 46.3% (12.1%–74.2%) of the prevaccination PPS14 and 71.2% (24.5%–68.1%) for PPS23F. The memory B cells were equally divided between IgM’CD27+ and switched-memory B cells. The IgM’CD27+ population represented 30.8% (8.5%–77%) of total B cells for PPS14 (P = .025) and 29.6% (13.1%–68.1%) for PPS23F; these findings were not significantly different from those for unselected B cells. The switched memory population represented 30.5% (2.9%–56%) and 41.6% (11.2%–63.7%) of the prevaccination PPS14- and PPS23F-labeled B cells, and both populations were significantly different as compared to unselected B cells (P < .001). The remainder of the B-cell population consisted of CD27− B cells, accounting for 39.3% of the PPS14-labeled cells and 28.8% of the PPS23F-labeled B cells; these findings were significantly different from those for unselected B cells (P < .01; Figure 1).

On day 7 after vaccination, the percentage of PPS-selected B cells increased significantly (4.60% for PPS14 and 4.65% for PPS23F; Table 2). The majority of postvaccination PPS-labeled B cells were memory B cells (CD27+), accounting for 70.4% for PPS14 and 78.7% for PPS23F (Figure 1). In contrast to prevaccination B-cell populations, in which IgM’CD27+ and switched memory B-cell phenotypes were equally divided, switched memory B cells were the predominant phenotype after vaccination. The IgM’CD27+ cells represented 24.1% (6.8%–38.5%) of the PPS14-labeled B cells and 25.2% (6%–38%) of the PPS23F-labeled B cells, both of which were less than prevaccination levels but not significantly so. The switched memory population represented 46.3% (12.1%–74.2%) for PPS14 and 53.5% (17.2%–88.4%) for PPS23F, both of which were significantly increased as compared to preimmunization levels (P < .05). Similar to prevaccination PPS-labeled B-cell populations, the minority of postvaccination PPS-labeled B-cell populations consisted of naive CD27− B cells, with 29.5% (5.5%–65.7%) for PPS14 and 21.2% (1.9%–46.4%) for PPS23F. The naive B-cell population consisted primarily of CD27−IgM− B cells, with 23.3% (5.5–49.8) and 16.6% (0.7–38) for PPS14 and PPS23F, respectively. A small percentage of B cells, 6.2% (0%–14.9%) for PPS14 and 4.6% (1.2%–8.4%) for PPS23F, were naive, class-switched CD27−IgM− B cells. Moreover, the predominant B-cell population responding to PPS14 and PPS23F in this elderly population on day 7 after vaccination consisted of CD27−IgM− or switched memory B cells.

**Phenotype of PPS-Specific B Lymphocytes Isolated From PBMCs From Elderly Individuals Versus That Among B Lymphocytes From Healthy Young Adults**

In our previous study [17], we identified the phenotype of B cells responding to PPV 7 days after vaccination in healthy young adults (age, 18–30 years). In prevaccination PBMCs, 1.1% and 1.2% of B cells before immunization and 5.0% and 4.2% after immunization were labeled with PPS14 and PPS23F, respectively. In elderly individuals, the pre- and postvaccination percentages of PPS14- and PPS23F-labeled B cells were similar, namely 1.85% and 2.01%, respectively, before immunization and 4.60% and 4.65%, respectively, after immunization (Table 2). Figure 2 compares the 4 B-cell populations—naive, class-switched, CD27−IgM+, and switched memory—isolated from elderly individuals to those isolated from healthy young adults in our previous study [17]. Before vaccination, there was no statistically significant difference between the young and elderly populations in any of the 4 B-cell subpopulations. After vaccination, young adults demonstrated a significant increase in CD27+IgM+ in response to PPS14 and PPS23F. However, in elderly individuals, the CD27+IgM+ population decreased in response to both PPSs, with a concomitant increase in the switched memory population.

Significant differences were noted in the B-cell response to PPS14 and PPS23F between elderly and young individuals. Young adults responded predominantly with a significant increase in IgM’CD27+ B cells (PPS14 range, 20.3%–53.1%; PPS23F range, 23.0%–62.4%). The elderly individuals, in contrast, responded to both PPSs with a predominantly switched memory B-cell response (PPS14 range, 30.5%–46.3%; PPS23F range, 41.6%–53.5%).

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<tr>
<th>Time Relative to PPV</th>
<th>Young Adults</th>
<th>Elderly Individuals</th>
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<tr>
<td></td>
<td>PPS14, Cells/μL</td>
<td>PPS23F</td>
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<tr>
<td>Before</td>
<td>Percentage</td>
<td>No.</td>
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<td></td>
<td>1.5 ± 1.1</td>
<td>5.5</td>
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<td>After</td>
<td>5.0 ± 2.8</td>
<td>18.4</td>
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Data denote the mean no. or mean percentage (±standard error of the mean) of CD19+ B cells stained with fluorescently labeled PPS14 and PPS23F in peripheral blood samples.

