Effect of Immunoglobulin G Isotype on the Infectivity of
Chlamydia trachomatis in a Mouse Model of
Intravaginal Infection

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It has been previously shown with an in vitro neutralization system that monoclonal antibodies (MAbs) to the major outer membrane protein (MOMP) of Chlamydia trachomatis, depending on the isotype of the MAb and the host cell used, can either neutralize or enhance the infectivity of this organism. MAbs to variable domain 4 (VD 4) of MOMP have been described that neutralize the infectivity of C. trachomatis when tested in a system in which either the host cell does not have detectable FcγRIII receptors or complement is added to block the interaction of the MAb with the receptor. However, if FcγRIII receptors are available, immunoglobulin G2b (IgG2b) MAbs to the VD 4 are able to enhance the infectivity of this pathogen. Two MAbs that recognize the sequence TLNPTIA in VD 4 of the MOMP but differ in isotype, E4 (IgG2b) and E21 (IgG1), were used to test whether in vivo the isotype of the MAb modulates the outcome of a vaginal infection in a murine model. A third MAb, CP33 (IgG2b), that recognizes the chlamydial lipopolysaccharide but does not neutralize infectivity of C. trachomatis, was also tested. Elementary bodies (EBs) of C. trachomatis, serovar E (BOUR), were pretreated with the three MAbs and were used to inoculate the vaginas of C3H/HeJ mice which had been pretreated with progesterone. Subsequently mice were monitored over a 5-week period with vaginal cultures. In the groups that were inoculated with EBs pretreated with MAbs directed to VD 4 of MOMP, there was a significant decrease (P < 0.05) in the number of mice infected. Only 30% of the mice were infected in the MAb E4-treated group, and 10% were infected in the MAb E21 group. This was in contrast to the groups inoculated with EBs pretreated with MAb CP33 and control untreated EBs, which resulted in 100 and 79% of the mice infected, respectively. Therefore, in this setting in which EBs were introduced in vivo coated with MAb, there was no enhancement of infection by IgG2b MAbs; rather, the results paralleled the in vitro neutralization results, in which cells lacking FcγRIII receptors were employed. Mice were also given the MAbs, as well as purified IgG as a control, by intraperitoneal injection before and after intravaginal inoculation with C. trachomatis. Despite relatively high levels of MAbs in serum and detectable levels of MAbs in the vagina at the time of infection, there was only modest protection in animals receiving MAb E21, with 60% of the mice infected in contrast to 90% of the mice receiving MAb E4, MAb CP33, and IgG. However, by the second week of infection compared to controls, there was a significant increase (P < 0.05) in the amount of chlamydiae recovered from the vaginas of mice that had received the two IgG2b MAbs, E4 and CP33. In summary, the presence of IgG2b MAbs directed to surface components of C. trachomatis at certain times during the course of infection may play a role in enhancing the infectivity of this pathogen.

Chlamydia trachomatis has been identified as a leading cause of sexually transmitted disease in the Western world. A major concern with these infections is the sequela of infertility that can accompany a genital infection (9). Therefore, in addition to screening programs designed to target the population at risk, a vaccine against this organism has been considered as a prophylactic measure (20, 27). Vaccination against trachoma with the whole organism has proved to be mostly ineffective (20). Recipients of the vaccine either had short-term, serovar-specific protection or, in some cases, developed a worse clinical picture upon infection with this pathogen. While the exact cause of the latter phenomenon is not known, laboratory experiments have suggested that there is an immunological basis for this involving the heat shock protein of this organism (13). Therefore, as an alternative approach, attention has been focused on the development of a chlamydial subunit vaccine. There has been considerable effort made to define the components of C. trachomatis that may induce protection as well as the critical host immunological factors involved in protection against chlamydial infections (13). So far, the host defense mechanisms appear to be multifactorial, and the key antigenic components of C. trachomatis are elusive. The major outer membrane protein (MOMP) of C. trachomatis has been the subject of much research in an effort to define the antigenic components that may be involved in protection against this organism. Monoclonal antibodies (MAbs) to MOMP have been described that are able to neutralize the infectivity of the organism in vitro (13, 16, 18, 31). Therefore, peptides or recombinant proteins representing the epitopes mapped with these neutralizing antibodies have been used in animal vaccinations and subsequent challenge experiments (21, 23, 29). To date, the results of such studies have been mixed. Tuffrey et al. (29), using recombinant MOMP to vaccinate mice by intramuscular and subcutaneous routes, showed upon an intruterine challenge the incidence of upper tract disease was decreased, while vaginal shedding of chlamydiae was not affected. However, when mice were vaccinated via a Peyer’s patch and then challenged, shedding of live chlamydiae and the duration of vaginal shedding were reduced. After vaccinating mice par-
enterally with peptides to MOMP, Su et al. (23) failed to show protection from lower tract disease after a vaginal challenge. Failure to protect from lower genital tract infection with parenteral immunization could be due to several factors, including the adjuvant systems used, the inoculation route, the ratio of immunoglobulin (Ig) subclass raised to the immunogens, the peptides chosen for these studies, or the need for the conformational determinants that may not be present in synthetic or recombinant antigens.

