Role of Retinal Pigment Epithelium in the Development of Experimental Autoimmune Uveitis

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Purpose. To determine the role of retinal pigment epithelium in the induction of S-antigen-induced uveitis by administration of sodium iodate (NaIO₃) to selectively damage the retinal pigment epithelium.

Methods. Forty-four Lewis rats were injected with 60 µg of S antigen in complete Freund's adjuvant. On postimmunization day 9 the rats were separated into four groups: three groups received NaIO₃ at doses of 50, 25, and 10 mg/kg body weight, respectively, and the fourth group (control) received diluent. In addition, separate groups of animals (three in each group) received various doses of NaIO₃ or diluent. All of the animals were killed on day 6 after NaIO₃ injection, and the eyes were enucleated and submitted for light and electron microscopic examination. In addition, two groups of Lewis rats (6 in each group) were immunized with 0.5 ml of guinea pig spinal cord homogenate in complete Freund's adjuvant to induce experimental allergic encephalomyelitis. On postimmunization day 7, one group received NaIO₃ at a dose of 50 mg/kg body weight, whereas the other group received diluent. All animals were killed between days 12 and 14, and spinal cord sections were obtained for microscopic examination.

Results. In the control group immunized with S antigen, severe (2+ to 4+) uveoretinitis developed in 70% of the animals. In contrast, only 18% of the animals injected with NaIO₃ at a dose of 50 mg/kg body weight exhibited disease, and this was a mild (1+) form. The groups injected with 25 mg/kg (1 + to 2+) and with 10 mg/kg ((2+ to 3+) of NaIO₃ showed a mild to moderate degree of uveoretinitis in 27% and 50% of the animals, respectively. In the remainder of the animals there was no evidence of uveoretinitis. All of the NaIO₃-treated animals showed selective necrosis of the retinal pigment epithelium; this was extensive in the higher dose group and focal in the lower dose groups. In the experimental allergic encephalomyelitis model there was no significant difference in incidence or histologic appearance of demyelinating disease in NaIO₃- vs diluent-treated groups.

Conclusions. These results indicate that the retinal pigment epithelium may play a role in the initiation and perpetuation of uveitis after sensitization with S antigen. The effect of NaIO₃ appears to be localized to the retinal pigment epithelium; it had no effect on immune reactive cells, as evidenced by the development of experimental allergic encephalomyelitis in animals treated with NaIO₃. Invest Ophthalmol Vis Sci. 1994;35:40-47

Experimental autoimmune uveitis (EAU), similar to other organ-specific diseases, can be initiated by resident antigen-presenting cells when the appropriately sensitized T cells are encountered. To be an effective antigen-presenting cell, a cell should have the necessary intracellular machinery to process and subsequently present the antigen to immune cells. In addition, the antigen-presenting cell should be able to express surface MHC class II antigens for proper interaction with T cells. However, not all of the cells with class II surface antigens can act as antigen-presenting cells and, in addition, it is not yet clearly known if class II antigen expression alone is sufficient for antigen-presenting cell function.
Within the eye, four resident cells are capable of expressing MHC class II antigens during intraocular inflammation.6-9 These are ciliary epithelial cells, Müller cells, retinal vascular endothelial cells, and retinal pigment epithelium (RPE) cells. However, if any or all of these cells act as antigen-presenting cells in the induction of uveitis is unknown.

The retinal pigment epithelium, as a part of its physiological function, continuously phagocytoses S-antigen–rich rod outer segments.10 In addition, RPE cells, like macrophages, have the intracellular lysosomal and hydrolytic enzymes, such as acid phosphatase and cathepsin D, that can distinguish, ingest, and digest various particles.11 It has also been demonstrated in vitro that isolated RPE cells express class II antigens in response to stimulation with interferon gamma,12 and coculture studies showed that RPE cells can present retinal as well as nonretinal antigen to lymphocytes.2 Because of these unique features, evaluated the role of the RPE in the development of uveitis by using a known RPE poison, sodium iodate (NaIO3).13-16 Accordingly, we monitored the incidence and severity of S-antigen–induced EAU in NaIO3-treated Lewis rats.

