

Immunologically induced purulent anterior segment inflammation of the guinea pig eye

Sompolinsky D, Lundberg L, Prause JU. Immunologically induced purulent anterior segment inflammation of the guinea pig eye. *Allergy* 1992; 47: 234–242.

A single conjunctival application of ovalbumin to inbred guinea pigs (IMM/S 209) immunized with the same antigen in Freund's complete adjuvant provoked an acute purulent inflammation of the anterior segment of the eyes with a duration of up to 1 week. Intense conjunctival injection and chemosis were followed by a purulent discharge. A corneal haze was observed regularly, and a considerable proportion of the animals developed a pronounced pannus and corneal ulcers. Tear fluid cytology revealed a rapid increase in cell concentration, from the normal level ($< 10^8/l$) to $> 10^{11}/l$. Seventy to 95% of the cells were polymorphonuclear leukocytes. Histological examination revealed an acute inflammatory reaction which radiated from the conjunctival fornices to the entire anterior segments of the eyes. The process was characterized by an intense oedema, vasodilation and perivascular aggregations of polymorphonuclear leukocytes, and to a lesser extent eosinophilic granulocytes which characteristically infiltrated and penetrated the epithelial layers. Neovascularization could be observed early after challenge in the stroma of all parts of the outer eye. Ulcerations of the conjunctival and corneal epithelia were observed frequently. After a number of reiterations of the antigenic challenge, a marked infiltration with lymphocytes and basophils/mast cells was observed, and significant scarring of the conjunctival mucosa developed. In several animals, a slight, but significant co-reaction of the contra-lateral, non-challenged eye was observed.

Clinical aspects

Vernal keratoconjunctivitis is a chronic inflammatory disease of the outer eye. It is characterized by intense tearing, thick mucous conjunctival discharge, giant papillary conjunctivitis, limbal infiltrates, and superficial keratitis which may lead to corneal ulceration. The disorder is probably connected with an IgE mediated hypersensitivity, but this alone cannot fully explain the chronic course during years. Some investigations have indicated that also IgG antibodies (5) and cellular immunological processes (3) are involved. We have developed a model for a chronic hypersensitivity disorder of the anterior segment of the guinea pig eye which expresses most of the clinical signs of the human vernal keratoconjunctivitis. The model may be of importance for the study of immunological disturbances of the anterior segment of the eye.

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Key words: allergy; anterior segment inflammation; conjunctivitis; guinea pigs; histology; keratitis; ovalbumin

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Accepted for publication 26 June 1991

An immediate allergic response can be provoked in systemic (4, 12) or topically (16) immunized guinea pigs simply by dripping the antigen solution onto the ocular surface. Clinically, the response is dominated by profuse tearing, conjunctival injection and chemosis. The symptoms appear very soon after the immunological challenge and fade usually after a couple of hours. In rats a late-phase cellular infiltration (after approx. 6 h) has been demonstrated histologically (1).

We present an apparently new experimental ocular syndrome, i.e., an aseptic acute, long-lasting purulent anterior segment inflammation (PASI) with proneness to develop corneal ulcers. PASI was elicited by dripping an ovalbumin-solution onto the ocular surface of guinea pigs immunized systemically with ovalbumin (oa) in Freund's complete adjuvant (FCA). Repeated challenges elicited a chronic inflammatory response with increased subconjunctival connective tissue. PASI does not resemble a

type IV allergic reaction since the inflammatory reaction is prompt and overwhelmingly dominated by invading polymorphonuclear neutrophil leucocytes (PMN) and some eosinophilic granulocytes (EOS), while the participation of lymphocytes is modest. PASI is also different from a type I allergic reaction in being a long-lasting and purulent process.

Material and methods

Two-3-month-old inbred albino guinea pigs of strain IMM/S 209 were used. This strain is one of 4 strains of guinea pigs selectively bred for about 30 generations for a high (IMM/S 209 and 740) or for a low (IMM/R 201.16 and 203) anaphylactic respiratory response to repeated inhalations of aerosolized oa (15). The intra-strain genetic homogeneity has been demonstrated by skin transplantation and by immunological studies (18). The ocular anaphylactic response has furthermore been shown to be under genetic control (16).

Animals were immunized by two i.p. injections, at 7 days' interval, of 10 µg oa (Sigma grade V) dissolved in 0.5 ml phosphate buffered saline and carefully emulsified with 0.5 ml FCA (Statens Serum-institut, Copenhagen).

Twenty-five days after the first i.p. injection, the right eye was challenged with a drop of 25 µl saline containing 5 mg oa. Contact between the tip of the pipette and the ocular surface was carefully avoided. After application of the oa solution, the antigen was distributed by gentle movements of the lids from the outside.

In one experiment, the ocular provocation was repeated once a week for 15 weeks. Non-immunized animals of the same strain and breed, but challenged as the experimental animals, served as controls.

