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Filamentary keratopathy: A non-contact photomicrographic *in vivo* study in the human cornea

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PURPOSE. *To investigate* in vivo *morphology of corneal filaments.*
MATERIALS AND METHODS. *Over a 12-year period, 19 patients with corneal filaments (7 with keratoconjunctivitis sicca and 12 with other surface diseases) were examined with the slit lamp and photographed by non-contact photomicrography.*
RESULTS. *The filaments appeared as variously long and thick threads, attached at one or both ends to the surface and carrying various amounts of granular and amorphous material. The attachment points and their surroundings showed abnormal cells and diffusion of tear fluid stained green with fluorescein sodium. The underlying stroma appeared normal. The remaining epithelium often showed abnormal surface cells and/or edematous or cystic changes.*
CONCLUSIONS. *The* in vivo *morphology of filamentary keratopathy is consistent with aggregations of mucus and cell debris adhering to the corneal surface. The underlying diseases seem to have in common corneal epithelial edema. The nature of additional factors, or their combination, precipitating mucus adherence to the surface is not clear. (Eur J Ophthalmol 2003; 13: 599-605)*

KEY WORDS. *Cornea, Human, Filaments*

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INTRODUCTION

Filamentary keratopathy (also termed filamentary keratitis) is a relatively rare condition causing ocular irritation and photophobia. It owes its name to corneal surface appendices termed filaments that, with the slit lamp, appear as variously long strands, or variously large vesicles. Filaments were first described in 1882 by Leber (1), and later reported in a vast number of conditions. Duke-Elder and Leigh (2) mention infections (such as adenovirus, herpes simplex, and vaccinia), trauma (abrasions, after short-wave diathermy, prolonged padding of an eye), edematous states (recurrent erosion, contact lens wear), degenerative conditions (keratoconjunctivitis sicca [KCS], keratoconus, neurotropic keratopathy, pemphigoid, erythema multiforme, advanced trachoma, keratitis of psoriasis, in advanced glaucoma, as a complication of chronic uveitis), and idiopathic cases. In a large study (3), filaments were observed in 200 patients with KCS, recurrent erosions, epithelial keratitis from various causes, epithelial edema after endothelial disturbance, superior limbal keratoconjunctivitis, chronic blepharospasm, aniridia, and ocular albinism, and after padding and after surgery without padding.

Historical surveys on theories on the origin of fila-

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ments have been given elsewhere (3-5). In short, filaments have been proposed to originate from three sources: extraneous material adhering to the corneal surface (fibrinous coagula (1), mucus (3, 6, 7)), the corneal epithelium (8-10), or the subepithelial stroma (5, 11, 12). In the present study, an attempt was made to investigate and describe the close *in vivo* morphology of filamentary keratopathy by a method requiring no contact with the corneal surface, and, if possible, to elucidate their origin and relation to disease.

PATIENTS AND METHODS

Nineteen patients, 7 with KCS (6 women, 1 man, mean age 48.5 years, range 27 to 64 years) and 12 with other conditions (1 each with anterior uveitis after herpes zoster, anterior uveitis after cataract extraction, superior limbic keratoconjunctivitis, subtarsal foreign body, trichiasis, blepharospasm, basal membrane dystrophy; 2 with keratitis photoelectrica; 3 idiopathic; 7 women, 5 men, mean age 57 years, range 20 to 81 years) were examined with the slit lamp and photographed by non-contact *in vivo* photomicrography (13) in various illumination modes. The photographs were taken at one or several occasions (in total, 31 occasions). An attempt was made to capture as many features as possible. Staining with fluorescein sodium was used at all occasions, with the addition of rose bengal at 20 (both dyes 1%, without preservative). Ektachrome 100 ASA film was used.

RESULTS

Slit lamp examination

The filaments appeared as variously long and thick surface appendices. The surfaces in areas outside their attachments showed in KCS diseased/abnormal surface cells staining yellow (nonfluorescent/adherent) with fluorescein sodium (14), or red with rose bengal, disruptions of the epithelial barrier (green flecks (15)), and small epithelial cysts. In conditions other than KCS, two patients showed punctuate green fluorescein staining, four epithelial edema, three epithelial erosion in the sense of missing substance; one patient showed both. In the three remaining patients, the condition of the surface was not noticed (Figs. 1, 2).