The possibility of different functional roles, in terms of neutralization or enhancement of the infection, of the subclass of Igs elicited by MOMP has been raised (17, 22). We have previously demonstrated that MABs mapping to the same epitope of MOMP that differ in subclass can give contrasting results with in vitro neutralization assays (17). Depending on the isotype and host cell used, enhancement of infectivity as well as neutralization can be observed with the same MAb. Su et al. (22) have presented evidence that suggests that these differences dependent on Ig subclass could be attributed to host cell expression of FcyRII receptors. Since these observations may have important implications for future vaccine development, in this report, using a mouse model of vaginal infection, we have attempted to take the initial steps to answer whether these observations have a role in vivo.

MATERIALS AND METHODS

Organisms.

*C. trachomatis* organisms, serovar E (BOUR) (American Type Culture Collection, Rockville, Md.), raised in HeLa 229 cells were used for the intravaginal inoculations. HeLa cells in 175-cm² flasks were removed 48 h after infection with glass beads, centrifuged for 45 min at 9,000 × *g*. The pellet was resuspended in 0.2 M sucrose–0.02 M sodium phosphate (pH 7.2)–5 mM gluthamic acid (SPG), sonicated, and frozen in aliquots at −70°C. The titer of the stock, as well as the inoculum used in each experiment, was established by centrifuging dilutions of the organism made in SPG onto monolayers of HeLa 229 cells contained in 1-dram (3.697-ml) glass vials. Chlamydial inclusion-forming units (IFU) were determined by staining the coverslips with MAb E4 as previously described (16).

MABS.

MABS were purified from ascitic fluid obtained from BALB/c mice as previously described with a protein A column (Bio-Rad Laboratories, Richmond, Calif.) (16). Fractions that had both a high protein content and inclusion immunofluorescent titer (14) to serovar E were pooled and extensively dialyzed. Purified MAB was frozen in aliquots at −70°C to serovar E were pooled and extensively dialyzed.

In vitro infectivity

In vitro neutralization assays. Complement-independent neutralization assays were performed as previously described with some modifications (5, 17). Dilutions of MAbs made in SPG were mixed with in vitro neutralization with complement (16). In vitro neutralization assay with HeLa cells and complement (16). In vitro neutralization assay with HeLa cells and complement (16). In vitro infectivity of *C. trachomatis* in each group for each of the two trials. In addition to culture, vaginal samples were tested by PCR for the presence of *C. trachomatis*. Samples (0.1 ml) were boiled for 10 min and then placed on ice, and 2 μl was used for the PCR as previously described (15). Briefly, the primers to open reading frame 2 of the 7.5-kb plasmid of *C. trachomatis* CGA CTG GTGTATACGAC AGC and CCA AGC TGA ATG GCG ATT TCT were used, resulting in a fragment size of 198 bp. PCR products were separated by electrophoresis on 3% NuSieve GTG–1% SeaKem agarose (FMC BioProducts, Rockland, Maine) and visualized with ethidium bromide (1 μg/ml).

Passive immunization.

*CHI/Hec* mice were pretreated with Depo-Provera as outlined above. On days 2 and 1 before challenge, the day of challenge, and the day after challenge, mice were given by intraperitoneal injection 100 μg of one of the three MABS in Table 1 or purified IgG from pooled normal mouse sera (Sigma, St. Louis, Mo.) as a control. On the second and third days after challenge, mice were given 50 μg of purified IgG. Mice were challenged intravaginally with 5 × 10⁸ IFU in 0.01 ml of SPG. Vaginal cultures were obtained over a 4-week period after challenge. The experiment was done twice with five mice per treatment group in each trial.