MATERIALS AND METHODS

Disease Induction

Forty-four female Lewis rats (Charles River, Wilmington, VA) weighing 175 to 200 g were injected in the hind foot pad with 60 μg of bovine S antigen in complete Freund’s adjuvant containing 2 mg/ml of Mycobacterium tuberculosis H37 RA (Difco, Detroit, MI) in a total volume of 0.12 ml. S antigen was isolated from bovine retina according to the method described by Dorey et al.17 All the procedures used were in accordance with the ARVO Statement for the Use of Animals in Ophthalmic and Vision Research.

Treatment

On day 9 after S antigen injection, rats were separated into four groups; three groups (groups 1, 2, and 3) received a tail vein injection of NaIO3 (Sigma, St. Louis, MO) in normal saline at doses of 50, 25, or 10 mg/kg body weight, respectively, in two doses administered 4 hours apart. NaIO3 (0.08 M) was prepared using normal saline as diluent, pH adjusted to a range of 7.3 to 7.5; the final solution was sterilized by filter-sterilization with a 3 μm filter (Nucleopore, Pleasanton, CA). The control group (group 4) received diluent only. In addition, separate groups of naive animals, three animals in each of three groups (groups 5, 6, and 7) received NaIO3 at doses 50, 25, or 10 mg/kg body weight. All of the animals were anesthetized and killed on day 6 after NaIO3 injection. Eyes from the immunized animals were fixed in 4% buffered formaldehyde and submitted for light microscopic examination. The severity of the intraocular inflammation was graded in a masked fashion according to the grading system described by Wetzig et al.18 One eye from each of the animals that received NaIO3 only was submitted for light microscopy in 4% buffered formaldehyde; the other eye was immersed in cold glutaraldehyde and formaldehyde fixative and processed for electron microscopy, as described previously.19 Briefly, the eyes were sectioned, postfixed in 1% osmium tetroxide buffered with phosphate, dehydrated through a graded series of ethyl alcohol, cleared in propylene oxide, and embedded in Epon. For electron microscopic studies, ultrathin sections were prepared, stained with uranyl acetate and examined with a Zeiss-10 microscope (Zeiss, Thornwood NY).

In a subsequent experiment, two groups of six animals each (groups 8 and 9) were immunized with 60 μg of retinal S antigen in complete Freund’s adjuvant. On postimmunization day 9, group 8 rats (experimental animals) received NaIO3 in the tail vein at a dose of 50 mg/kg body weight, and the control animals (group 9) received diluent. Animals in both groups 8 and 9 were injected intradermally with 100 μg S antigen in 0.1 ml of phosphate-buffered saline in the shaven dorsal regions 36 hours before death to study in vivo delayed-type hypersensitivity. All animals were killed on day 6 after injection of NaIO3. The delayed-type hypersensitivity reaction was studied (in a masked fashion) just before death by measuring square area of induration.30 The results were analyzed by the one-tailed Student’s t test. The eyes were enucleated and processed for histopathologic studies, spleens were removed for lymphocyte proliferation assay, and sera were obtained to determine the levels of antibodies to S antigen.

Lymphocyte Proliferation Assay

Mononuclear cells were isolated by Ficoll-Paque gradient (Pharmacia, Piscataway, NJ) from spleen cell suspensions of each animal in groups 8 and 9. Proliferation assays were performed in flat-bottomed 96-well culture plates (Costar, Cambridge, MA) using RPMI 1640 supplemented with 10% fetal calf serum and 2-mercaptoethanol, as described previously.21 The mononuclear cell suspension and appropriately diluted S antigen or mitogen (concanavalin or phytoheamagglutinin) were incubated for 5 days at 37°C. At the end of the culture period the cells were pulsed for 5 hours with 1 μCi 3H-thymidine and incorporated counts per minute were assessed using a scintillation counter. Results were expressed as stimulation index: stimulation index = counts per minute with S antigen or mitogen/counds per minute with medium. Results were analyzed by the one-tailed Student’s t test.
Detection of Antibodies to S Antigen