Morphology

Composition

The filaments appeared as variously thick and long threads or strands, optically dense and light reflecting, sometimes naked but mostly supporting various amounts of adhering or enveloping material. This material showed two components: one granular, optically dense, and light reflecting, and one amorphous and translucent. The two components were represented in various proportions. Some filaments seemed to contain predominantly or (almost) exclusively the amorphous material; others appeared granular with the amorphous material difficult to discern. Several filaments showed optically dense bulbous expansions with no discernible substructure.

Shapes and sizes

The shapes of the filaments varied largely. The threads or strands were coiled and/or twisted, or stretched. The attached material was located anywhere on the threads, often on their free ends but also in the middle leaving a free protruding end, or along their whole lengths. Some filaments appeared as short threads ending in a large clump. The shapes of larger filaments varied from round and bulky to stretched and slender, or irregular. Complex figures appeared as bulbous expansions interconnected by strands or cemented together. The lengths of the filaments varied between approximately 60 µm and ≤3 mm; the bulky ones measured between about 50 and 450 µm in diameter. The surfaces of some filaments appeared rough; of others, smooth. In some filaments was captured a surrounding layer of a transparent substance (see also below).

Surface attachments

The threads were usually attached at one, but sometimes at both ends to the surface. Fine threads were attached to abnormal/stainable surface cells. In thicker threads, the centripetal ends were clearly visible but their location in depth could not be estimated. The immediate surroundings showed grayish surface