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Table 2. Pneumococcal Polysaccharide-Selected CD19+ B-Cell Percentages and Counts Among Young Adults and Elderly Individuals Before and 7 Days After PPS Vaccine (PPV) Receipt

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DISCUSSION

We recently determined that the PPV-responding population in healthy young adults consisted of CD27⁺IgM⁺ B cells [17]. However, the PPV-responding B-cell subset for at-risk populations such as elderly individuals had not been previously analyzed. The goal of this study was to characterize the phenotype of responding B cells in elderly individuals after PPV vaccination. We analyzed the immune response to PPS14 and PPS23F because both are present in PPV23; PPS14 represents an immunogenic serotype that elicits excellent Ab responses, whereas PPV23F represents a poorly immunogenic serotype.

To ascertain the immunocompetence of our elderly volunteers and their ability to respond to PPV, we studied pre- and postvaccination PPS-specific immunoglobulin concentration and OPA. Although all but 1 individual displayed a significant increase in anti-PPS IgG concentration after vaccination, the IgM concentration increased significantly only in response to PPS23F. This is in stark contrast to the results obtained in healthy young adults, who demonstrated a significant increase in all immunoglobulin isotypes after vaccination for both PPSs [17].

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<tr>
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<th>Young</th>
<th>Elderly</th>
<th>PPS14</th>
<th>Young</th>
<th>Elderly</th>
<th>PPS23F</th>
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<tr>
<td>CD27⁺IgM⁺</td>
<td>30.2 (3.85-72.0)</td>
<td>21.1 (5.7-35.8)</td>
<td>30.5 (2.96-56.0)</td>
<td>46.3 (12.1-74.1)</td>
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<tr>
<td>CD27⁺IgM⁻</td>
<td>20.3 (7.69-37.2)</td>
<td>53.1 (12.0-68.5)</td>
<td>30.8 (8.46-40.4)</td>
<td>24.1 (6.82-38.5)</td>
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<tr>
<td>CD27⁻IgM⁺</td>
<td>40.1 (8.0-76.9)</td>
<td>19.7 (0.0-41.2)</td>
<td>27.4 (6.25-59.0)</td>
<td>23.3 (5.56-49.8)</td>
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<tr>
<td>CD27⁻IgM⁻</td>
<td>9.5 (4.0-22.0)</td>
<td>6.1 (0.96-7.6)</td>
<td>11.9 (1.48-24.2)</td>
<td>6.2 (0.0-14.9)</td>
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Figure 2. Pneumococcal polysaccharide (PPS)-labeled B-cell phenotypes in elderly individuals, compared with young adults. The phenotypes of B lymphocytes that respond to vaccination with PPS vaccine were determined by flow cytometry. Before vaccination and 7 days after vaccination, circulating peripheral blood mononuclear cells were isolated and labeled fluorescently with different anti-surface marker Abs. The phenotype of pre- and postvaccination PPS14-selected (A) and PPS23F-selected (B) B cells was compared in young and elderly individuals. In each sample, 100 000 events were recorded. Abbreviation: IgM, immunoglobulin M.
Several studies have documented an association between decreased efficacy and increased age among PPV recipients [2, 22]. Despite adequate Ab concentrations, the OPA is markedly decreased in elderly individuals [8, 23–25]. Decreased vaccine efficacy is likely related to alterations in functional Ab activity and specificity rather than to IgG Ab concentrations [24, 26]. Several investigators [8, 9, 27] recently reported a significant reduction in the PPS-specific IgM response in elderly individuals. Moreover, depletion of IgM from serum significantly reduced OPA against PPS14 and PPS23F. Others have made similar observations in the response to encapsulated organisms, emphasizing the important role of IgM antibodies in protective immunity [23, 24, 28–30]. The results of our Ab and opsonophagocytic studies are thus similar to those of previous studies that demonstrated a loss of IgM Ab and OPA in elderly individuals.

We used fluorescently labeled PPS in conjunction with flow cytometry for identification and analysis of PPS-specific B lymphocytes. We have previously shown that fluorescently labeled PPSs retain their functional activity and specificity [17]. The use of directly labeled PPS minimizes potential cross-reactivity with linking agents, resulting in lower background binding and more-accurate phenotype analysis. Phenotypic analysis of unselected CD19+ B cells in elderly individuals demonstrated a predominance (68.5%) of naive B cells. Memory B cells, characterized by the presence of the CD27 marker, represented approximately 34% of PBLs, with an equal distribution between IgM+CD27+ and switched memory B-cell phenotypes.

In healthy young adults, unselected PBLs also predominantly consist of naive B cells (68%), and IgM+CD27+ and switched memory B cells each represented approximately 15% [17]. There was no significant difference between elderly and young individuals in memory B-cell percentage. However, elderly individuals had a significantly lower absolute number of B cells (Table 1), and consequently the numbers of IgM+CD27+ and switched memory B cells were significantly lower. Several investigators have studied IgM+CD27+ B cells in elderly individuals, because loss of IgM+CD27+ B cells is associated with impaired immune responses [7, 31]. In concordance with our findings, Colonna-Romano et al and others reported no change in the IgM+CD27+ B-cell percentage with increased age [32, 33]. However, a significant reduction in the absolute number of B cells was reported [33], resulting in decreased numbers of B cells in all phenotype subpopulations.

