Adenovirus Epithelial Keratitis
and Thygeson’s
Superficial Punctate Keratitis
Adenovirus Epithelial Keratitis and Thygeson’s Superficial Punctate Keratitis

In Vivo Morphology in the Human Cornea
This book treats the in vivo morphology of human adenovirus corneal epithelial infections and of Thygeson’s superficial punctate keratitis (TSPK), both captured in high-magnification photographs.

The two diseases are apparently disparate: adenovirus eye infections are very common, caused by a known agent, and highly infectious; TSPK is comparatively rare, its cause unknown, and it seems non-contagious; also, the course of the two diseases is different. Why, then, are they so often confused in clinical practice? The reason is the similarity between adenovirus epithelial infiltrates and ‘coarse’ TSPK epithelial lesions.

Part I of this book shows corneal epithelial changes caused by various adenovirus serotypes captured in different individuals at various points of time. The accompanying case reports highlight the importance of familiarity not only with the well-known picture of adenovirus epithelial keratitis, but also with the early manifestations of the infection. An early diagnosis is particularly difficult but of paramount importance in infections superimposed on the patients’ preexisting diseases because such an event might herald a nosocomial outbreak of epidemic keratoconjunctivitis with its well-known disastrous consequences. A sequela of adenovirus epithelial keratitis is subepithelial opacities (infiltrates), which may persist for many years or even indefinitely; the included series shows a sequence of events occurring in them during 3 years following the infection.

Part II of this book shows corneal epithelial changes occurring in TSPK, both typical and atypical; the case reports demonstrate the long-term nature of the disease and highlight the importance of the patient’s history in differentiating TSPK from adenovirus infections and, particularly so in atypical TSPK, also from herpes simplex virus infection.

The interpretation of the findings partly relates to corneal epithelial disturbances caused in human by the two other major viruses (herpes simplex and varicella-zoster) observed in vivo by the same method. Additionally, a scrutiny of sequences of events sheds some light on the mechanisms behind the similarity between epithelial changes occurring in adenovirus infections and TSPK.

I hope that this book showing the natural course of adenovirus epithelial keratitis and TSPK will not only serve as a diagnostic tool but, as no curative treatment has been found yet for either of them, also as a reference when effects of new drugs are evaluated.
Contents

Part I Adenovirus Epithelial Keratitis

1 The Morphology of Adenovirus Epithelial Keratitis .......................... 3
   Adenovirus Cytopathic Effect in Cell Cultures .............................. 4
   Rounded/Abnormal Cells in Human Adenovirus Epithelial Keratitis .... 5
   Cyst-Like Structures; Fluorescein Staining .................................. 6
   Fluorescein and Rose Bengal Staining ........................................... 7
   Epithelial Infiltrates 1................................................................. 8
   Epithelial Infiltrates 2................................................................. 9
   Addendum 1. Toxic Effect of Rose Bengal Dye ................................. 10
   Addendum 2. Conjunctival Changes .............................................. 11

2 Adenovirus Type 8 Epithelial Keratitis: The Development, Accompanying
   Signs, and Sequelae ................................................................. 13
   Case 1: EKC: An Occupational Hazard .......................................... 14
   Case 2: A Sequel of a Friendly Visit ............................................ 18
   Case 3: Anterior Uveitis and Nosocomial Infection ...................... 22
   Case 4: A Case of a Caring Wife ................................................. 23
   Case 5: Nosocomial Infection After Suture Removal ..................... 24
   Case 6: Nosocomial Infection After Applanation Tonometry .......... 28
   Case 7: A Woman Infected by a Caring Relative ......................... 29
   Case 8: A Potential Source of a Nosocomial Outbreak ................. 30
   Case 9: Nosocomial Infection in a Contact Lens Wearer ............... 32
   Case 10: Nosocomial Infection in Corneal Erosion ...................... 34