Serum samples from the animals in groups 8 and 9 were titrated for antibody to S antigen by enzyme-linked immunosorbent assay using a technique similar to that described by Mochizuki et al.2 Briefly, 96-well polyvinyl chloride plates (Dynatech Laboratories, Alexandria, VA) were coated with S antigen, 50 ng/well, in carbonate buffer. Plates were incubated at 4°C overnight and then washed three times with phosphate-buffered saline containing 0.05% Tween 20. After incubation with phosphate-buffered saline/1% bovine serum albumin at 37°C for 30 minutes, diluted serum samples were added to the wells. After incubation for 1 hour at 37°C, plates were washed three times with phosphate-buffered saline/Tween; peroxidase-conjugated rabbit anti-rat immunoglobulin G (Cooper Biomedical, Malvern, PA) at a dilution of 1:6000 was added to each well, after which the plates were incubated at room temperature for 1 hour. The plates were then washed as before and o-phenylenediamine (Sigma) in citrate buffer containing 3% H2O2 was added to the wells. The reaction product was measured by absorbance at 490 nm. Antibody levels were expressed as the absorbance values at 1:100 dilution for each serum sample in triplicate, and the results were analyzed by one-tailed Student's t test.

NaIO₃ in Experimental Allergic Encephalomyelitis

To eliminate possible toxic effects of NaIO₃ on the immune cells, another prototype T-cell-mediated disease, experimental allergic encephalomyelitis (EAE), was studied. Two groups of female Lewis rats (groups 10 and 11), six in each group, were immunized with a 1:1 emulsion of freshly isolated guinea pig spinal cord homogenate in normal saline and complete Freund's adjuvant containing 2 mg/ml of Mycobacterium tuberculosis (Difco). This emulsion (0.5 ml) was injected intra-dermally in the shaven nuchal region at five different sites. On postimmunization day 7, the experimental group received NaIO₃ intravenously at a dose of 50 mg/kg of body weight, similar to group 1; the control group received diluent. All animals were killed between days 12 and 14. Optic nerves and cervical and lumbosacral spinal cords were obtained for histopathologic examination; the tissue sections were stained with luxol fast blue-hematoxylin and eosin.

RESULTS

Histopathologic examination results of animal groups 1 to 4 are shown in Table 1. Severe uveoretinitis developed in only seven of ten control animals (group 4) that received diluent only. The intraocular inflammation was graded to be 2+ to 4+. One animal died on postimmunization day 10. All seven rats with uveoretinitis showed diffuse infiltration of acute and chronic inflammatory cells in the uvea, associated with exudative retinal detachment and extensive destruction of the outer retina (Fig. 1). The ocular inflammation was found to be 2+ to 4+ in these rats. In contrast, only 2 of 11 animals injected with the high dose of NaIO₃ (group 1) exhibited ocular disease, and this was a mild form (grade 1+) characterized by choroidal thickening and slight vitritis (Fig. 2). None of these animals showed inflammation involving the retina. The retinal pigment epithelium showed eosinophilic changes with pyknosis of nuclei; the photoreceptor outer segments were present but were disorganized.

Of the animals injected with 25 mg/kg of NaIO₃ (group 2), 3 of 11 revealed a moderate degree of uveoretinitis (1+ to 2+) characterized by choroidal thickening and focal destruction of photoreceptors. In group 3, treated with NaIO₃ at a dose of 10 mg/kg body weight, one animal died on day 10 after injection of NaIO₃; 5 of 10 animals developed a moderate to severe degree of uveoretinitis (2+ to 3+) with marked

| Table 1. Histopathologic Analysis of Intraocular Inflammation and Retinal Damage in Experimental Groups 1 to 4 |
|---|---|---|
| Group | Treatment | Disease Incidence | Severity and Grading of Inflammation |
| 1 | NaIO₃ 50 mg/kg | 2/11 (18%) | Mild thickening of choroid, iris and ciliary body 1+ |
| 2 | NaIO₃ 25 mg/kg | 3/11 (27%) | Mild thickening of uvea and focal extension of inflammation into the outer retina 1+ to 2+ |
| 3 | NaIO₃ 10 mg/kg | 5/10 (50%) | Marked thickening of uvea with outer retinal damage from inflammatory cell infiltration 2+ to 3+ |
| 4 | Diluent | 7/10 (70%) | Marked thickening of uvea with extensive retinal damage and serous detachment of the retina 2+ to 4+ |

NaIO₃ was injected on day 9 post-immunization and animals were sacrificed six days later.
thickening of the uvea. There was destruction of photoreceptors and infiltration of inflammatory cells was noted in the outer retinal layers. Even though the animals in groups 2 and 3 showed multifocal necrosis of the RPE, the extent of RPE involvement was less in groups 2 and 3 than in group 1. Animals in groups 5, 6, and 7, which were treated with NaIO₃ only, demonstrated variable amounts of RPE damage that was more marked in the higher dose group (Fig. 3). Electron microscopic examination of these eyes demonstrated damage to the RPE, which showed loss of the basal and apical folds, disorganization of mitochondria, and other intracellular organelles (Fig. 4) in contrast to normal RPE (Fig. 5). Electron microscopy also revealed the presence of rod outer segments on day 6 after injection of NaIO₃; however, these outer segments appeared disorganized. None of these NaIO₃-treated animals exhibited intraocular inflammation.

