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, tularema, tuberculosi, 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.1 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.

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

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 and 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 smears for inclusion bodies.

A diagnosis was made of acute fulminating necrotic conjunctivitis due to herpes simplex.2 Two days later he developed indurated areas of bulbar conjunctiva palpated through the upper and lower lids.

The patient left hospital before further histological examination. The histological report confirmed a secondary conjunctival infection with areas of necrosis and epitheloid 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.3

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 polyoid exocrescence of bulbar conjunctiva in the superior temporal quadrant.

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1 Parinaud H. Infective conjunctivitis of animal origin. Ar d'oc 1889; 252.

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 ophthalmoscopy for retinal capillary blood flow studies.4 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 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.5 By changing the filter setting of the imaging system a conventional fluorescent 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 fluorescent blood cell velocities 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, intracocular 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 better understood if this phenomenon is to be used for quantitative retinal capillary blood cell flow measurements.

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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.

Reply

Sir,—Biomicroscopic recordings of conjunctival (Fig 1) and periangual capillaries clearly show segmentation corresponding to erythrocytes versus plasma. From these findings and our experience in conjunctival video
angiographic observations we conclude seg-
mentation in the fluorescence intensity corres-
ponds to segments of erythrocytes and cell-free
plasma. The figures of Ben-nun and Constable do
d not necessarily contradict our assumption.
The segmentation of fluorescence intensity
seems to correspond to packed cells. Theinterpreta-
tion 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-
tioned is very interesting. Those findings may
clarify the interpretation of our report. 
Recently Tanaka at al.1 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/noise ratio.

In conclusion, we think that our interpreta-
tion 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.

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

Figure 2 Perifoveal capillary network with
hyperfluorescent gap (arrow) in macular capillary
(modified from Wolf et al.)

Peri orbital necrobiosis lipoidica

Str.-I read with interest the case reported by
Mr Lavy and colleagues.2 An important dif-
ferential and possible alternative diagnosis to
that suggested which does not appear to have
been considered is that of necrobiotic xantho-
granuloma (NXG). This now well described
condition is a non-X histiocytic disease
characterised by a chronic granulomatous inflamma-
tion with a particular predilection for the peri-
orbital tissues. Prior to its description in 1980 by
Kossard and Winkelmann,3 it had previously been
described in a variety of ways including atypical
necrobiosis lipoidica.

As in the case discussed NXG presents with
painless non-pruritic papules that progress to
nodules and plaques which may vary in appear-
ance 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 dysproteinæmia, usually a monoclonal para-
proteinæmia 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.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 cholestérol 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 compl-
ent 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 necrobiotic
process affecting the periorbital region.

Reply

Str.-I note with interest Mr Luck’s suggestion that
a diagnosis of necrobiotic xanthogranu-
лома 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

Graves’ Ophthalmopathy: Current issues in endocrinology and metabolism. Eds Jack R

In 1989 the first international meeting devoted
to thyroid eye disease was held in Montreal.
In addition to endocrinologists and ophthalmo-
logists there were immunologists, pathologists,
atologists, otorhinolaryngologists and oculo-
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
specificity, 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’ ophthalmo-
pathy follows the reaction of a primarily
thyroid-directed cytotoxic antibody with an
antigen present on the surface of the eye muscle
membrane. 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 propensity 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 Kress confirms the value
of 2000 cGy of megavoltage irradiation in
fractionated doses over a two-week period.
Recent results from (West) Germany claim

1 Jung F, Körber N, Kiesewetter H, Printhe C, Wolf
S, Reim M. Measuring the microcirculation in
the human conjunctiva bulbi under normal and
hyperperfusion conditions. Graefes Arch Clin

2 Lavy TE, Fink AM. Periorbital necrobiosis

3 Kossard S, Winkelmann RK. Necrobiotic
xanthogranuloma. Austral J Dermatol 1980;

4 Rose GE, Patel BC, Garner A, Wright JE. Orbital

5 Luck J, Layton A, Noble BAN. Necrobiotic
xanthogranuloma with orbital involvement. J

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