3 Adenovirus Epithelial Keratitis Caused by Various Serotypes
   (Ad3, 4, and 7) ............................................................................. 43
   Case 1: Adenovirus: Which Serotype? ........................................ 44
   Case 2: Pharyngoconjunctival Fever .......................................... 48
   Case 3: Adenovirus Type 7 in a Contact Lens Wearer and Her Family. 49
   Case 4: Red Eye: A Diagnostic Clue .......................................... 50
   Case 5: Adenovirus or Thygeson’s Keratitis? .............................. 51
   Case 6: Adenovirus or HSV Epithelial Keratitis? ....................... 52
   Case 7: Adenovirus Infection: A Clinical Diagnosis ................... 53
### Part II  Thygeson’s Superficial Punctate Keratitis

#### 5  The Morphology of Thygeson’s Superficial Punctate Keratitis (TSPK) .......................................................................................... 79
- Shapes and Sizes of TSPK Epithelial Lesions ........................................................................... 80
- Rounded/Abnormal Cells in TSPK .......................................................................................... 81
- Fluorescein Sodium Staining of TSPK Epithelial Lesions ......................................................... 82
- Rose Bengal Staining of TSPK Epithelial Lesions .................................................................. 83
- The In-between Areas in TSPK (1) .......................................................................................... 84
- The In-between Areas in TSPK (2) .......................................................................................... 85

#### 6  Typical Cases of Thygeson’s Punctate Epithelial Keratitis (TSPK) ............................ 87
- Case 1: A 24-Year History of TSPK ....................................................................................... 88
- Case 2: A 27-Year History of TSPK with Remissions and Exacerbations ...................... 90
- Case 3: A Happy End (?) After 25 Years of TSPK ............................................................... 92
- Case 4: A 20-Year History of TSPK ....................................................................................... 94

#### 7  Three Atypical Cases of Thygeson’s Superficial Punctate Keratitis (TSPK) .................. 97
- Case 1: A Recurrence of an HSV Dendrite? ......................................................................... 98
- Case 2: Who Dares to Operate the Cataract? ....................................................................... 104
- Case 3: A Peculiar Epithelial Keratitis ................................................................................. 112

Final Remark .......................................................................................................................... 127

Bibliography ............................................................................................................................ 129

Index ........................................................................................................................................ 131
About This Book

The photographs presented in this book have been chosen to show:

**Part I: Adenovirus (Ad) Epithelial Keratitis**

- The *in vivo morphology* of epithelial keratitis caused by various Ad serotypes, accompanying signs and sequelae (Chap. 1)
- The *in vivo morphology and dynamics* of epithelial keratitis caused by *Ad type 8* (Chap. 2)
- The *in vivo morphology and dynamics* of epithelial keratitis caused by *some other Ad serotypes* (Chap. 3)
- The *in vivo morphology and dynamics* of *subepithelial opacities/infiltrates* (Chap. 4)

**Part II: Thygeson's Superficial Punctate Keratitis (TSPK)**

- The *in vivo morphology* of TSPK (Chap. 5)
- The *in vivo morphology and dynamics* of *typical TSPK* (Chap. 6)
- The *in vivo morphology and dynamics* of *atypical TSPK* (Chap. 7)

The photographs were taken by *non-contact in vivo photomicrography*, a method that requires neither contact with the epithelium nor the use of anaesthetics. By this method are visualized structures that optically differ from their regularly organized surroundings; a normal corneal epithelium or stromal cells cannot be discerned. As there is no contact with the ocular surface, the architecture of epithelial changes is not disturbed by the examination, and there is no risk of spreading infections. The technique allows the use of various illumination modes to complement each other and a free application of *diagnostic dyes* to expand the information, e.g., 1% fluorescein sodium and 1% rose bengal (preservative-free solutions). These dyes are commonly used in clinical practice.

The *adenovirus diagnosis* (except for one case) was verified in conjunctival swabs by virus isolation in cell culture, and the isolates were typed by conventional neutralisation tests.

The photographs of *cell cultures* were taken by the same method. The *bars* indicate 200 µm throughout the book.
Abbreviations

Ad  Adenovirus
Ad  3,4,7,8 Adenovirus type
CPE  Cytopathic effect
EKC  Epidemic keratoconjunctivitis
Fluorescein  Fluorescein sodium
HSV  Herpes simplex virus
KCS  Keratoconjunctivitis sicca
TSPK  Thygeson’s superficial punctate keratitis
VZV  Varicella-zoster virus