**Delayed-Type Hypersensitivity Reaction**

Delayed-type hypersensitivity test performed 36 hours before death and measured as the square area of induration revealed no significant difference between NaIO₃- and diluent-treated groups. NaIO₃-treated animals (group 8) had an average area of induration of
FIGURE 5. Electron micrograph of retinal pigment epithelium obtained from control animal. Note normal cytoarchitecture of retinal pigment epithelium (original magnification ×4704).

2.39 ± 0.80 cm² whereas the diluent treated control group (group 9) showed 2.5 ± 1.23 cm² (P > 0.05).

Lymphocyte Proliferation Assay

Results of assays of in vitro proliferation of lymphocytes in response to S antigen and to nonspecific antigens are shown in Table 2. The stimulation index for S antigen was 16.65 ± 4.96 in the NaIO₃-treated group and 47.72 ± 18.17 in the diluent-treated control group (P < 0.005). The stimulation index with phytohemagglutinin was 12.06 ± 3.95 in the NaIO₃-treated group and 27.02 ± 6.02 in the diluent-treated control group (P < 0.005). However, stimulation index with Concanavalin A was significantly higher in the NaIO₃-treated group, 9.52 ± 2.58, than in the diluent-treated group, 3.42 ± 1.16 (P < 0.005).

Enzyme-Linked Immunosorbent Assay

Enzyme-linked immunosorbent assay for S antigen showed positive reactivity as measured by absorbance at 490 nm in 1:100 dilution of all serum samples (groups 8 and 9). Serum samples from normal animals demonstrated an average value of 0.15 or less (a final corrected value of 0.30 or greater was used as the cutoff for positivity). There was no significant difference in the production of antibodies to S antigen in NaIO₃-treated and diluent-treated animals. The average value in the NaIO₃-treated group was 1.26 ± 0.08, whereas in the control group the value was 1.23 ± 0.10 (P > 0.05).

NaIO₃ in Experimental Allergic Encephalomyelitis

On day 10 after immunization with guinea pig spinal cord emulsion, two animals in the NaIO₃-treated group developed grade 3 disease and two animals developed grade 2 disease. Grade 1 disease developed in the remaining two animals by day 14. Similarly, in the diluent-treated control group, on day 10 two animals developed grade 3 clinical disease and two developed grade 2 disease. The remaining two animals exhibited 0.5 to 1 disease between days 12 and 14 (grade 0.5; flaccid tail; 1; ataxia; 2; paresis of hind legs; 3; frank paralysis. The grading system was adopted from Carbon et al(24). Histopathologic examination of optic nerve and spinal cord sections showed focal demyelination and infiltration of inflammatory cells in both groups 10 and 11 (See table 3). At the site of this inflammatory cell infiltrate, luxol fast blue staining revealed loss of myelin. The inflammatory process appeared to be similar in both groups.

DISCUSSION

Selective damage of RPE by intravenous injection of NaIO₃ produced a significant decrease in the incidence and severity of S-antigen–induced EAU. In the current experiment severe uveitis developed in 70% of the control animals injected with S antigen and diluent. This intraocular inflammation was associated with exudative retinal detachment and diffuse infiltration of mononuclear cells admixed with polymorphonuclear leukocytes in the retina and uvea. In contrast, mild uveitis developed in only 18% of the animals treated with NaIO₃ at a dose of 50 mg/kg body weight. Moreover, this intraocular inflammation caused only mild choroidal thickening, with preservation of the overlying retina. In addition, the incidence and severity of inflammation was inversely proportional to the dose of NaIO₃, that is, lower incidence and milder disease in the higher dose group (group 1) and moderate to se-

