Summary
A study of a syndrome characterised by deficient or inadequate Meibomian gland secretions, minimal or transient symptoms suggestive of ocular dryness, fluorescein staining of the cornea (often detected only after delayed observation or sequential instillation of stain), and contact lens intolerance is described. Clinical and cytological studies indicate that the syndrome is due to obstruction of the Meibomian gland orifices by desquamated epithelial cells that tend to aggregate in keratotic clusters, which results in alteration of the Meibomian glands' contribution to the precorneal tear film. Further complication may result from bacterial proliferation in the desquamated keratotic cells and the release of the bacteria and their toxic products into the precorneal tear film from these reservoirs in the excretory pathways of the Meibomian glands.

This study investigated the Meibomian glands of patients with the primary complaint of contact lens intolerance. Age and sex matched patients who showed optimal contact lens tolerance served as controls. We describe a syndrome characterised by deficient or inadequate Meibomian gland secretions, minimal or transient symptoms suggestive of ocular dryness, fluorescein staining of the cornea (often detected only after delayed observation or sequential instillation of stain), and contact lens intolerance. The present communication reports the pathological findings from cytological and bacteriological examination of smears obtained before, during, and after sequential expression of the Meibomian glands of patients with the syndrome, and reports that a significant percentage of patients showing contact lens intolerance without obvious cause have this syndrome. A more detailed clinicopathological description of these studies is in press.

Materials and methods
We investigated the Meibomian glands of 38 consecutive patients referred to us for evaluation of contact lens intolerance for which all conventional diagnostic techniques had failed to reveal a definitive cause. Twelve age and sex matched patients who showed optimal contact lens tolerance served as controls for bacteriological and cytological studies. Only the Meibomian glands of the lower lid were studied. Samples of the Meibomian gland secretion were collected at the lid margin with the corner of a glass slide after gentle and forceful expression (Fig. 1). The sample was then smeared on to another glass slide, fixed for 20 minutes in (Harleco) Diff-Quik, and stained by the Wright-Giemsa method for cytological study. Permanent slides were made by covering the sample with 1 drop of (Fisher Scientific) Permount histological mounting medium and a glass coverslip. These slides were viewed under a light microscope at 200, 400, and 1000 times magnification.

Results and discussion
The superficial oily layer of the tear film is primarily the result of Meibomian gland secretion. The Meibomian glands are located within the tarsal plate of the eyelids (Fig. 2), and belong to the category of holocrine glands (glands whose secretion is composed of entire cells that are released upon maturation). These cells originate in the most remote part of the glands. As they grow, their cytoplasm accumulates minute droplets of sebaceous material, which result in a characteristic foamy appearance (Fig. 3). At the same time the nucleus shrinks, and when the cell reaches full maturity the membrane ruptures and releases all its contents. In this way the sebaceous secretion is expelled into the excretory duct, where it mixes with the desquamated epithelial cells from the ductal lining.

Analysis of full-thickness biopsies of eyelids and tissue obtained from cadavers and exenteration
specimens reveals that the lining of the Meibomian glands' excretory ducts is made up of a multilayered squamous epithelium similar to that of the epidermis (Fig. 4). The product collected in the excretory duct is delivered to the tear film at the lid margin. If the orifice is either partially or totally obstructed, 2 problems may arise: stagnation and infection.

Stagnation of the sebaceous secretion, especially in the lower lid, may occur by external compression from an adjacent expanding mass (such as a granuloma or tumour) or by internal obstruction due to plugging of the excretory duct. Our concern will be directed to the latter. Certain skin diseases, such as seborrhoeic dermatitis and acne rosacea, are characterised by increased epithelial turnover. Large amounts of cells are produced, which detach from the epidermal surface in the form of small scales (Fig. 5). The mechanism is similar to that of dandruff production. The excretory duct of the Meibomian glands is lined by the same type of epithelium as the epidermal surface. Therefore it is reasonable to assume that obstruction of the duct is more likely under these circumstances of increased epithelial turnover because of the accumulation of desquamated epithelial cells—particularly near the lid margin (Fig. 6).

When stagnation occurs, the duct dilates (Fig. 7) because of the accumulation of sebaceous material and cellular debris from the Meibomian gland and the ductal lining. These changes are not always accompanied by pouting of the orifices or inflammatory signs (or both) along the lid margin, and the condition may easily be dismissed. In these circumstances, however, expression of the gland would release inspissated material containing numerous desquamated epithelial cells (Fig. 8), often aggregated in clusters or plugs (Fig. 9). Plugging of the excretory ducts of the Meibomian glands is usually insidious, often inapparent, and may lead to dysfunction and eventual atrophy of the gland. Clinically, stagnation of the Meibomian gland secretions has been said to be responsible for a form of superficial punctate keratitis similar to that seen in syndromes with a known unstable tear film. Keratitis and blepharoconjunctivitis were also described in patients with Meibomian gland dysfunction. Abnormalities of Meibomian secretions have traditionally been considered an important cause of conjunctivitis. We are now presenting evidence that these patients with obstructed orifices or stagnated secretions, or both, show a significantly higher prevalence of contact lens intolerance.

The presence of dead, desquamated epithelial cells in the stagnated secretion of the Meibomian glands may provide an excellent culture medium for bacteria, as shown in this study (Fig. 10). The presence of bacteria in the smears was not always accompanied by clinical signs of inflammation on the lid margin or inflammatory cells in the collected Meibomian gland secretion. Bacteria were usually found to grow in small amounts only in dead, desquamated epithelial cells and not in neighbouring
nucleated cells (Fig. 11). This finding may also explain why infections of the Meibomian glands are sometimes extremely resistant to either systemic or topical antibiotic treatment. Large amounts of bacteria were seen in smears from only 4 specimens from 4 patients who showed no inflammatory changes. However, the findings suggest the presence of a bacterial reservoir inside the Meibomian excretory pathways, which in turn may represent a continuous source of irritation to the anterior segment of the eye.

Several mechanisms of contact lens intolerance associated with Meibomian gland dysfunction are suggested. One appears to be due to the mechanical obstruction of the Meibomian glands by keratotic plugs, which probably results in an alteration of their oily secretion. The second mechanism may be related to the release of bacteria or their toxic products, or both, from the Meibomian glands into the precorneal tear film. The bacteriological studies indicated that the most frequent organisms identified were Staphylococcus epidermidis and Staphylococcus aureus. The role of these bacteria in causing inflammation in the anterior segment has been demonstrated.7

The possibility of Meibomian gland dysfunction is usually not investigated unless significant symptoms or gross signs are present. Symptoms are usually not present unless the integrity of the tear film is stressed, possibly by either a contact lens or by a dramatic change in the humidity or temperature of the environment. Thus, an apparently normal eye may unexpectedly show contact lens intolerance.

Treatment of Meibomian gland dysfunction should be directed toward relieving the obstruction of the ducts and orifices, thus allowing normal flow...
of Meibomian gland secretion on to the precorneal tear film. Treatment is best accomplished by professional expressing of the Meibomian glands at appropriate intervals. Home therapy, consisting of hot compresses and scrubs of the lid margins, should be instituted on a daily basis, particularly in the initial stages.

References