The ocular response was graded 0-5 (Fig. 1). This grading fits the usual symptoms of PASI, and is not identical with the evaluation of the symptoms of

acute ocular anaphylaxis, developed in guinea pigs immunized with oa-Al(OH)₃ as we have reported previously (16).

Tear fluid was collected from the inner canthus with graded disposable micropipettes (Brand, Germany). By careful handling, the animals showed no signs of annoyance. Two samples of 2 µl tear fluid were obtained. One sample was smeared uniformly on a premarked area (324 mm²) of a slide and used for total cell counts. The other sample was smeared gently to conserve the cell morphology for a differential cell count. The two smears were air-dried and stained with solutions of May-Grünwald and Giemsa. The exact area of a microscopic field was assessed with a graduated slide. The total cell count per litre tear fluid was obtained by counting a) all cells in the 2 µl portion (if < 3000), or b) the cells in 40 microscopic fields.

In the differential count, the following cell-types were noted: epithelial cells, PMN, EOS and lymphocytes. The following cell types were only encountered occasionally: monocytes, macrophages and Kurloff cells (mononuclear leucocytes particular for guinea pigs). Erythrocytes, if occurring, were not included in the count.

Histological techniques

The animals were killed at different intervals after provocation. Both eyes with all conjunctiva and lids were immediately obtained and immersion fixed in buffered formalin or Carnoy's fixative. The upper pole of each eye was removed to facilitate infiltration, and the whole tissue block was processed according to the routine paraffin technique. Sections of 4 µm were cut, and representative slides were stained with haematoxylin and eosin, PAS, haematoxylin-phloxine-saffran, toluidine blue and Giemsa. Sections were examined in a masked fashion by light microscopy, and the amount of different cells, necrosis and neovascularization was expressed semiquantitatively (in scores of 0-3). From each eye, 10 fields from each of 5 sections were calculated.

Experiments

Two experiments were performed:

A single challenge experiment, in which 12 experimental animals and 10 controls participated. The animals were challenged once in the right eye. Clinical evaluation, tear sampling and subsequent killing of the animals were performed at various intervals after challenge.

A multiple challenge experiment, in which 7 experimental animals and 7 controls participated. After the first ocular challenge, the animals were further

Clinical evaluation

Grade	Signs
0	No reaction
1	Conjunctival hyperaemia
2	Marked hyperaemia, chemosis
3	As 2 but in addition with cornea covered by chemotic conjunctiva
4	As 3 in addition with an excess of turbid tear fluid
5	As 4 but in addition with the ocular surface covered by thick purulent discharge

The score was raised by 0.5 by one or more of the symptoms: Pronounced lid hyperaemia; hazy or ulcerated cornea. Maximum score was, however, limited to 5.0.

Fig. 1. The grading system used for the clinical evaluation of PASI.

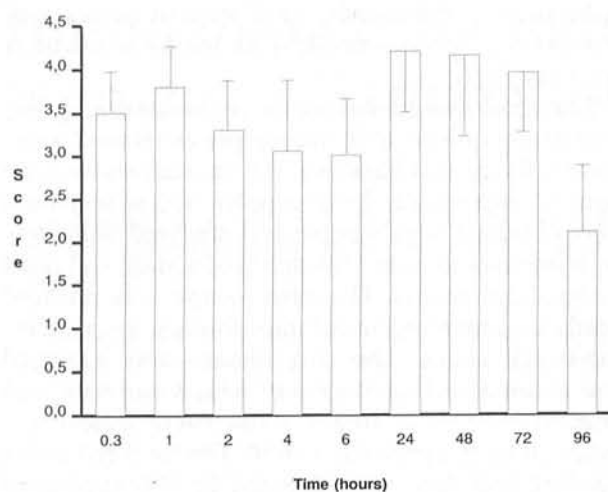


Fig. 2. Severity of clinical symptoms after a single challenge with ovalbumin in the right eye (Bar = SD).

challenged once a week for 15 weeks in the right eye. The histological evaluations were performed after 2–3 h and after 1 week.

Statistical evaluation

The data obtained fitted the normal distribution. Differences between groups were evaluated using the t-test and a probability level of $p < 0.05$ was considered significant.

Results

Clinical symptoms

Non-immunized animals did not react upon application of oa onto the conjunctival surface.

Single-challenged experimental animals developed clinical symptoms, consisting of marked vasodilation and oedema of the palpebral and bulbar conjunctiva within 60 s of the challenge. During the next 20–40 min, the cornea became partly covered by the chemotic conjunctiva, the upper lids became thick and red, and excess turbid tear fluid coated the ocular surface (Fig. 2). Within 6–24 h a turbid viscous discharge containing lumps and stripes of pus developed, and often pasted the lids together. A marked pannus was frequently observed (Fig. 3) and sometimes phlyctenaeous limbal lesions. In 10 of the challenged eyes, the cornea became opaque, and in 5 eyes a distinct paracentral corneal ulcer developed after 1–2 days. Typically, the ulcer was round or oval with a diameter of 0.5–2.0 mm. All symptoms, including the corneal ulcers, recovered spontaneously, and after 5–7 days the challenged eye had an entirely normal appearance.