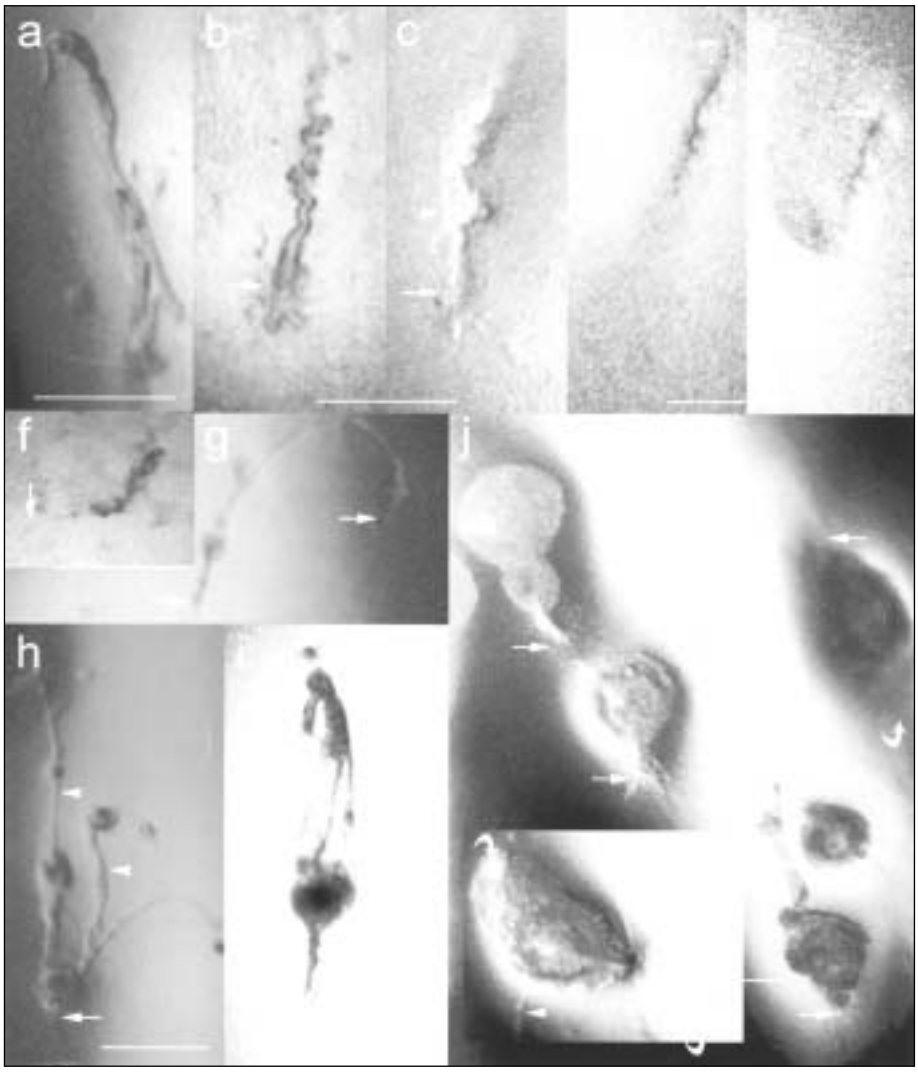

Fig. 1 - Filamentary keratopathy. *Examples of morphologic features captured by non-contact* in vivo *photomicrography in patients with various surface diseases. The filaments appear as surface appendices consisting of variously thick and long threads, or strands, attached at one or several points to the surface, and supporting various amounts of amorphous (translucent) and granular (light-reflecting) material. The attachment points (straight arrows) show no discernible underlying stromal opacities (***a-e** *and* **g-j**, *without staining;* **f**, *rose bengal 1%; bars 200 µm).* **(a) Mucus alone**: *A piece of formed mucus moving freely in the tear film. Its optical properties resemble those of the threads constituting the backbones of the filaments (keratoconjunctivitis sicca).* **(b-f) Figures with simple structures**: *A partly coiled thread, optically dense* **(b)** *and light reflecting* **(c)**, *ends abruptly at the attachment point (***b**, *arrow). The dark lines surrounding the attachment* **(b)** *correspond to swollen cells* **(c)**. *The thread carries a small amount of amorphous material (***c**, *arrowhead). Basal cell edema is visible in the left upper* **(b)** *and right lower* **(c)** *corners (anterior uveitis).* **(d, e)** *A coiled and optically dense thread supporting translucent and poorly organized amorphous material (***d**, *arrowhead), better visible when turned upward after a blink (***e**, *arrowhead) (subtarsal foreign body).* **(f)** *A minifilament, consisting of a thin thread attached to a diseased surface cell (arrow) and of attached granular material. Amorphous material cannot be discerned (keratoconjunctivitis sicca).* **(g-j) Figures with complex structures**: **(g)** *A thicker thread, stretching upward like a bow, shows two optically dense bulbous expansions close to the attachment points (arrows). The interconnecting part of the thread appears naked (keratoconjunctivitis sicca).* **(h)** *Variously thick naked threads (arrowheads) connecting bulbous expansions. At the only one visible attachment point (arrow), the epithelium shows two fine lines converging toward a short thread emanating from the expansion (keratoconjunctivitis sicca).* **(i)** *This filament seems just now detached from the surface at its upper end, leaving a small clump of optically dense material (bowed arrow). From the upper end emanate threads/strands toward an optically dense bulbous expansion with no discernible details. A shorter thread connects the figure with the surface (straight arrow) (keratoconjunctivitis sicca).* **(j)** *Several rounded bulky filaments with granular appearance attached to the surface via short threads. The attachments show swollen cells and fine radiating lines (visible in the filament located centrally in the photograph). Two filaments are connected by a long strand (arrowhead). The filament in the right upper corner (out of focus) is flipped down. Inset: The same filament, flipped upward, seems to be a conglomerate of two rounded bodies, one of which has detached from the surface, leaving swollen cells (bowed arrow) (keratoconjunctivitis sicca).*

