Corneal pannus (chronic superficial keratitis) in the German Shepherd Dog

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ABSTRACT
The clinical features, histopathology and treatment of corneal pannus (chronic superficial keratitis) in a series of eighty-four German Shepherd Dogs are reported. The aetiology of the condition and its therapeutic management are discussed in the light of these findings.

INTRODUCTION
The term 'pannus' is used to refer to tissue changes characterized either by cellular infiltration and extensive vascularization or by the replacement of normal tissue by granulation tissue. In orthopaedics pannus refers to the granulation tissue present in some forms of inflammatory joint disease, whilst in ophthalmology use of the term is related to the clinical appearance of a lesion generally accepted to be one of chronic keratitis. In man, the aetiology and histopathology of corneal pannus vary considerably (Hogan & Zimmerman, 1962; Duke-Elder, 1965; Grayson & Keates, 1969), but in the dog common usage of the term is usually confined to a distinct disease entity which demonstrates a breed specificity for the German Shepherd Dog (GSD). Similar or identical canine ocular lesions have been described variously under the names of keratitis pannosa and pigmentosa (Veenendaal, 1928), chronic superficial kerato-conjunctivitis (Überreiter, 1959), Überreiter's Disease or Syndrome (Überreiter, 1959; Schmidt, 1973; Saunders & Rubin, 1975; Slatter et al., 1977) and chronic superficial keratitis (Überreiter, 1961; Voigt, Dietz & Schmidt, 1965; Steinfeld, 1967; Amman, 1966, 1968; Runquist & Henrisson, 1970; Bethlen, 1972; Jenny, 1972, Krähenmann, 1972; Campbell & Snyder, 1973; Campbell et al., 1975; Saunders & Rubin, 1975; Peiffer et al.,
Since the pathological change is chronic inflammation of the superficial corneal stroma, the term 'chronic superficial keratitis' is more appropriate. However, in this report the authors have taken note of the common usage of the term 'pannus' by clinicians in the United Kingdom, and have used this term throughout.

The aetiology of pannus in the dog remains obscure, but recent work in the U.S.A. has demonstrated that environmental conditions are possibly of considerable importance in determining the severity of the disease and its response to therapy (Slatter et al., 1977). The purpose of this paper is to describe the clinical and histopathological features of pannus observed in GSD patients in the United Kingdom, and to report the results of an evaluation of treatment for the disease.

MATERIALS AND METHODS

Population details

This study is based on a series comprising eighty-four GSD patients seen by referral to one of us (P.G.C.B.) over a 4-year period: 83% of the dogs were from southeast England, but subjects from the southwest and north of England, and south Wales were also included. All but five patients in the series were aged between 4 and 9 years (Fig. 1) and there was a female to male ratio of approximately 2:1 (55 female, 29 male). Eighty-two percent of the females had been spayed and all the males were entire. Ninety percent of the patients had been

![Fig. 1. Age analysis in a series of 84 GSD patients.](image-url)
routinely vaccinated (canine distemper, viral hepatitis and leptospirosis), and apart from the ocular condition no other recognizable disease process was present at the time of examination. The dietary and management patterns were so variable that their importance from an aetiological standpoint was negated. The duration of the anamneses ranged from 5 days to approximately 6 months at the time of initial referral examination.

**Clinical examination**

The routine clinical examination included slit-lamp biomicroscopy. Microbiological examination of corneal and conjunctival swabs, conjunctival scrapings and surgically excised corneal material for aerobic and anaerobic bacteria, chlamydia, mycoplasmas and fungi was completed whenever possible. Cytological evaluation of such material is not undertaken at this college at present.

The assessment of treatment involved regular re-inspections either directly or through the referring veterinary surgeons up to 6 months post-initial therapy.

