**LETTERS TO THE EDITOR**

**Cowpox virus**

Sir,—In 1889 Parinaud described a unilateral conjunctivitis acquired by close contact with infected animals. It was a granular conjunctivitis accompanied by swollen eyelids and a mucopurulent secretion. The parotid region was swollen and inflamed. The granulation tissue persisted for months and histologically there were epitheloid and mast cells present. A variety of agents have been implicated—for example, cat-scratch disease, tularemia, tuberculosis, blastomycosis, coccidioidomycosis, syphilis, and actinomycosis, etc.

We report a necrotic granulomatous conjunctivitis caused by the cowpox virus, a virus closely related but not identical to vaccinia. There is no recorded case of cowpox conjunctivitis occurring in the United Kingdom.

A 15-year-old boy who lived on a farm was referred with 1 week's history of swollen sore left upper and lower eyelids with inflamed conjunctiva. Initially he noticed slight erythema on the left lower lid. One day later the conjunctiva had become inflamed and both lids swollen and the GP noticed a small red spot on the lower lid and tiny blisters on the conjunctiva. The lid swelling had increased until after 7 days he could not open the eye and the left side of his face became swollen (Fig 1). There was no history of trauma to the eye and the condition had not responded to systemic antibiotics.

The fornices were totally free of adhesions. The bulbar conjunctiva was approximately 7 mm thick and there was a 5 mm cuff of perilimbal necrotic conjunctiva. This was excised and an area of thickened conjunctiva was sent for histology. The cornea, the fundi, and the media were normal. Swabs were taken for viral tissue culture and smear for inclusion bodies. A diagnosis was made of acute fulminating necrotic conjunctivitis due to herpes simplex.

Two days later he developed indurated areas of bulbar conjunctiva palpatited through the upper and lower lids. The patient left hospital before further histological examination. The histological report confirmed a severe conjunctival infection with areas of necrosis and epithelioid and round cell infiltration. The indurated areas were considered to be granulation tissue with a marked fibrotic response. The tissue culture grew a cowpox virus. The carrier of cowpox virus is thought to be a domestic cat.

Three months later the visual acuity was 6/6 in each eye and the bulbar conjunctiva under the superior and inferior eyelids remained swollen, red and indurated, but not tender. There was a 7 mm area of symblepharon affecting the lower lid and a 5 mm polypoid excrecence of bulbar conjunctiva in the superior temporal quadrant.

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**Segmentation of fluorescence in the retinal microcirculation — is it a valid indicator of blood cell flow?**

Sir,—We read with interest the article of Arend et al on the use of scanning laser ophtalmoscopy for retinal capillary blood flow studies. Perifoveal capillary blood cell velocities were found to be reduced in diabetic patients compared with normal subjects. The basic assumption for the blood flow measurements was that the segmentation in the fluorescence intensity corresponded to segments of erythrocytes in the form of rouleaux formation (low fluorescence) and cell-free plasma (high fluorescence).

Using Desmarre's retractors a very chemosed conjunctiva with mucopurulent discharge on the surface was exposed. The cornea was covered by the swollen conjunctiva. A provisional diagnosis of purulent conjunctivitis with preseptal cellulitis was considered. The following day the patient was examined under general anaesthesia. Despite appearances both upper and lower lids were of normal thickness.

Figure 1 Appearance of patient 7 days after onset of conjunctivitis.

Figure 2. The same retinal location as in Figure 1 illuminated with white light to show the red blood cells. The density of the blood cells in the capillaries does not necessarily correlate with the alterations in the fluorescence intensity.

Using our vascular trichrome method we noticed that segmentation in the fluorescence intensity does not necessarily correspond to the erythrocytes versus plasma assumption. Figure 1 shows a retinal capillary (rat) with alterations of the fluorescence intensity along the vessel. In Figure 2 the same vessel is illuminated with white light, demonstrating that erythrocytes are seen throughout both high and low fluorescence areas. We might have regarded these findings as post mortem artefacts were they not supported by other experimental data. We recently developed a new method, named fluorescent blood cell angiography, for in vivo dynamic observation of fluorescent labelled erythrocytes in the retinal capillary net. By changing the filter setting of the imaging system a conventional fluorescein angiography of the same capillary net can also be performed.

These observations were recorded on a video tape for later analysis. Using this new method we found that the fluorescein segmentation velocity in the capillary net does not necessarily correspond to the blood cell velocity. While in some capillary paths the labelled blood cell velocity did correspond to the segmentation velocity, in other capillary paths in the same retina these velocities did not correspond. Moreover, factors such as systemic blood pressure, hyperglycaemia, intraocular pressure, and capillary architecture seem to have an unpredictable effect on the ratio between blood cell flow and the phenomenon of fluorescent segmentation. In summary, we think that the scanning laser ophthalmoscope is a promising tool in future analysis of capillary blood flow. Nonetheless, capillary fluorescence segmentation has to be understood if this phenomenon is to be used for quantitative retinal capillary blood cell flow measurements.

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**Reply**

Sir,—Biomicroscopic recordings of conjunctival (Fig 1) and periangular capillaries clearly show segmentation corresponding to erythrocytes versus plasma. From these findings and our experience in conjunctival video...
angiographic observations we conclude segment-
ation in the fluorescence intensity corre-
ponds to segments of erythrocytes and cell-free plasma. The figures of Ben-nun and Constable
do not necessarily contradict our assumption.
The segmentation of fluorescence intensity seems to correspond to packed cells. The interpretation of the postmortem findings could be clarified if the illumination was changed from white to green light. With green light illumination the contrast between red blood cells and plasma is best, owing to the maximum of absorption of haemoglobin.