In addition to the mice that were challenged, three mice in each MAB treatment group that were not challenged were bled, and vaginal samples were collected by washing the vagina twice with 0.02 ml of PBS. These samples were used to determine the amount of MAB present the day of the challenge and 1 and 7 days after challenge. To determine the amount of MAB in the serum and vaginal samples, a standard enzyme immunoassay (EIA) curve was generated for each of the three MABS. Here, twofold dilutions of purified MAB ranging from 10 to 0.04 μg/ml were used to assay a microtiter plate coated with EBs (1 μg/well) of serovar E (16). Sera obtained from the test animals were diluted 1:200, vaginal wash samples were diluted 1:2, and the concentration of MAB in the samples was calculated from the standard curve for the corresponding MAB.

**RESULTS**

In vitro pretreatment of EBs with MABS before inoculation.

In the first series of experiments, *C. trachomatis* was pretreated with each of the three MABS in Table 1. Based on previous work with this model in our laboratory, two doses of inoculum were used: 5 × 10⁷ IFU, with which <25% of the animals are infected, and 5 × 10⁸, which infects >75% of the animals. We chose these doses in order to be able to detect enhancement of infection in the case of the lower dose and attenuation of infection with EBs treated in vitro with MABS. *CHI/Hec* (H-2k) female mice (Jackson Laboratories, Bar Harbor, Maine) 7 to 8 weeks of age received 2.5 mg of Depo-Provera (Upjohn, Kalamazoo, Mich.) subcutaneously 10 and 3 days prior to inoculation with *C. trachomatis* (28). The inocula were incubated at 37°C for 45 min before inoculation and weekly for the next 2 weeks. Calcium alginate swabs were inserted in the vagina, rotated 10 times, and placed in 0.4 ml of SPG. Specimens were cultured within an hour on HeLa 229 cells contained in 1-dram (3.697-ml) glass vials, and IFU were detected as described above. At the time of sacrifice, blood was collected from the cardiac puncture from all animals. The experiment was performed twice with five to seven animals in each group for each of the two trials.

In addition to culture, vaginal samples were tested by PCR for the presence of *C. trachomatis*. Samples (0.1 ml) were boiled for 10 min and then placed on ice, and 2 μl was used for the PCR as previously described (15). Briefly, the primers to open reading frame 2 of the 7.5-kb plasmid of *C. trachomatis* CGA CTG GTGTATACGAC AGC and CCA AGC TGA ATG GCG ATT TCT were used, resulting in a fragment size of 198 bp. PCR products were separated by electrophoresis on 3% NuSieve GTG–1% SeaKem agarose (FMC BioProducts, Rockland, Maine) and visualized with ethidium bromide (1 μg/ml).

**TABLE 1. Characteristics of the MABS used for the mouse challenge experiments**

<table>
<thead>
<tr>
<th>MAB</th>
<th>Antigen recognition</th>
<th>Isotype</th>
<th>Neutralize Fc&lt;sup&gt;+&lt;/sup&gt;</th>
<th>Enhance Fc&lt;sup&gt;+&lt;/sup&gt;</th>
<th>50% Neutralization (μg/ml)&lt;sup&gt;+&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>E4</td>
<td>MOMP VD4 (TLNPTIA)</td>
<td>IgG2b</td>
<td>Yes</td>
<td>Yes</td>
<td>0.40</td>
</tr>
<tr>
<td>E21</td>
<td>MOMP VD4 (TLNPTIA)</td>
<td>IgG1</td>
<td>Yes</td>
<td>No</td>
<td>0.41</td>
</tr>
<tr>
<td>CP33</td>
<td>LPS</td>
<td>IgG2b</td>
<td>No</td>
<td>Yes</td>
<td>&gt;50</td>
</tr>
</tbody>
</table>

* In vitro neutralization assays performed: Fc<sup>+</sup>, cells without FcyRII receptors or assays in which complement interferes with MAB binding to Fc receptors; Fc<sup>−</sup>, cells with FcyRII receptors.