**Histopathological examination**

Tissue from twelve patients was submitted for histopathological evaluation. The tissue was obtained by superficial keratectomy: under a general anaesthetic a number 15 scalpel blade was used to cut down through normal anterior cornea approximately 0.5–1.00 mm beyond the periphery of the pannus lesion and to a level just below its vascular bed. The whole lesion was removed by splitting the interlamellar substance of the cornea, using sharp dissection. The diseased tissue was thus stripped back to the limbus, and thence removed using scissors. Biopsy material was stored in buffered formalin, and routinely stained, using the haematoxylin/eosin and periodic-acid-Schiff methods. Masson's trichrome stain was used to identify fibrous tissue, and a Perl's reaction was utilized to look for haemosiderin.

**RESULTS**

**The clinical features**

In the majority of patients, pannus was seen as a bilateral disease (93%), and the lesion always involved the corneal tissue on the temporal aspect of the globe, the ventro-lateral quadrant being the most commonly affected (95%) (Fig. 2). The extent and appearance of the lesion varied considerably between patients, and occasionally bilateral lesions in the same patient differed between the two eyes. In some patients the lesion was seen as primarily an area of extensive vascularization, but in the majority of dogs it was marked by the organization of connective tissue elements, cicatrization and a resultant dense corneal opacity. Further variation in appearance was due to the presence of varying amounts of pigment. Additionally, there was often well defined melanin pigmentation of the adjacent bulbar conjunctiva (81% of dogs) (Fig. 2), and a follicular conjunctivitis, or a
conjunctivitis characterized by gross macroscopic thickening and hyperaemia of the palpebral and membrana mucous membranes was present in some patients (10%). However, it was possible to establish four distinct stages of the disease based on the clinical appearance of the cornea; and the authors have adopted terms of reference more commonly used in the human literature to differentiate these four stages. The terms are *pannus tenuis* (cellular infiltration of corneal tissue), *pannus vasculosus* (vascularization of corneal tissue), *pannus en epaulette* (*pannus crassus*: organization of connective tissue elements within corneal tissue), and *pannus siccus* (scar formation).

*Pannus tenuis*. This, the earliest and least severe stage of the disease, was seen in eight dogs, and it was characterized by the development of a greyish haze in the superficial corneal stroma at the ventro-lateral limbus (Fig. 3). There was no indication of irritation for there was no attendant blepharospasm, photophobia or excessive lacrimation, and vision was not affected.

*Pannus vasculosus*. The initial stage is followed by a vascularization, *pannus vasculosus*, of the area of corneal haze. This lesion was seen in eighteen dogs, and slit-lamp examination established that the new blood vessels were confined to the superficial stroma, and that they arose from limbal-based capillary loops to form a dense vascular mass beneath the corneal epithelium (Fig. 4). The lesions stained patchily with fluorescein, indicating that in areas the epithelium had apparently been lost.

*Pannus en epaulette*. The *pannus vasculosus* stage is followed by an apparent partial regression of the vascular pattern, and the organization of sub-epithelial connective tissue elements. Most patients were presented at this stage of the
Fig. 3. *Pannus tenuis*. 5 year GSD Left eye.

Fig. 4. *Pannus vasculosus*. Vascular invasion of the cornea. 6 year GSD Left eye.
disease (forty-six dogs), and the lesions seen were opaque, basically pink and slightly elevated above the normal corneal surface (Fig. 2). Varying amounts of pigment were present. In many instances the lesion limited itself to the lower temporal quadrant covering about one-quarter to one-third of the total corneal surface. However, larger areas and even the whole cornea were sometimes involved, with an associated impairment of vision (fourteen dogs) and even total blindness (six dogs). Throughout the whole course of the disease, this factor of vision impairment was the only one which notably detracted from the patient's well-being; at no stage was there any evidence of associated pain or discomfort.

_Pannus siccus._ Eventually, some resolution of the inflammatory reaction and a further shrinkage of the blood vessels occur in the longer standing cases (4 months' duration plus, twelve dogs), but some of this change may be related to the use of corticosteroid therapy. The lesions seen were not obviously elevated from the normal corneal surface, remained opaque but greyish-white in appearance and considerable further pigmentation had occurred (Fig. 5). No further changes in the disease process were noted in this series, and in this stationary, presumed final, stage of _pannus siccus_ the clinical appearance of the lesion suggested that it was pigmented cicatricial tissue only.