<table>
<thead>
<tr>
<th>GROUP (n*)</th>
<th>TREATMENT</th>
<th>S-Ag</th>
<th>CON-A</th>
<th>PHA</th>
</tr>
</thead>
<tbody>
<tr>
<td>8 (6)</td>
<td>NaIO₃ (50 mg/kg)</td>
<td>16.65 ± 4.96</td>
<td>9.52 ± 2.58</td>
<td>12.06 ± 3.95</td>
</tr>
<tr>
<td>9 (6)</td>
<td>Diluent</td>
<td>47.72 ± 18.17</td>
<td>3.42 ± 1.16</td>
<td>27.02 ± 6.02</td>
</tr>
</tbody>
</table>

* n = number of animals in each group.
NaIO₃ was injected day 9 post-immunization and animals were sacrificed 6 days later.
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The selective toxic effect of NaIO3 on RPE has been attributed to several mechanisms. NaIO3 inhibits the lactate dehydrogenase, succinyl dehydrogenase, alcohol dehydrogenase and acid phosphatase activity of RPE. The zona occludens, which is the anatomic basis for the blood–retinal barrier function of RPE, is also destroyed by treatment with NaIO3. Heavy and diffuse fundus fluorescence was reported 24 hours after NaIO3 administration, indicating damage to the blood–retinal barrier; this effect was found to persist for 7 to 8 days. In addition, NaIO3 also destroyed anionic sites on both sides of the basal membrane of the RPE cells. The c-wave of the electroretinographic response, which originates mainly in the RPE, was abolished within minutes of NaIO3 injection.

Due to the aforementioned effects, the RPE cannot participate in receptor outer segment turnover in NaIO3-treated animals. Subsequent to the loss of its intracellular enzyme activities, the RPE in NaIO3-treated animals may also be incapable of effectively processing antigen. Light microscopic as well as electron microscopic studies showed the presence of photoreceptors even after 6 days of NaIO3 treatment, indicating the availability of S antigen to the antigen-presenting cells, because S antigen is localized predominantly in photoreceptors. Similar findings of preserved photoreceptor outer segments were reported by Ashburn et al. Even in the presence of sensitized T cells, the NaIO3 treatment prevented development of uveitis in the majority of animals when a high dose (50 mg/kg) of this selective RPE poison was administered, which suggests that local antigen presentation may have been prevented by the NaIO3 treatment. However, additional studies, in particular adoptive transfer studies using this agent, may help to further define the role of the RPE in the induction and/or perpetuation of uveitis.

Previous studies from our laboratory demonstrated that EAU in Lewis rats peaks at between 12 and 14 days postimmunization with S antigen. This, together with reports that the damaging effects of NaIO3 on RPE begin 24 hours after administration and last 7 to 8 days, and the repair process commences by day 6, led us to administer NaIO3 on day 9 after immunization with S antigen. In the current study, this 1-week "window" of RPE damage was used to study the role of RPE in the development of S-antigen–induced EAU. More studies are underway to determine the significance of this timing on inhibition of uveitis development.

The current electron microscopic studies and several previous studies indicate selective damage to the RPE from NaIO3 during the initial period after systemic administration of this agent. This selective effect appears to last about 5 to 7 days. Subsequent to or during the latter part of this period, there is clear evidence of damage to photoreceptor outer segments and the choriocapillaris. The damage to these structures could play a role in suppression of uveitis. However, the current study was designed to avoid the effects of NaIO3 on the photoreceptors and choriocapillaris by killing the animals on day 6 after administration of NaIO3. Although such design could minimize the effects of photoreceptors and choriocapillaris on the development of uveitis, because of inherent limitation it is not possible to completely eliminate the effects of NaIO3 on these structures in modulation of uveitis.

There have been reports of toxic effects of NaIO3 on the kidneys of experimental animals. However, to our knowledge there are no published accounts of toxic effects of NaIO3 on immune cells. Because the decrease in severity and incidence of EAU in our model could possibly be due to a direct toxic effect of NaIO3 on these cells, we used NaIO3 in a different

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**TABLE 3. Clinical and Histopathologic Analysis of Experimental Groups 10 and 11 (EAE Model)**

<table>
<thead>
<tr>
<th>Group</th>
<th>No.</th>
<th>Immunization</th>
<th>Treatment</th>
<th>Clinical Disease</th>
<th>Demyelination</th>
</tr>
</thead>
<tbody>
<tr>
<td>10</td>
<td>6</td>
<td>GPSC homogenate</td>
<td>NaIO3</td>
<td>6/6</td>
<td>6/6</td>
</tr>
<tr>
<td>11</td>
<td>6</td>
<td>GPSC homogenate</td>
<td>Diluent (NaCl)</td>
<td>6/6†</td>
<td>6/6</td>
</tr>
</tbody>
</table>

GPSC, guinea pig spinal cord.