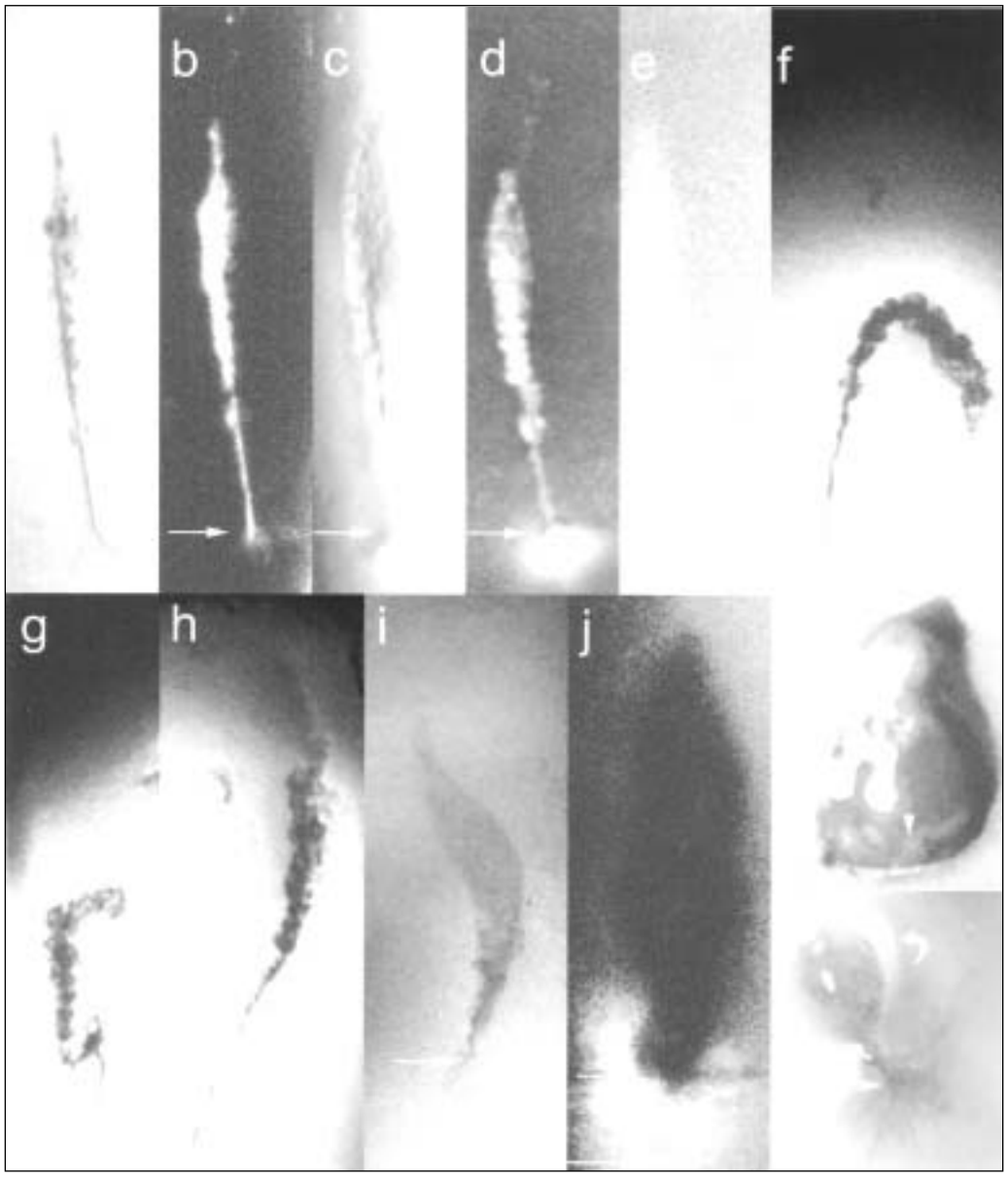

Fig. 2 - Filamentary keratopathy. *Examples of optical, staining, and dynamic features of corneal filaments captured by non contact* in vivo *photomicrography (***a***,* **b***, no staining;* **d***,* **e***,* **j***,* **k***, fluorescein sodium 1%;* **f-i***,* **l***, rose bengal 1%;* **e***,* **j***,* **k***, blue filter; bars 200 µm).* **(a-h)** *A slender filament, captured in different illumination modes, without and after staining, shows* **(a)** *an optically dense (dark) central thread (short arrow) partly covered by a mixture of granular (dark) and amorphous (translucent) material,* **(b)** *a strong light-reflecting property,* **(c)** *nonfluorescent (yellow) fluorescein sodium staining,* **(d)** *faint fluorescent fluorescein sodium staining in white light and* **(e)** *with the blue filter, and* **(f-h)** *red staining with rose bengal. The surface appears rough, and the centripetal end shows a free protruding thread (arrowhead), faintly* **(a, b)** *or clearly visible* **(c, d,** *and* **f-h)**. *The attachment point (long arrow) shows* **(a)** *irregularities implying swollen cells,* **(b)** *a few grayish surface cells staining* **(c)** *yellow with nonfluorescent fluorescein sodium and* **(f-h)** *red with rose bengal; the cell- and thread stainings are continuous. Additionally* **(d, e)**, *there is diffusion of fluorescein sodium into the surrounding and underlying tissues. Lacking reference points, the location in depth of the attached end of the thread cannot be estimated. The free end of the filament moves with blinks,* **(f-g)** *approaches the attached one, and* **(h)** *stretches again (keratoconjunctivitis sicca).* **(i)** *For comparison, a filament composed of thread and amorphous material staining red with rose bengal; no granular material is discernible (subtarsal foreign body).* **(j, k)** *Variations in fluorescent staining with fluorescein sodium.* **(j)** *In this filament, the absence of the green fluorescence contrasts with the green staining at the attachment point (anterior uveitis).* **(k)** *This filament shows green fluorescence, a few light-reflecting squames (arrowhead), and a light reflection (bowed arrow) probably originating from a surrounding clear zone (keratoconjunctivitis sicca).* **(l)** *A red stained rounded filament composed of predominantly amorphous material shows a smooth surface and a surrounding clear zone (bowed arrow). Red stained abnormal cells are converging toward the attachment point (idiopathic).*