![Fig. 5. Pannus siccus. Pigmented cicatricial tissue only. 6 year GSD Left eye.](image-url)
Microbiological investigations were conducted at all stages of the disease, but nothing of significance can be reported. The bacterial organisms isolated were normal commensals for the canine eye, whilst mycoplasma, chlamydial and fungal agents were not seen.

Vaccination, dietary, management and other disease factors could not be directly correlated with the presence of the disease.

The histopathological features

The histopathological findings in this series linked well with the clinical appearance of the disease, but although it is possible to describe the dominant features at cell level for each stage, it must be stressed that no clear dividing lines exist. Thus in a pannus en epaulette lesion, there are areas in which the histological appearance is more typical of pannus vasculosus or pannus siccus.

Pannus tenuis. The lesion was seen as a mononuclear sub-epithelial cellular infiltrate consisting mainly of plasma cells; some lymphocytes and macrophages were also present. Polymorphs, in particular, were seen to have accumulated beneath the epithelial basement membrane, this structure seemingly acting as a barrier to intra-epithelial cellular migration during this stage. The epithelium itself showed a catarrhal proliferation, but remained intact.

Pannus vasculosus (Fig. 6). The sections demonstrated an extensive prolifer-

*Fig. 6. Pannus vasculosus. 6 year GSD ×300. A heavy infiltrate of plasma cells and lymphocytes (d) together with many small blood vessels (c) can be seen in the superficial stroma (b). Polymorphs (e) can be seen in the region of the basement membrane of the epithelium (f), within its structure (a), and collected on its surface.*
Fig. 7. *Pannus en epaulette*. 6 year GSD × 300. A more localized monocytic reaction (a) can be seen underneath an epithelium that appears to be returning to normal (d). Fewer larger blood vessels (b) can be seen, together with pigment in both the stroma and the epithelium (c).

Fig. 8. *Pannus siccus*. 6 year GSD × 300. Melanin pigmentation in both the stroma and the epithelium.
ation of blood vessels of limbal origin within the corneal stroma, and there was a massive cellular infiltration of this tissue. The predominant cell was still the plasma cell, but lymphocytes, macrophages and polymorphs were also present. The polymorphs were seen sequestered within the stromal capillaries and immediately beneath, within and occasionally on the surface of the epithelium.

The epithelium showed metaplastic and degenerative changes including rete peg formation, swelling and vacuolation of the basal and polyhedral cells, early keratinization and shedding of the outermost cells, and, in some places, complete loss of the whole structure. Epithelial basement membrane material was thickened when visible; however, it was not recognizable in many places.

Pigment, chiefly melanin, was observed scattered throughout both the stroma and the epithelium.

_Pannus en epaulette_ (Fig. 7). The cellular infiltration was restricted to a few foci in the stromal tissue, and the blood vessels were fewer but larger. The epithelial basement membrane material again appeared thickened and folded at this stage. The epithelium itself looked almost normal apart from a variability in the number of cell layers present. Pigment was present in much larger quantities in both the epithelium and the stroma.

_Pannus siccus_ (Fig. 8). An irregular arrangement of healing scar tissue was present in the stromal tissue, but there was little evidence of inflammatory change. The irregularity of the scar tissue would seem to contribute to the corneal opacity. The epithelium exhibited a variable thickness, and both this and the stroma contained liberal quantities of pigment.

**Treatment**

In this series (Table 1) the therapeutic measures employed were evaluated from two aspects:

(i) their effectiveness in removing the presenting lesion, and (ii) their effectiveness in preventing recurrence of the disease.

The medical treatment regimens were not produced as the result of a carefully controlled study. The efficacy of different corticosteroid preparations has not been compared, but the drug combinations herein advocated were considered to be more efficacious than treatment in which corticosteroid preparations were used individually.