The multiple-challenged animals reacted differently. After 4–5 challenges, the acute symptoms became more mitigated but signs of chronic alterations occurred, i.e., hypertrophic papillae on the upper tarsal mucosa, frequent mucosal ulcerations and scars, particularly near the rims, and heavily thickened upper eye-lids. Corneal ulcers remained a fre-

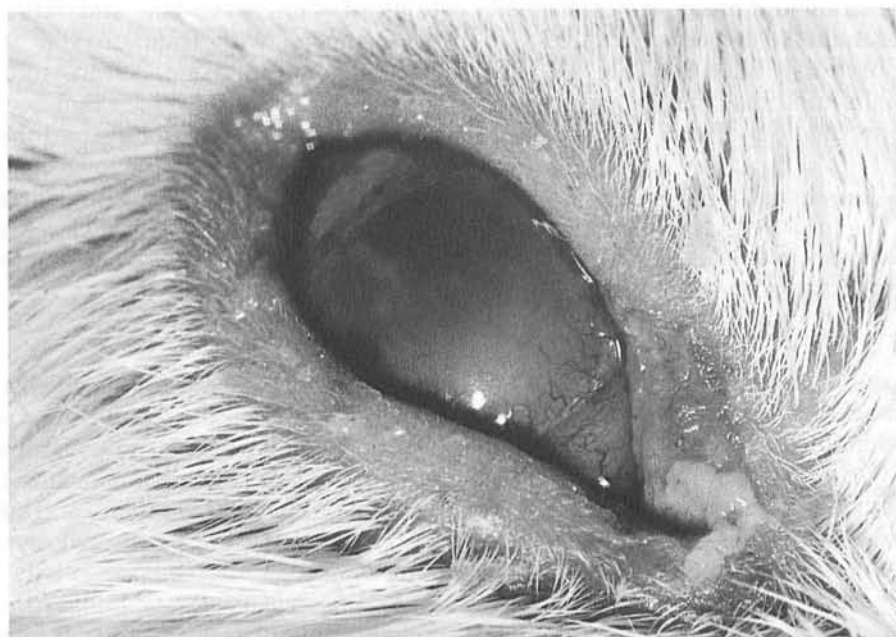


Fig. 3. Guinea pig with PASI. Severe corneal pannus on challenged eye.

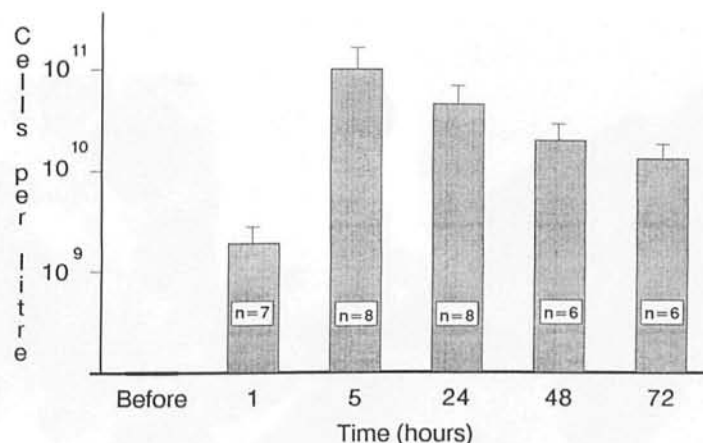


Fig. 4. Mean cell count (Bar = SD) in tear fluid of challenged eye after topical challenge with ovalbumin. Ciphers in squares indicate the number of animals evaluated at the given time.

quent phenomenon, and could recur on the same eyes. In a number of cases, an inflammatory co-reaction occurred in the contralateral eye, although less severe than in the challenged eye. However, in 2 animals we observed bilateral corneal ulcerations.

Cytology of tear fluid

In tear samples from the healthy non-immunized guinea pigs, the mean concentration of cells was $7.3 \times 10^7/l$ (SD = $7.5 \times 10^7/l$), with a range of $0-39 \times 10^7/l$. Epithelial cells accounted for 70%, and the remaining cells were lymphocytes and PMN, EOS were rarely seen.