cells, swollen cells, and fine radiating lines. The underlying stroma appeared normal. The grayish cells surrounding the attachments stained yellow with fluorescein sodium and red with rose bengal. In both cases, the staining was continuous with that of the threads. Additionally, the surrounding and underlying tissues stained brilliantly green with fluorescein sodium.

Staining properties

With fluorescein sodium, the majority of the filaments appeared yellow on retroillumination, and green (fluorescent) on focal illumination, without and with the blue filter; in some, the fluorescent hue could not be elicited. With rose bengal, the filaments showed various hues of red. The transparent zone surrounding some of the filaments initially stained with either dye but the staining disappeared rapidly.

Dynamics

With blinks, the filaments moved around their attachment points, swept over the surface, or flipped up and down. Double attached threads often stretched like a bow, and sometimes coiled forming a loop. Slender filaments stretched and collapsed, and some folded and appeared bulky before stretching again. One filament suddenly stretched and increased its length several times, and another one increased its size considerably by newly attached material. Double attached filaments occasionally detached at one end, one interconnecting strand ruptured and coiled on the surface, and one filament detached during the examination. Some long strands left stainable surface imprints.

Additional findings

In one area was captured a short protruding thread staining yellow with fluorescein sodium and red with rose bengal; the remainder of the filament and the green diffuse fluorescein staining were missing. Another area, from which a filament had detached during examination, showed disrupted surface, swollen cells, and green fluorescein staining. Surface erosions adjacent to a filament were captured in three patients. In one, the filament was located about 1 mm from the edge of the erosion, in another it was attached to its edge, and in the last one it was avulsed; the apparently denuded stroma appeared clear.

DISCUSSION

The optical features of the filaments were similar, regardless of the underlying condition. In all, they implied aggregates of material visible in the precorneal tear film as excess mucus. In a previous study (in patients with KCS (16)), such material was found to consist of three discernible components: two optically different varieties interpreted as mucus - one with definite forms, optically dense, light reflecting, and resembling mucus normally present on the conjunctival surface, and the other amorphous - and granular material probably representing cell debris. The only phenomenon related to the underlying disease seemed to be various amounts and relative proportions of the incorporated material, particularly cell debris, abundant in KCS but relatively scarce in other conditions. The *in vivo* appearance of the filaments compared well with histologic examinations showing a homogenous central core with features similar to mucus in the precorneal tear film and the mucous thread in the conjunctival fornices, acellular material, and epithelial squames caught up in various parts of filaments (3).

The filament composition implied an affinity between the threads, the amorphous material, and detached surface cells. It might be that the amorphous material, within the filaments apparently acting as cementing substance, also promoted surface adherence. Fine threads, rolling between the corneal and tarsal surfaces, seemed to adhere at random to abnormal/stainable surface cells, rip off exfoliating ones, and remain attached to those still firmly anchored (16). Whether thicker threads also adhered to such cells was impossible to discern because in these staining of abnormal superficial cells was more extensive and continuous with that of the threads. Although the centripetal ends of the threads were clearly visible, their location in depth could not be estimated in the absence of reference points. Still, as the only discernible opacities at the attachment points were relatable to abnormal surface cells, and as the underlying stroma appeared uninvolved, the attachments seemed to be located no deeper than at the epithelial level.

The presence of abnormal surface cells in combination with an absence of discernible stromal changes implied no active participation of corneal structures in filament formation. Epithelial changes shown

by the attachment points - fine radiating lines suggestive of stretched cells, abnormal/stainable surface cells apparently streaming toward the attachments, rounded/swollen cells, and diffuse green fluorescein staining indicating disruptions of the epithelial barrier - seemed secondary to traction. It should be noted, however, that in patients with KCS, preformed epithelial disruptions (green flecks (15)) could not be distinguished from secondary changes.