**<sup>+</sup> In vitro neutralization assay with HeLa cells and complement.**
infection with the higher dose. Immediately before inoculation into mice, the pretreated EBs were assayed with an in vitro system in which enhancement can be demonstrated. Here the MAb E4- and CP33-treated EBs had six times the infectivity of the non-treated and MAb E21-treated EBs. In contrast, in vivo, as can be seen in Table 2 based on vaginal culture results, pretreatment of the higher dose of organisms with MAbs E21 and E4 conferred statistically significant (P < 0.05) protection, whereas with MAb CP33, no protection was observed. In order to further substantiate the negative vaginal cultures in the MAb E21- and E4-treated groups, the vaginal samples were also tested by PCR. Samples taken 1 and 3 weeks after challenge were tested by PCR, and there was an exact correlation with the vaginal culture results.

In the case of the lower inoculum, none of the 10 mice pretreated with MAb E4 and MAb E21 were infected, as determined by vaginal shedding and PCR. This was compared to 21% (3 of 14) of the control mice and 30% (3 of 10) of the mice inoculated with MAb CP33-treated EBs. Therefore, there was no enhancement of infection seen with these groups of mice.

**Passive immunization with MAbs.** Mice were administered the three MAbs or IgG as a control by daily intraperitoneal injections. The passively immunized animals were then challenged after 3 days of antibody administration. Three mice in each treatment group were used to measure the amount of MAb in the serum and vagina at the time of infection and 1 and 7 days after infection. An EIA in which known concentrations of the purified MAbs were used as standards to quantitate the amount of MAb in the serum and vaginal wash yielded the concentrations seen in Table 3. These serum MAb concentrations resulted in immunofluorescent antibody titers of 12,800 for the sera from the MAb E4 and E21 groups and titers ranging from 1,600 to 800 for the MAb CP33 group. These serum MAb concentrations were much higher than that needed to produce neutralization in vitro (Table 1). When tested with an in vitro system in which a source of complement was present that could presumably block MAb attachment to FcγRIII receptors, both the sera from mice inoculated with MAb E4 and MAb E21 neutralized chlamydia infectivity, while sera from mice given MAb CP33 had no effect on infectivity (Fig. 1). Neutralization titers of the MAb E4 and MAb E21 groups were both >256 for the three time points tested. However, when tested by a system in which a complement source was not present, there was marked enhancement with sera obtained from mice given either of the IgG2b MAbs, E4 or CP33, with IFU counts nearly three times that of the control (Fig. 1).

The concentrations of the MAbs in vaginal wash as determined by EIA were considerably lower than the concentrations in serum. We were not able to measure the amount of MAb CP33 in the vaginal wash samples in the quantitative EIA because of the limit of detection for this MAb, which is consistent with the weaker binding of MAb CP33 to EBs when measured on a protein basis. When vaginal samples from the day of inoculation were tested at a 1:2 dilution by inclusion IFA, samples from all mice in both MAb E21 and MAb E4 groups were positive, and one of the three mice in the MAb CP33 group was positive.

After inoculation with EBs, 90% (9 of 10) of the mice in all groups except the MAb E21-treated group shed chlamydiae. While not statistically significant, in the MAb E21 group, fewer mice were infected after the challenge, with only 60% (6 of 10) being culture positive during a 3-week period. The total numbers of IFU shed by mice infected in the control and MAb E21 groups were very similar (Fig. 2). However, as illustrated in Fig. 2 and 3, MAb E4- and CP33-treated groups had on average higher numbers of chlamydiae shed per infected animal on days 12 and 15 after infection than did control and MAb E21-treated groups (P < 0.05), which returned to the same level as the other two groups by the end of the third week. For the most part, those animals infected in each group shed over the first 3 weeks, with a decrease in positive animals seen in all

<table>
<thead>
<tr>
<th>TABLE 2.</th>
<th>Overall results from inoculation of mice with EBs pretreated with MAbs*</th>
</tr>
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<tbody>
<tr>
<td>Treatment group</td>
<td>Total no. of mice</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td>14</td>
</tr>
<tr>
<td>MAb E21</td>
<td>10</td>
</tr>
<tr>
<td>MAb E4</td>
<td>10</td>
</tr>
<tr>
<td>MAb CP33</td>
<td>10</td>
</tr>
</tbody>
</table>

* A total of 5 x 10^6 IFU/ml were pretreated with 100 μg of each MAb per ml for 45 min at 37°C prior to intravaginal inoculation with 5 x 10^3 IFU/mouse.