Fig. 4 shows the cell concentrations of tears after one challenge. In spite of excess tearing, the mean level of cells increased steeply to a peak of $> 10^{11}/l$ in the course of only 5 h, thereafter it decreased steadily, although it was still $5 \times 10^9/l$ after 96 h. One hour after challenge, the cell population was composed of PMN 71%, EOS 12%, lymphocytes 8% and epithelial cells 9%. At 5, 24 and 48 h, the PMN accounted for $\geq 95\%$ of the cells of the tear fluid, and EOS for 1% or less. After 72 and 96 h, lymphocytes accounted for 5 and 14%, respectively. The PMN were thus the predominant cell type in tear fluid at all sampling times. The PMN often aggregated so that their number could be difficult to

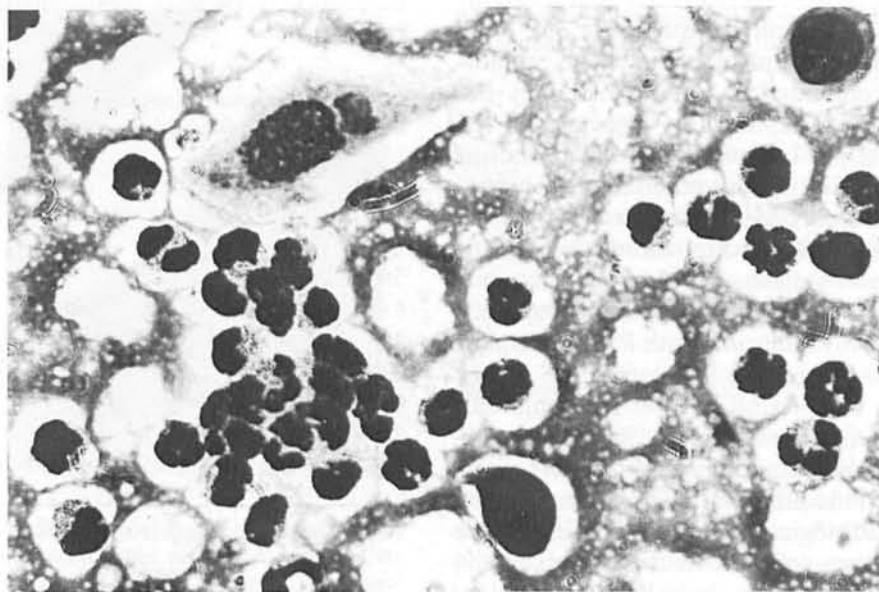


Fig. 5. Smear of purulent tear fluid from guinea pigs with PASI-syndrome 24 h after topical challenge. Groups of polymorphonuclear leukocytes and a few epithelial cells. May-Grünwald Giemsa staining, $\times 400$.

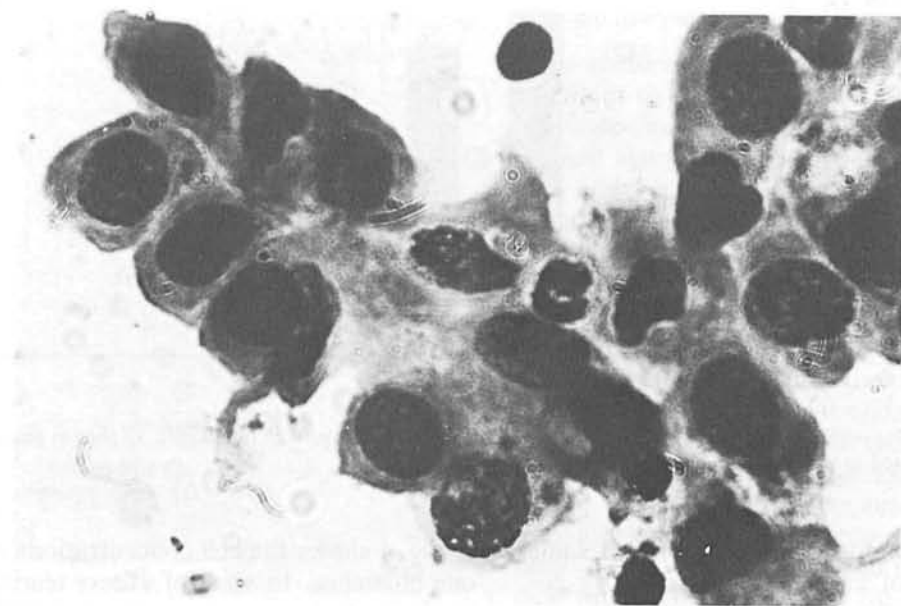


Fig. 6. Smear of tear fluid from guinea pigs with PASI-syndrome 24 h after topical challenge. Coherent epithelial cells with invading polymorphonuclear leukocytes (arrow heads). May-Grünwald Giemsa, $\times 1000$.

count (Fig. 5). From samples with aggregated PMN, minimum values were estimated for Fig. 4. Scales of coherent epithelial cells from the conjunctiva and cornea were also quite commonly seen during the first hours after challenge, and often with PMN in the space between adjacent cells (Fig. 6).

Histological examination, single challenge experiment

The conjunctival tissue reacted faster and more intensely than the other ocular tissues (Fig. 7).

In eyes obtained 30 min after challenge, inflammatory cells accumulated in and immediately beneath the conjunctival epithelium especially in the limbal region (Fig. 7). In a few cases small foci of necrosis could already be discerned. The conjunctival stroma appeared oedematous and the vessels dilated, although these features cannot be quantitated in histological sections.