The fluorescent blood cell angiography men-
tion is very interesting. Those findings may clarify the interpretation of our report. Recently Tanaka et al. observed fluorescent dots in perifoveal capillaries. They proposed that these dots correspond to leucocytes and platelets in the circulating blood. We do not agree with their conclusion. They are using the automatic gain control in the set-up of the scanning laser ophthalmoscope which leads to decreased signal-to-noise ratio.

In conclusion, we think that our interpretation of the observed phenomenon (Fig 2) seems to be acceptable. In addition until now our method is the only one that measures flow velocities and morphological parameters in the perifoveal capillaries objectively.

3 Tanaka T, Murakawa K, Shimasu K. Fluorescein fundus angiography with scanning laser ophthal-
4 Wolf S, Arend O, Tonnen H, Bertram B, Jung F, Reim M. Retinal capillary blood flow measure-
ments by means of scanning laser ophthalmo-

Figure 1 Conjunctival capillary vessels (magnification ×100) showing the segmentation plasma versus corpuscular formation.

Periorbital necrobiosis lipidica

Str.,—I read with interest the case reported by Mr Lavy and colleagues.1 An important differ-
ential and possible alternative diagnosis to that suggested which does not appear to have been considered is that of necrobiosis xanthogranu-
loma (NXG). This now well described condition is a non-X histiocytic disease characterised by reticulin and collagen formation with a particular predilection for the periorbital tissues. Prior to its description in 1980 by Kossard and Winkelmann,2 it had previously been described in a variety of ways including atypical necrobiosis lipidica.

As in the case discussed NXG presents with painless non-pruritic papules that progress to nodules and plaques which may vary in appearance but usually have a xanthomatosum element. These lesions may remain subclinical for extended periods but can pursue an aggressive course with recurrent severe ulceration of the skin lesions. These usually have pronounced telangiectasis in the ulcerative phase.

The importance of this alternative diagnosis is that NXG is invariably associated with a dysproteinemia, usually a monoclonal para-
proteinemia of the IgG class. This may follow a benign course but malignancies, typically multiple myeloma and chronic lymphatic leukaemia, may develop. The lesions may also involve the orbit posing a potential threat to vision.3,4

The histopathological findings in the case described could be consistent with a diagnosis of NXG. The features found in NXG of a non-
specific lymphocytic and plasma cellular infiltrate with palisading granuloma formation, together with areas of collagen necrobiosis and giant cell formation are similar to the biopsy illustrated. More specific features of NXG would be xanthogranulomatous panniculitis, and distinct palisading cholesterol cleft formation.

In view of this, further investigation of this patient that may be warranted would include serum protein and lipoprotein electrophoresis, urinalysis for Bence-Jones protein, and a computed tomographic scan of the orbits to rule out any intraorbital pathology. Other less consistent findings in NXG that may be of limited value are a cryoglobulinaemia, a positive rheumatoid factor, depressed serum comple-
ment levels, and a reduced level of C1 esterase inhibitor. (If a review of the histology were carried out monoclonal antibody studies may identify the presence of T-helper cells within the granulomas which has been described in NXG.)

The increasing recognition of NXG as a specific clinicopathological entity with serious systemic associations means that this diagnosis must be considered in any case of a necrotic process affecting the periorbital region.

2 Kossard S, Winkelmann RK. Necrobiosis xanthogranu-

Reply

Str.,—I note with interest Mr Lavy’s suggestion that a diagnosis of necrobiosis xanthogranu-
loma should be included. This is a condition that I was not previously familiar with and I am grateful to him for drawing my attention to it.

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BOOK REVIEWS


In 1989 the first international meeting devoted to thyroid eye disease was held in Montreal. In addition to endocrinologists and ophthalmol-
ogists there were immunologists, pathologists, radiotherapists, otoaryngologists and ocu-
plastic surgeons, geneticists, biochemists, and statisticians.

Despite such an array of expertise the first 78 pages, which are devoted to trying to expound the pathological processes, are far from conclu-

sive. Autoantibodies to eye muscle can be demonstrated, but they show incomplete specificit,

y, with some cross reactivity with diaphragm muscle and with thyroid antigens.

Connective tissue antibodies and cell mediated immunity are also considered. Wall proposes a working hypothesis that Graves’ ophthal-
moscopy follows the reaction of a primarily thyroid-directed cytotoxic antibody with an antigen present on the surface of the eye muscle cell mem-
brane. Studies of T-lymphocyte reactivity to retrobulbar antigens is emerging as one of the key areas. However, the very protracted natural history of the condition and the prob-
lem of unilaterality of the prognosis in many patients are questions that will have to be answered by any proposed pathogenic mechanism.

The remaining 109 pages cover the problems of clinical management. Unfortunately there is still no universally agreed scheme to describe the various forms and levels of involvement of the eye and orbit in this condition. There is a useful chapter on the structure and mode of action of cyclosporin, but another chapter is given over to plasmapheresis, though most workers have abandoned this as a mode of treatment.

The long term follow-up of patients treated by orbital radiotherapy at Stanford under the direction of the late J P Kri,, confirms the value of 2000 cGy of megavoltage irradiation in fractionated doses over a two-week period. Recent results from (West) Germany claim
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