The staining properties of the filaments paralleled the staining properties of the incorporated material. Additionally, with fluorescein sodium, green fluorescence, similar to that shown by the tear film stained with the dye, could be elicited in the majority of the filaments. Its absence in some was suggestive that in these the dye was enmeshed in a material precluding its fluorescence. The additional zone surrounding some of the filaments seemed to consist of tear fluid.

The actual appearance of the filaments captured in the photographs was clearly related to their dynamics. Attached at one or two points, the threads swept over the corneal surface with blinks with options like stretching, twisting, coiling, engaging in another filament, growing by collecting further material, or rupturing and leaving a short protruding end, detaching and leaving swollen surface cells, alternatively avulsing and leaving a clean erosion and a clear underlying stroma. The alternatives of filament removal seemed to reveal a relationship among the strength of the threads, their epithelial bonds, and epithelial coherence. In histologic preparations, recognizable sheets of epithelial cells at the base of (forcibly removed) filaments have been found only in recurrent erosions and filaments with associated gutters (3).

Altogether, the morphology and the dynamics indicated an absence of active participation of corneal structures in filament formation. The present findings support the hypothesis that filamentary keratopathy is due to mucus adherence to the corneal surface (1-3, 6), and suggest that random adherence of formed mucus of presumably conjunctival origin is the primary event. The reasons for this adherence are obscure. The present patients, as well as those reported in the literature, seem to have in common corneal epithelial edema, similarly to filamentary keratopathy a non-specific and potentially reversible condition. Examples of contemporaneous resolution of both - spontaneous (as in keratitis photoelectrica), with treatment of underlying disease (as in anterior uveitis), or with treatment with hypertonic saline (17) - let to suspect that epithelial edema may be an important factor, but the nature or combination of additional factors precipitating the development of filaments is difficult to recognize.

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REFERENCES

1. Leber T. Präparate zu dem Vortrag über Entstehung der Netzhautablösung und über verschiedene Hornhautaffectionen. Ber Dtsch Opth Ges 1882; 14: 165-6.
2. Duke-Elder S, Leigh AG. Epithelial filaments. In: System of Ophthalmology. Vol. 8, P. II. London: Henry K. Kimpton; 1965: 697-701.
3. Wright P. Filamentary keratitis. Trans Ophthalmol Soc UK 1975; 95: 260-6.
4. Theodore FH. Filamentary keratitis. Contact Intraocul Lens Med J 1982; 8: 137-46.
5. Kowalik BM, Rakes JA. Filamentary keratitis-the clinical challenges. J Am Optom Assoc 1991; 62: 200-4.
6. Czermak W. Über Fadenbildung an der Cornea. Klin Monatsbl Augenheilkd 1891; 29: 229-258.
7. Jones BR, Coop HV. The management of keratoconjunctivitis sicca. Trans Ophthalmol Soc UK 1965; 85: 379-90.

8. Roeder DR. Auswachsen des Corneal-Epithels. Klin Monatsbl Augenheilkd 1887; 25: 279-81.
9. Hess C. Beiträge zur Kenntniss der Fädchen-Keratitis. Graefes Arch Ophthalmol 1892; 38: 160-70.
10. Nuel J-P. La kératite filamentaire. Arch d'Ophtalmologie et Revue Génerale d'Ophtalmologie 1892; 12: 593-623.
11. Uthoff W. Beiträge zur Pathologischen Anatomie des Auges. Graefes Arch Ophthalmol 1883; 29: 167-190.
12. Weskamp C. Parenchymatous origin of filamentary keratitis. Am J Ophthalmol 1956; 42: 115-20.
13. Tabery HM, Holm OC. Photography *in vivo* of epithelial lesions in the human cornea with non-contact high magnification technique. Acta Ophthalmol 1987; 65: 513-5.
14. Tabery HM. Dual appearance of fluorescein staining *in vivo* of diseased human corneal epithelium. A non-contact photomicrographic study. Br J Ophthalmol 1992; 76: 43-4.
15. Tabery HM. Corneal surface changes in keratoconjunctivitis sicca. Part I: the surface proper. A non-contact photomicrographic *in vivo* study in the human cornea. Eye 2003; 17: 482-7.
16. Tabery HM. Corneal surface changes in keratoconjunctivitis sicca. Part II: the mucus component. A non-contact photomicrographic *in vivo* study in the human cornea. Eye 2003; 17: 488-91.
17. Hamilton W, Wood TO. Filamentary keratitis. Am J Ophthalmol 1982; 93: 466-9.