Eyes obtained 6 h after challenge had conjunctival epithelium heavily infiltrated with PMN, lymphocytes/plasma cells, histiocytes and some EOS. Areas of focal necrosis were found both in the conjunctival epithelium and stroma (Figs. 7, 9), and the latter showed a marked eosinophilic infiltration (Fig. 7).

After 24 h the inflammatory reaction reached its first maximum, histologically, in the conjunctiva. The epithelium had large areas of necrosis, and in the stroma, basophils/mast cells could be recognized by light microscopy in addition to the other inflammatory cells (Fig. 7). At the same time, an inflammatory

co-reaction of the same type, although to a lesser extent, was observed in the collateral eye.

During the subsequent 6 days, the conjunctival inflammation decreased slowly having a slight second maximum at 72 h. The process was followed by the formation of new vessels in the corneo-limbal zone, and by fibrosis of the submucosa (Fig. 7).

The corneal inflammation had a quieter course, histologically (Fig. 8). Stromal inflammation was not detectable until after 24 h, and the entire reaction

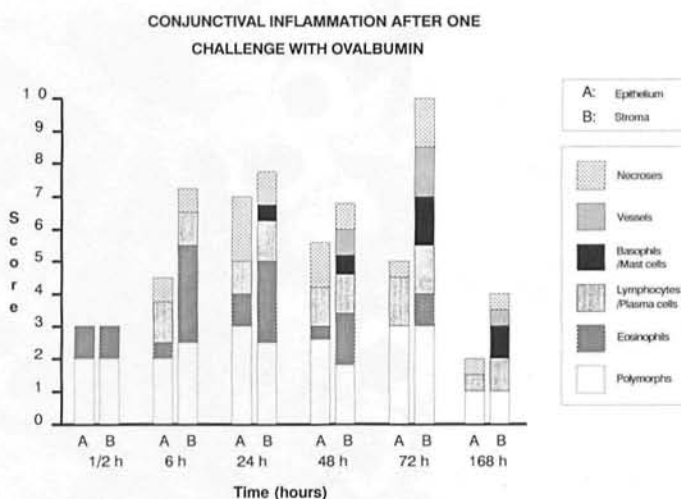


Fig. 7. Each of the histologically evaluated variables were scored semiquantitatively (0–3). Ten fields from each of 5 sections were calculated.

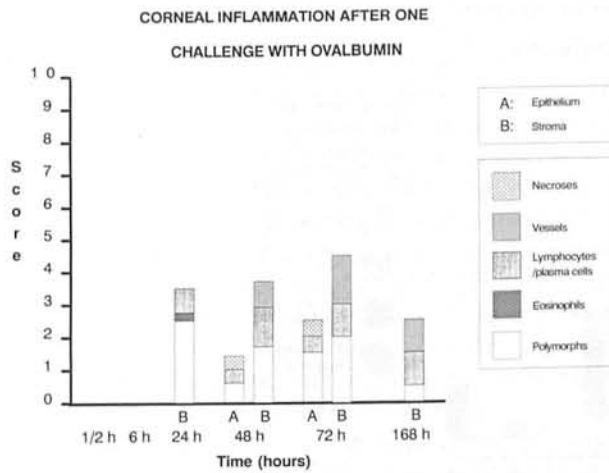


Fig. 8. Each of the histologically evaluated variables were scored semiquantitatively (0–3). Ten fields from each of 5 sections were calculated.

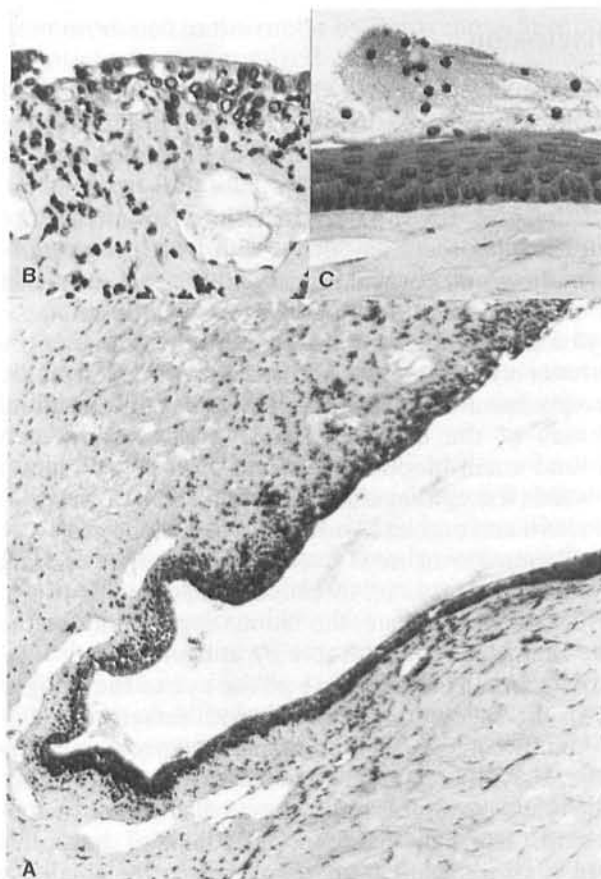


Fig. 9. Right cornea and conjunctiva of single challenged animal, 6 h after a single conjunctival challenge with oa. A: survey of inferior fornix (ØPI No 434/87, $\times 150$, HE); B: detail of conjunctiva with necrosis and oedema ($\times 300$, HE); C: detail of cornea – deposits of debris and slight shedding of epithelial cells ($\times 300$, HE).