**TABLE 3.** Estimated concentration of MAbs in serum and vaginal wash specimens at different times after challenge.

<table>
<thead>
<tr>
<th>MAB</th>
<th>Serum (μg/ml)</th>
<th>Vaginal wash (ng/ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Day 0</td>
<td>Day 1</td>
</tr>
<tr>
<td>E4</td>
<td>84</td>
<td>88</td>
</tr>
<tr>
<td>E21</td>
<td>100</td>
<td>200</td>
</tr>
<tr>
<td>CP33</td>
<td>90</td>
<td>100</td>
</tr>
</tbody>
</table>
groups by day 19 (Fig. 4). Therefore, it appears that compared to controls passively administered IgG, MAb E21 conferred modest protection when the total numbers of mice infected in each group are considered. However, once a mouse was infected, none of the MAbs either reduced duration or lowered the number of chlamydiae shed from infected animals. Furthermore, in the cases of MAbs E4 and CP33, the two IgG2b MAbs, there was a significant increase in the quantity of chlamydiae shed from infected mice during the second week following challenge.

**DISCUSSION**

Subunit vaccines have been one of several approaches taken to develop immunization schemes for the prevention or attenuation of chlamydial infections (20). Su et al. (23) have immunized mice with a peptide representing a surface-exposed region of MOMP and subsequently challenged the mice by an intravaginal inoculation of *C. trachomatis*. Tuffrey et al. (29) have used recombinant MOMP as an immunogen followed by intrabursal challenge. In both trials, when mice were immunized parenterally, there was no protection from lower genital tract infection as measured by vaginal shedding of *C. trachomatis* and does not show the enhancement effect when cells express FcyRIII receptors (16, 17). As an additional control, we employed an IgG2b MAb to the lipopolysaccharide (LPS) of *C. trachomatis*, which also appears to enhance infectivity when FcyRIII receptors are present but which, unlike the other two MOMP MAbs, does not have the ability to neutralize infectivity in a culture system void of these receptors.

From the experimental data, it is clear that if EBs are precoated with MAbs and then used to infect mice through the vaginal route, there is no enhancement of infection by the two IgG2b MAbs tested, E4 and CP33. In contrast, there is a perfect correlation between the in vitro assays in which FcyRIII receptors are absent or blocked in the presence of complement where MAbs to the VD4 of MOMP, E4 and E21, have been shown to effectively neutralize the infectivity of *C. trachomatis*. One explanation for these observations of neutralization by MAb E4 and not enhancement of infection could be that the organisms have been killed by the MAb pretreatment before challenge. However, when EBs pretreated with MAb E4 were assayed immediately before infection in a system in which FcyRIII receptors are present, there was enhancement of infection over nontreated control EBs and MAb E21-treated EBs. Therefore, viability was not compromised by the MAb treatment prior to infection. Another explanation for the lack of enhancement is that the permissive epithelial cells during the early stages of infection do not display Fc receptors to which the EB-IgG2b complex can bind and eventually gain entry into the host cell. Therefore, the actual chlamydial attachment site on the permissive cell is blocked by the MAbs that recognize MOMP. Recently, Su et al. (24) have presented evidence that the binding of EBs to epithelial cells is through the interaction of MOMP on the surface of the EB and heparan sulfate proteoglycans on the host cell. Therefore, blocking of this interaction by MAbs directed to VD 4 of MOMP is a plausible explanation for our findings of protection from a vaginal challenge.

Another approach for examining the effect in vivo on infection by MAbs that enhance or neutralize infectivity in vitro was to passively administer MAbs to the animal. With this approach, MAb E21 appeared to afford modest protection, as evidenced by a lower number of mice infected. This modest difference may be the result of a low titer of MAb demonstrated in the vaginal tract at the time of infection. While it is difficult to measure the quantity of MAb in the vaginal tract, the vaginal samples contained 7 ng of MAb E21 per ml on the day of challenge. However, this number was derived from the 0.04 ml that was used to wash out the vaginal tract. Therefore, if one assumes that this represents approximately a 1:40 dilution of the vaginal contents, then the actual concentration in
The vaginal mucosa is closer to 0.28 μg/ml. This concentration is just below the amount, 0.4 μg/ml, determined by an in vitro system to decrease by 50% the infectivity of C. trachomatis compared to that of non-MAb-treated EBs. By the same calculation, MAb E4 would have been present at 0.08 μg/ml, well below the amount necessary to result in neutralization. In both of these cases, serum antibody concentrations ranged from 84 to 100 μg/ml and gave neutralization results similar to those.