In all the _pannus tenuis_ and _vasculosus_ patients, and in approximately 60% of the patients in which some epaulette formation had occurred, corticosteroid therapy was seen to be completely effective in producing a clear cornea. The various regimens used were as follows:

_Pannus tenuis_: a combination of topical and systemic corticosteroid preparations produced complete resolution within 7 days. A 5-day course of triamcinolone (Adcortyl, E. R. Squibb & Sons) at a dose rate of 1 mg/20 lb body weight b.i.d. was followed by a 2-day course at half this dose rate, and topical betametha-
**TABLE 1. An analysis of pannus therapy in a series of eighty-two patients**

<table>
<thead>
<tr>
<th>Type of pannus: number of cases</th>
<th>Therapeutic success: numbers</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pannus tenuis</td>
<td>Medical treatment only</td>
</tr>
<tr>
<td>6</td>
<td>6</td>
</tr>
<tr>
<td>16</td>
<td>14 (2 results unavailable)</td>
</tr>
<tr>
<td>40</td>
<td>21 (3 results unavailable)</td>
</tr>
<tr>
<td>Pannus vasculosus</td>
<td>Pannus en epaulette</td>
</tr>
<tr>
<td>6</td>
<td>10</td>
</tr>
<tr>
<td>14</td>
<td>10 (3 results unavailable)</td>
</tr>
<tr>
<td>40</td>
<td>10 (2 results unavailable)</td>
</tr>
<tr>
<td>Pannus siccus</td>
<td>Combined surgical and medical treatment</td>
</tr>
<tr>
<td></td>
<td>13</td>
</tr>
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*The twelve patients used for biopsy samples are not included in the breakdown.*
sone (Betnesol-N, Glaxo) was used during this 7-day period and for a further week at two drops q.i.d.

**Pannus vasculosus:** the same combination therapy was used, the lesion resolving completely within 7 days.

**Pannus en epaulette:** the most efficacious medical regimen for these patients was a combination of depot (sub-conjunctival) methyl prednisolone acetate (Depo-medrone, Upjohn), topical betamethasone and systemic triamcinolone. Using topical anaesthesia (Ophthaine, 0.5%, E. R. Squibb & Sons) and occasionally sedative restraint (Acetyl Promazine, C-Vet. Ltd), 2.0 mg methyl prednisolone acetate was injected under the lateral bulbar conjunctiva, using a 26-gauge needle. The systemic therapy was the same as that used for the *tenuis* and *vasculosus* patients, but the topical corticosteroid preparation was used until the cornea had cleared, or up to a maximum of 25 days. In the majority of patients resolution occurred within 10–14 days.

**Pannus siccus:** the same topical, systemic and subconjunctival corticosteroid preparations were used in these patients as were used in the *en epaulette* patients. Some clearing of the corneal opacity and pigmentation was achieved in most instances, but overall the improvement was slight.

It was found that pannus always recurred following initial corticosteroid therapy but the intervals varied from as 4 weeks to 5 months. However, owner vigilance resulted in prompt treatment and resolution was usually easily achieved at this stage using the same combined topical and systemic corticosteroid regimen as that described for the *tenuis* and *vasculosus* patients. Similarly, subsequent recurrences were treated in the same way, and in doing so effective disease control was maintained.