Fig. 10. A: Right fornix of multiple-challenged eye, 72 h after last challenge with oa. Note the increased amount of connective tissue and lymphocytic predominance (ØPI No. 104/88, $\times 150$, HE). B: High power of conjunctival mucosa with newly formed vessels, inflammatory cells and fibrotic tissue ($\times 300$, HE).

had only one peak around 72 h (Fig. 8). Only the epithelium had necrotic foci. The cellular invasion was dominated by PMN and lymphocytes, and it involved both the stroma and the epithelium. The keratitis was followed by a slight lymphocytic iridocyclitis detectable 72 h after challenge.

Multiple-challenge experiment

A comparison between the composition of the inflammatory reaction of the single challenged eyes and the reaction after multiple topical challenges, shows a significant shift from PMN to lymphocytes/plasma cells as the most frequent cells in the conjunctival and corneal stroma (Figs. 7, 8 and 11). Also basophils/mast cells were more frequent in the chronic reaction, while EOS were almost absent.

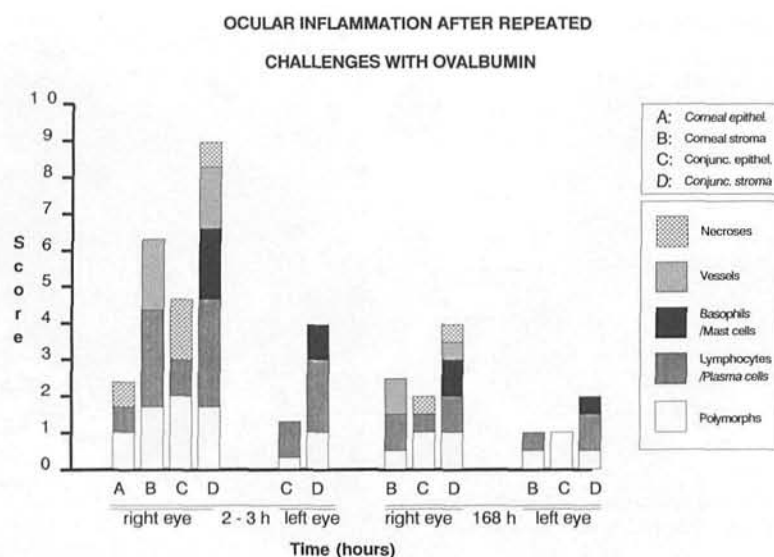


Fig. 11. Each of the histologically evaluated variables were scored semiquantitatively (0-3). Ten fields from each of 5 sections were calculated.

The immediate corneal reaction was significantly more severe in the multiple challenged eyes than in the single challenged eyes 2-3 h after the last challenge (evaluated by the total score: $p < 0.001$). Corneal epithelial ulceration and stromal neovascularization were prominent together with a marked fibrosis when compared with the singly challenged animals.

In addition, the non-challenged fellow eye of multi-challenged experimental animals reacted also significantly more severely than the fellow eyes of single challenged animals. The histological picture was that of a chronic inflammatory reaction with pannus formation, fibrosis and lymphocytic infiltration (Fig. 10).

Bacteriology

The possibility that the purulent discharge of PASI was caused by bacterial infection was ruled out by the following observations:

1. Microscopic examination of the tear fluid samples only exceptionally revealed microorganisms and then only micrococci.
2. All multiple-challenged guinea pigs were treated with 3 mg/kg gentamicin intramuscularly every second day, starting on the day of challenge. The PASI syndrome developed in the usual fashion with purulent discharge.
3. Eight samples of ocular purulent discharge were examined by routine bacteriological technique. Six were sterile while 2 yielded colonies of coagulase negative staphylococci.

Discussion

The ocular syndrome, in this article designated PASI, was provoked by topical antigenic challenge of guinea pigs immunized by 2 i.p. injections of oA-FCA.

Clinically, PASI is characterized by an intense purulent keratoconjunctivitis with frequent pannus-formation, and corneal ulcers. The general condition of the experimental animals seemed little affected. Cytological studies of tear fluid and histology of the anterior eye segment indicated that PMN was the predominant cellular element involved in the initial phases of the disorder. These cells accumulated around small blood vessels and seemed to migrate towards the epithelial linings of all parts of the conjunctiva and cornea. Another feature of interest, was the formation of new vessels, apparently radiating from the limbus in all directions, including the uvea. Of the ocular surface, the limbus region may be the site that is most penetrable by antigens.