* On day 10 post-immunization, two animals developed 4+ disease, two animals developed 3+ disease. On day 14, two animals developed 2+ disease.
† On day 10, two animals developed 4+ disease, two animals developed 3+ disease. On day 14, two animals developed 1+ disease.

1+ = Flaccid tail.
2+ = Weakness of hind legs.
3+ = Paralysis of hind legs.
4+ = Quadriplegia.
T-cell–mediated autoimmune disease model, namely EAE.35,36 EAE is a well-established T-cell–mediated process, similar to S-antigen uveitis. It has been reported that microglial cells may present the antigen myelin basic protein to sensitized T cells in the EAE model. Unlike what occurred in the S antigen disease, NaIO3 had no effect in preventing development of encephalomyelitis or in reducing the signs and histologic changes of demyelination. EAE is an organ-specific disease, similar in its pathogenic mechanism to EAU. A major difference between the diseases is a lack of participation of the RPE in induction or perpetuation of EAE. This adds credence to the selective action of NaIO3 on the RPE, because the incidence of EAU was dramatically reduced, but the drug appeared to have no effect on EAE development. This observation clearly indicates lack of any significant toxic effect of NaIO3 on the immune cells, thus evincing the significance of the RPE in initiation or perpetuation of uveitis. In addition, a similar delayed-type hypersensitivity response to S antigen developed in control animals and those treated with NaIO3, indicating once again that the observed effects of NaIO3 in S antigen EAU are not due to deleterious effects on immune cells.

Enzyme-linked immunosorbent assay for detection of antibodies to S antigen showed no significant difference between the groups, indicating that NaIO3 did not affect the production of antibodies in EAU. However, results of in vitro lymphocyte proliferation assays demonstrated a significant difference in the response to S antigen, phytohemagglutinin and concanavalin A between the NaIO3-treated group and the control animals. The responses to S antigen and to phytohemagglutinin were significantly greater in the control animals than in NaIO3-treated rats, although the response to concanavalin A was greater in the NaIO3-treated animals. This may not reflect significantly on the clinical results of the current study because it has been demonstrated by other investigators that in vivo disease induction does not necessarily correlate with in vitro lymphocyte responses.37

Damage to RPE from NaIO3 can lead to altered barrier between the choriocapillaris and outer retina. Such alteration could facilitate entry of serum inflammatory mediators and cells into those animals immunized with retinal antigen and treated with NaIO3. However, none of the animals treated with NaIO3 developed significantly more inflammation than did the control S-antigen–immunized animals (Table 1). In fact, they revealed markedly less inflammation. These findings suggest that the inflammatory amplification factors, such as cytokines, adhesion molecules, and oxygen metabolites, could not have been produced at the site of RPE damage. It is recognized that RPE, on activation, can produce interleukin-1, interleukin-6, gamma interferon, and oxygen metabolites,38,39 so it is tempting to speculate that damage to the RPE from NaIO3 could have prevented generation of these proinflammatory mediators, thereby preventing amplification of uveitis even in the presence of altered RPE barrier.

It appears that in organ-specific autoimmune diseases, the antigen presentation takes place locally in the resident cells. These antigen presenting cells express class II antigens. In the eye, four distinct class II antigen expressing cells have been identified: retinal vascular endothelial cells, RPE cells, Müller cells, and ciliary epithelial cells.6-9 Among these, in vitro coculture studies have revealed that RPE can present retinal antigens to lymphocytes.2 In contrast, vascular endothelium in similar studies showed no evidence of retinal S antigen presentation.40 However, activation of lymphocytes by endothelial cells was noted, and thus was independent of antigens, but may be due to T-cell–endothelial-cell ligand interactions.

In conclusion, this study showed that selective destruction of RPE by sodium iodate resulted in a disease that was significantly lower in incidence and of lesser severity when compared with that in untreated animals. The results indicate that the RPE may play an important role in the initiation and perpetuation of uveitis in this experimental model of uveitis.

Key Words
RPE, uveitis, S antigen, sodium iodate

References