**FIG. 3.** Distribution of culture-positive mice by number of IFU recovered from the vaginal culture. The groups represented were passively immunized with the MAb indicated or IgG (control) before and after a vaginal challenge. There were 10 animals per group, and animals that were culture negative are not included in the graph.
obtained in experiments in which we have immunized mice with peptides representing VD 4 of MOMP (6). Therefore, the IgG levels present in the vaginal mucosa are due to transudation of serum antibodies and are not locally produced, and therefore, they are most likely representative of IgG levels produced from systemic immunizations with chlamydial peptides. Su et al. (23) immunized mice by a subcutaneous route using an oligopeptide representing MOMP and found vaginal antibody EIA titers to EBs to be 100 to 150 times lower than those in the serum. Despite high neutralizing antibody titers in the serum, they failed to find any evidence of protection from a vaginal challenge with C. trachomatis. By comparing Ig types found in the vaginal wash and in the serum, they concluded that the IgG present in the vaginal mucosa was a result of transudation and not local production. Therefore, corroborating their findings, we have seen despite high titers of neutralizing MAbs in the serum, that the level achieved in the vaginal area appears to be too low to afford significant protection.

Cotter et al. (7) used a backpack tumor hybridoma system to test the effect of an IgA- and IgG3-producing hybridoma directed to the MOMP of the mouse pneumonitis biovar of C. trachomatis to protect against infection from a challenge with the mouse pneumonitis biovar of C. trachomatis. Using this system, they were able to detect the MAbs in the vaginal secretions; however, the concentration was on average 100- to 200-fold lower than that in the serum. Here, they found only a marginal protective effect on colonization and shedding from the genital tract.

In the animals passively immunized, the two IgG2b MAbs, E4 and CP33, appeared to enhance infection, as determined by the number of IFU present in vaginal cultures taken during the second week of infection. While similar numbers of mice in the control and MAb E4 and CP33 groups were infected and shed comparable amounts of viable EBs during the first week of infection, there appeared to be a significant increase in shedding of viable EBs by the two groups given the IgG2b MAbs, E4 and CP33. A possible explanation for this observation is that permissive cells during the course of infection due to the inflammatory process express FcγRIII receptors, resulting in more efficient uptake of IgG2b-coated EBs. Induction of Fc receptor expression in epithelial cells has been previously documented (1–3, 8). Polymeric IgA receptors have been shown to increase in response to inflammation and infection (8). It has also been demonstrated that IL-4 and gamma interferon can act synergistically to increase IgA receptor levels in human intestinal epithelial cells (8). Epidermal keratinocytes have also been shown to express an Fc IgE receptor on their surface after stimulation in vitro with IL-4 and gamma interferon (2). Recently FcRn, which transports IgG in an apical to basolateral direction, had been demonstrated to be functionally expressed on the surface of intestinal epithelial cells of adult rat hepatocytes (3). Ulstein et al. (30) have demonstrated the presence of Fcy receptors on the glandular epithelium of the human endometrium. Their work suggested that the expression of FcR varies during different stages of the menstrual cycle. In addition, the presence of FcγRIII receptors on the surface of cultured HeLa cells has already been documented by Su et al. (22). Therefore, it remains to be proven whether genital mucosal epithelial cells, permissive for C. trachomatis in vivo, actually express Fc receptors on their surface in response to infection. If so, then this may be a mechanism that chlamydiae could benefit from by facilitating their entrance into the host cell. At this point, one can only speculate as to what advantage such receptors might give the host, but they could be a response to infection in order to transport Ig into the lumen of the genital tract in an attempt to attenuate infection.

In summary, it is clear that IgG MAbs that neutralize the infectivity of C. trachomatis if present in a high enough concentration on the surface of C. trachomatis can protect from in vivo infection, presumably by blocking entrance into permissive cells. However, despite achieving high serum antibody levels, the amount of IgG antibody that can reach the genital mucosa is too low to afford significant protection. These findings suggest that immunization strategies to attenuate vaginal infection that rely to some degree on antibody will have to be targeted to the genital mucosa in order to favor local antibody production. This may favor not only the production of a protective IgA response but also higher levels of IgG than that afforded by parental immunization. In addition, this study presents further in vivo evidence that antibodies directed to C. trachomatis that are of the IgG2b isotype may actually play a role in enhancing a chlamydial infection.

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