After repeated exposure of the eye to the antigen (oa), the formation of new blood vessels was followed by collagen formation, particularly around the vessels. At this point, a considerable number of lymphocytes, basophils and mast cells could be observed. The light microscopical lack of basophils and mast cells in the early phases after challenge may have been due to an intensive degranulation, making the cells difficult to recognize. This suggestion is supported by such observations in similar animal models (11). However, during the first phases of this inflammatory disorder, PMN were clearly predominant. The invasion of these cells as well as

EOS, and the release of the contents of their granules may be one cause of the physical and chemical injury exerted on the mucosal stroma and epithelium. These cells may have been attracted by immune-complexes and platelet activating factor (PAF-acether) (17) accumulating following the application of antigen. The serum titre of IgG₂-anti-oa was 10–100 times higher in animals immunized with oa-FCA than in similar animals immunized with oa-Al(OH)₃, and the titres of IgG₁- and IgE-antibodies were only little influenced by the type of adjuvant used (unpublished results). IgG₁ of guinea pigs is a homocytotrophic immunoglobulin. It is possible that the initial reaction of hyperaemia and oedema appearing almost immediately upon antigenic challenge was due to homocytotrophic antibodies (IgG₁ and IgE); however, the prolonged inflammation of up to 1 week duration may have involved other mechanisms. In a study of oa-immunized rats, showing a similar reaction to the one presented in this paper, IgG₁ and IgE were also found in increased serum titres (11).

A sudden increase in vascular permeability has been produced in the rabbit by intravenous injection of antigen into immunized animals, or by administration of antigen-antibody complexes to non-immunized rabbits (14). Tissue injury may be due to complement activation by immunocomplexes and complement fractions because C5a are chemotactic for PMN. The accumulated PMN may be activated to increased superoxide release by both IgE- and IgG-immune complexes (10, 23). In a report of a supposedly cell-mediated response of the outer eye of guinea pigs to tuberculin, the histology of the limbal region showed a predominantly mononuclear cell infiltration with "some PMN" (12). In our experiments, the prompt onset, the sparse participation of mononuclear cells, and the clinical course are not in favour of a plain tuberculin-type delayed hypersensitivity reaction (type IV). It should be noted that the PMN component of delayed type hypersensitivity is reported to be particularly low in guinea pigs (13).

It seems, therefore, likely that PASI is the pathological consequence of several interacting types of hypersensitivity, sharing most of its signs with the late-phase of allergic reactions, however, a more exact assessment of the immunopathology must await further studies. After clarification of the immunological mechanisms involved, the value of this syndrome for studies of human atopic eye diseases may become evident. The presented model shares with the oa-challenged rat model (11) the advantage, that they do not require either invasive conjunctival challenge like many useful models (2, 8, 9), pre-treatment with mucolytic agents (19, 22) or haptens (6, 20, 21). The immediate appearance in the tear fluid of high amounts of PMN and later also of EOS,

which is characteristic for the PASI model, further resembles the human allergic conjunctival lesions (7). In any case, some severe immunological eye disorders such as vernal keratoconjunctivitis and contact lens hypersensitivity probably develop after frequent exposure to antigens. This reflection emphasizes the interest in the nature of the clinical and histopathological pictures observed in the animals after multiple challenges with antigen. If a single exposure to allergen imposes an inflammation of several days' duration in the human patient, as was the case in the experimental animals, then each new exposure will damage already inflamed tissue. This may explain the stubborn chronicity of *vernal* keratoconjunctivitis in contrast to *hay fever* conjunctivitis.

The use of cytology on tear fluid has been of significant, though limited, usefulness for elucidation of the nature of this ocular disorder. It has served as an objective measure of the inflammation and the assessment is obtained without killing the animals. By and large, the cell concentration found in tear fluid corresponded well with the scores for cell infiltration in the histological examination. The occurrence of large amounts of PMN and scales of coherent epithelial cells from the conjunctiva and cornea, was confirmed by the histological studies. However, comparison between the differential cell count of tear fluid and score of cells infiltrating the conjunctival stroma indicated that tear cytology underestimates the amount of lymphocytes and EOS involved in the inflammatory process. The permeability of the inflamed mucosa for cellular elements seems to be selective to a certain degree. In any case, the complete morphology of the pathological process can only be studied by classic histological technique.

Acknowledgements

Statens lægevidenskabelige Forskningsråd and Landsforeningen til bekæmpelse af Øjensygdomme og Blindhed gave valuable financial support. The authors thank N. Hoiby for bacteriological examinations.