Medical therapy alone did not produce complete resolution in 40% of the patients in which there was epaulette formation, and was of no significant value in *pannus siccus* patients. Surgical removal of the lesion proved necessary to produce a completely clear cornea and to correct any impairment of sight, but corticosteroid therapy was used during the healing phase and was also necessary to control subsequent recurrence of the disease. The keratectomy technique used throughout was a simple procedure (see Materials and Methods), and the whole of the lesion in both depth and width was removed to ensure the best results. It was found easier to remove the larger lesions in two or more pieces, but the results of total keratectomy in three patients were very poor; healing here was marked by extensive granulation of the corneal surface. Surgery was repeated up to a maximum of three times in these patients but severe scarring remained, and severely impaired vision. Thermal and excisional peritomy *per se* were not used in this series, but a 2-mm wide strip of perilimbal episcleral tissue and overlying conjunctiva was routinely included in the dissection. Tarsorraphy and membrana flaps did not prove necessary adjuncts to surgery, for corneal repair was effected without discomfort within 14–20 days. However, corneal repair by re-epithelialization, rather than by neovascularization, was deemed necessary to minimize the
degree of post-operative keratitis; therefore sub-conjunctival methyl prednisolone acetate and topical betamethasone therapy was utilized during the healing phase to suppress the expected neovascular repair response to surgery. The topical betamethasone was used for a 25-day period after surgery and topical antibiosis (Chloromycetin Ophthalmic Ointment, Parke-Davis) was maintained throughout the healing period.

Recurrences of corneal pannus following surgery varied again from approximately 6 weeks to 5 months. However, early recognition of the condition on these occasions prompted the rapid institution of the combined topical and systemic therapy, and further surgery was not necessary.

DISCUSSION

Clinical features

In a recent survey of the disease conducted in the U.S.A., 82.47% of the patients being GSD, the majority of the affected animals were aged between 3 and 6 years (51%); the disease occurred most frequently during the fourth year of life and thereafter gradually decreased (Slatter et al., 1977). For the GSD the average patient age was 4.8 years with a standard deviation of ±2.6 years. In the present series the disease was more common at a somewhat later age, 65% of the patients being between 5 and 9 years old, with an incidence peak during the sixth year. (Comparison data concerning the frequency distribution by age of the general GSD hospital population is not available.) However, the disparity between these two sets of age incidence figures may be significant. Slatter et al. (1977) consider that exposure to excessive ultraviolet light is an important aetiological factor, and that the severity of pannus varies according to the amount of exposure. Thus the apparently later onset of the disease in the United Kingdom may be related to the gross climatic differences between the two environments in which these surveys were conducted.

Previous studies have not indicated a sex predisposition for the disease; however, although details of sex distribution within the GSD breed in southern England are not known, it is noteworthy that in this series the disease was twice as common in the female.

Pannus was seen to be a bilateral affection in this series; only 7% of the patients presented with a unilateral involvement, and the corticosteroid treatment instituted for the diseased eye was possibly effective in preventing second eye involvement. Patients were not seen in which the nasal aspect of the globe only was diseased; there was always a temporal involvement whenever the nasal aspect was affected. Four stages of the disease process were demonstrated in this series, the clinical appearance of the lesion dictating the type of therapy required to some extent. It is suggested that because of the absence of corneal irritation, pannus tenuis is often not noticed by the owner, and that in the majority of patients only the obvious lesions of pannus vasculosus, pannus en epaulette and pannus siccus are seen.
Adequate examination of the lesion should involve the use of an illuminated magnification system, and the slit-lamp is ideal for gauging the depth of the lesion. The persistence of blood vessels is an important factor in treatment, and the value of biomicroscopy in detecting their presence cannot be overstressed.

Aetiological considerations

The aetiology of this disease in the GSD remains obscure. A number of workers have looked for infectious or hereditary causes without success (Überreiter, 1959, 1961; Voigt et al., 1965; Steinfeld, 1967; Runquist & Henriksson, 1970; Campbell & Snyder, 1973). Überreiter was unable to demonstrate a bacterial cause and the isolation of chlamydial agents reported by Voigt et al. (1965) has not been repeated subsequently (Überreiter, Sibalin & Bürki, 1971; Campbell & Snyder, 1973). Steinfeld (1967) could not demonstrate a genetic influence, and on the basis of his histological findings only, has suggested a viral aetiology. Anderson et al. (1974) have demonstrated a deficiency of an immunoglobulin (IgGd) in affected dogs, and have suggested that such a deficiency may impair the ability of the eye to tolerate environmental changes. Recently, Slatter et al. (1977) have used the results of a disease survey conducted in the Rocky Mountain area of the U.S.A. to suggest that ultraviolet light may be a particularly important aetiological factor. In addition, Peterhans (1978) has noted that the high eosinophil content of limbal corneal tissue in the GSD may be a response to exposure to ultraviolet light. Indeed, it was Überreiter (1961) who first suggested the possible importance of environmental factors and interpreted his belief in the practical use of prophylactic 'goggles' for some of his patients.