The preimmunization PPS-selected B-cell population, in response to both PPSs, consisted predominantly of memory B cells, divided between IgM+CD27+ and switched memory B-cell populations, with a concomitant decrease in the fraction of naive B cells. In contrast, the preimmune PPS-labeled B-cell fraction in young adults closely resembled the unselected B-cell phenotype [17], with a predominance of naive B cells. The shift in phenotype from unselected to preimmunization PPS-labeled B cells and from the PPS-specific B-cell phenotype in young individuals to the PPS-specific B-cell phenotype in elderly individuals may reflect the magnitude of prior contact, either through natural exposure or vaccination. It should be noted that Ab concentration, opsonophagocytic Ab titer, and B-cell phenotype distribution were similar between vaccine-naive and vaccine-experienced elderly individuals (data not shown). These data suggest that age is the single most important factor in the shift in preimmunization phenotype distribution of PPS-labeled B cells.

The effect of IgM+CD27+ B-cell deficiency in elderly individuals was accentuated in the postimmunization studies. The majority of PPS-specific B cells after vaccination expressed the switched memory B-cell phenotype. In contrast, the predominant phenotype of PPS-labeled B cells after vaccination in young adults was IgM+CD27+ (Figure 2). The absence of IgM+CD27+ B cells 7 days after vaccination with PPV in elderly individuals correlated with a lack of anti-PPS IgM Ab in serum and with diminished opsonophagocytic Ab titer 30 days after vaccination. Despite the predominance of PPS-specific switched memory B cells after vaccination, both anti-PPS IgG Ab concentration and opsonophagocytic Ab titer were significantly lower in elderly individuals as compared to young adults. Furthermore, there was no correlation between the absolute number or percentage of PPS-specific switched memory B cells and the IgG Ab concentration. The increase in PPS-specific switched memory B cells does not appear to compensate for IgM+CD27+ deficiency in terms of functional Ab activity.

Most previous studies evaluating postvaccination alterations in B-cell phenotype examined unselected B-cell populations [9, 34, 35], rather than antigen-selected B cells. Recently, Clutterbuck et al [36] studied the immune response to either PPV or pneumococcal conjugate vaccine (PCV) followed by PPV in adults aged 50–70 years. PPS-labeled B cells were obtained using biotinylated PPS/streptavidin beads, and cells were analyzed 1 month after vaccination. However, this phenotype analysis is not suitable for comparison to our study because of substantial differences in B-cell capture techniques and timing. We specifically analyzed PBMCs 7 days after vaccination, when the highest number of antigen-specific Ab-secreting cells are found in the peripheral circulation [37, 38]. We examined PPS-specific B cells 30 days after vaccination in 16 young adults and 8 elderly adults (unpublished observations). These studies demonstrated that, 30 days after vaccination, antigen-specific B cells are at preimmunization levels. In addition, the phenotype of PPS-specific B cells was not significantly different from the preimmunization phenotype in young, PPV-naive elderly individuals and previously immunized elderly individuals. These data suggest that, 30 days after vaccination, antigen-specific B cells are by and large absent from the peripheral circulation and reside elsewhere in the B-cell compartment. Findings of phenotype analysis obtained 30 days after vaccination were thus
similar to those reported by Clutterbuck et al [36]. However, this time point is likely not an accurate representation of the cellular immune response to PPV, because it reflects the PBMCs rather than the bone marrow or spleen, which are more likely reservoirs of antigen-specific B cells 30 days after vaccination. We recognize that a limited number of elderly individuals were studied and that this group consisted of 10 PPV-naïve and 4 PPV-experienced individuals (who were immunized >5 years previously). Although the number of individuals enrolled limits the power of our statistical analyses, we found no difference in immune response between the naïve and experienced groups. These results are supported by recently reported studies of PCV13 in elderly individuals [39].

The data presented here demonstrate decreased anti-PPS IgM Ab concentrations, OPA, and absolute and relative numbers of IgM+CD27+ B cells in elderly individuals, compared with young adults. Moreover, clinical studies have established the decreased protective efficacy of PPV in elderly individuals [2, 22]. We hypothesize a direct link between these observations, suggesting a critical role of PPS-specific IgM+CD27+ B cells in protective immunity against S. pneumoniae. The recent change in pneumococcal vaccination practices will let us study the immune response following pneumococcal conjugate vaccination in elderly and immunocompromised individuals. The analysis of the B-cell repertoire will allow us to dissect differences between PCV and PPV responses at a cellular level, providing increased insight into the role of IgM and switched memory B cells in protective immunity.

Notes

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D. J. L. performed experiments, analyzed the data, and contributed to writing the manuscript; R. S. T. assisted with experimental procedures and contributed to writing the manuscript; N. M. K. performed experiments, analyzed the data, and contributed to writing the manuscript; A. S. I. performed experiments and analyzed the data; M. A. J. W. conceived and designed experiments and contributed to writing the manuscript.

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Potential conflicts of interest. All authors: No reported conflicts.

All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

References