References

1. ALLANSMITH MR, BAIRD RS, GREINER JV, BLOCH KJ. Late-phase reactions in ocular anaphylaxis in the rat. *J Allergy Clin Immunol* 1984; 73: 49–55.
2. ALLANSMITH MR, BLOCH KJ, BAIRD RS, SINCLAIR K. Ocular anaphylaxis: Induction by local injection of antigen. *Immunology* 1981; 44: 623–7.
3. ALLANSMITH MR, ROSS RN. Ocular allergy. *Clin Allergy* 1988; 18: 1–13.
4. ARONSON SB, MARTINET AC, YAMAMOTO EA, BEDFORD MJ. Mechanisms of the host response in the eye. II Variations in ocular disease produced by several different antigens. *Arch Ophthalmol* 1966; 76: 266–73.
5. BALLOU M, MENDELSON L, DONSHIK P, ROOKLIN A, RAPACZ P. Pollen-specific IgG antibodies in the tears of

- patients with allergic-like conjunctivitis. *J Allergy Clin Immunol* 1984; 73: 376-80.
6. BARNEY NP, KLEINMAN RE, TROCME SD, BLOCH KJ, ALLANSMITH MR. Attenuation of rat conjunctival response by repeated hapten applications. *Curr Eye Res* 1988; 7: 843-8.
7. BONINI S, VECCHIONE A, NAIM DM, ALLANSMITH MR, BALSANO F. Inflammatory changes in conjunctival scrapings after allergen provocation in humans. *J Allergy Clin Immunol* 1988; 82: 462-9.
8. CORNELL-BELL AH, HANN LE, BLOCH KJ, ALLANSMITH MR. Characterization of a localized basophil hypersensitivity lesion in guinea pig conjunctiva. *Cell Biol* 1986; 97: 1-12.
9. CORNELL-BELL AH, HUANG AY, HANN LE, ALLANSMITH MR. Sequential development of a conjunctival basophil hypersensitivity lesion in guinea pig. *Invest Ophthalmol Vis Sci* 1987; 28: 1970-7.
10. DE CLERCK LS, GIGASE PL, BRIDTS CH, STEVENS WJ. Neutrophil activation by IgE-containing immune complexes of patients with connective tissue diseases. *J Allergy Clin Immunol* 1988; 81: 95-9.
11. DOHERTY MJ, EASTY DL. Inflammatory and immunological cell profiles in a rat model of conjunctival immediate hypersensitivity. *Clin Exp Allergy* 1989; 19: 449-55.
12. DWYER RSC, TURK JL, DAROUGAR S. Immediate hypersensitivity in guinea pig conjunctiva. I. Characterization of the IgE and IgG1 antibodies involved. *Int Arch Allergy* 1974; 46: 910-24.
13. GREEN MI, SCHATTEN S, BROMBERG JS. Delayed hypersensitivity. In PAUL, WE (ed.): *Fundamental immunology*. Raven Press, New York, 1984: 685-96.
14. HOWES EL, MCKAY DG. Circulating immune complexes. Effects on ocular vascular permeability in the rabbit. *Arch Ophthalmol* 1975; 93: 365-70.
15. LUNDBERG L. Guinea pigs inbred for studies of respiratory anaphylaxis. *Acta Pathol Microbiol Scand [C]* 1979; 87: 55-66.
16. LUNDBERG L, BERTELSEN C, ZAVARO A, SAMRA Z, SOMPOLINSKY D. Experimental allergic conjunctivitis in inbred guinea pig strains with high respectively low bronchial allergic activity. *Allergy* 1987; 42: 262-71.
17. PRETOLANI M, LELLOUCH-TUBIANA A, LEFORT J, BACHELET M, VARHAFTIG BB. PAF-acether and experimental anaphylaxis as a model for asthma. *Int Arch Appl Immunol* 1989; 88: 149-53.
18. SØRENSEN M, JØRGENSEN PN, LUNDBERG L. Characterization of two strains of selectively bred guinea pigs. I. Skin transplantation experiments and screening for erythrocyte enzyme polymorphism. *Acta Pathol Microbiol Immunol Scand [C]* 1983; 91: 181-5.
19. TROCME SD, BAIRD RS, BLOCH KJ, ALLANSMITH MR. Worm antigen-induced ocular anaphylaxis in rats infected with *Nippostrongylus brasiliensis*. *Exp Eye Res* 1986; 42: 219-26.
20. TROCME SD, BONINI S, BARNEY NP, BLOCH KJ, ALLANSMITH MR. Late-phase reaction in topically induced ocular anaphylaxis in the rat. *Curr Eye Res* 1988; 7: 437-43.
21. TROCME SD, BONINI S, TROCME MC, BARNEY NP, BLOCH KJ, ALLANSMITH MR. A hapten model of topically-induced ocular anaphylaxis in the rat. *Invest Ophthalmol Vis Sci* 1987; 28: 264-9.
22. TROCME SD, TROCME MC, BLOCH KJ, ALLANSMITH MR. Topically induced ocular anaphylaxis in rats immunised with egg albumin. *Ophthalm Res* 1986; 18: 68-74.
23. WEISS SJ, WARD PA. Immune complexes induced generation of oxygen metabolites by human neutrophils. *J Immunol* 1982; 129: 309-13.

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