Very little information of aetiological significance was gathered from the current series of patients. There was no evidence to suggest an infectious basis to the disease; mycoplasma, chlamydial and fungal agents were not seen, and the bacterial isolations were unspectacular. The possibility of a virus origin was not investigated. Some of the patients were related, but evidence for a genetic involvement requires much wider research. Vaccination, dietary, management and systemic disease factors were not involved, and a seasonal incidence for the disease to support the suggested role of ultraviolet light could not be demonstrated.

Histopathological features

The histological picture described in this series, that of an inflammatory response dominated by cells of the lymphoid system, was largely similar to that reported by other workers (see Saunders & Rubin, 1975). In the light of current knowledge of immune and inflammatory responses, this picture strongly suggests than an immune reaction is mediating the observed changes. Campbell et al. (1975) have looked at cell-mediated immunity (CMI) to certain ocular agents, and have demonstrated that in the affected GSD there is significantly more CMI to corneal and iridal proteins than in the normal dog. The avascular cornea is an
immunologically privileged site, i.e. it is isolated from the immune system, a fact that has been used to good advantage for many years in corneal transplantation. However, if due to exposure to ultraviolet light or to some other triggering factor, the cornea is no longer isolated, it might be possible for the animal to make an immune response to its own corneal tissue. The likelihood of an immune-mediated phenomenon is further suggested by the therapeutic efficacy of corticosteroid preparations.

Treatment

Whilst the aetiology of this disease in the GSD remains unknown, without correction of the specific cause treatment, at best, remains symptomatic. There is, then, no cure at present, but corneal pannus can be controlled successfully in the majority of cases. In the U.S.A. the success of the various treatment methods available varies from one area of the country to another, the severity of the disease apparently varying with the prevailing climatic conditions (Slatter et al., 1977). In the current series, effective treatment in the early stages of the disease was easily obtained by using a combination of topical and systemic corticosteroid preparations, but recurrence can only be prevented by owner awareness, routine and repeated therapy. Recurrence times vary from patient to patient in this series between 4 weeks and 5 months, and, as such, the schedule of examination and therapy should be determined on an individual basis. The alternative to this schedule is the continuous use of corticosteroids, and whilst the effects of sustained systemic therapy are well recognized, the possible complications of superinfection, glaucoma and cataract formation should be borne in mind when long-term local therapy is used.

Similarly, pannus en epaulette will respond dramatically to corticosteroid therapy, and even large lesions which interfere with sight may be effectively treated so as to restore useful vision. In the pannus siccus patient useful vision may be present even though the cornea is extensively pigmented and scarred. However, should lesions in these two stages of the disease persist to interfere with vision after initial corticosteroid treatment, or should the production of a completely clear cornea be required, the physical removal of the lesion must be accomplished. Chemical cautery was not used in this series, whilst peritomy and keratoplasty techniques were not found to be necessary. Superficial keratectomy is easily accomplished, but corticosteroid therapy must be maintained during the immediate post-operative healing phase to suppress the vascular repair response, and ensure that repair is by epithelialization. Local and topical corticosteroids are employed, and although there is an initial short delay in corneal epithelial regeneration (Krähenmann, 1973), in practical terms this effect is negligible. Subsequent corticosteroid therapy is again necessary to control the expected recurrence, and this combination of initial surgical excision and subsequent medical suppression offers a readily effective practical approach to the control of the disease. Resistant lesions will also respond well to beta irradiation, but
similarly the problem again is the recurrent nature of the disease, and the general availability of such therapy in the United Kingdom negates this approach on purely practical grounds.

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REFERENCES


