Unusual Keratitis

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Please cite your position

1. Cornea Fellow
2. Resident in Ophthalmology
3. Cornea Surgeon
4. General Ophthalmologist
5. Paramedic/Nurse/Eye Health care worker
6. Others
Microbial Keratitis

Corneal Blindness is a significant cause of ocular morbidity in Africa and Asia
# Microbial Keratitis

## Incidence

<table>
<thead>
<tr>
<th>Country</th>
<th>Incidence / (million pop)</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nepal</td>
<td>7990</td>
<td>Br J Ophth 2001</td>
</tr>
<tr>
<td>India</td>
<td>1130</td>
<td>Br J Ophth 1997</td>
</tr>
<tr>
<td>Myanmar</td>
<td>7100</td>
<td>*Country report</td>
</tr>
<tr>
<td>Bhutan</td>
<td>3390</td>
<td>*Country report</td>
</tr>
<tr>
<td>USA</td>
<td>530</td>
<td>Arch Ophth</td>
</tr>
</tbody>
</table>

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840,000 new cases of corneal ulcer cases occur each year in India

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Slide Courtesy- Dr Prashant Garg
Microbial Keratitis

Microbiology is significant if-

Same organism in 2 solid media, 1 solid media and turbidity in liquid media

Confluent growth in one solid media and consistent with microscopy

Growth of same organisms on repeat scraping
Microbiology of corneal ulcers

Microscopy
- CFW mount
- Gram stain
- Giemsa stain

Culture
- 5% Sheep Blood agar (Aerobic)
- 5% Sheep Blood agar (Anaerobic)
- Chocolate agar (5% CO₂)
- Potato Dextrose agar
- Sabouraud Dextrose agar
- Thioglycolate broth
- Brain Heart Infusion broth

Slide Courtesy - Dr Chetan Videkar
Sensitivity and specificity

Table 4: Sensitivity and specificity of corneal scraping smears in the detection of microorganisms with culture as gold standard

<table>
<thead>
<tr>
<th>Smears n*</th>
<th>Bacteria</th>
<th></th>
<th>Fungi</th>
<th></th>
<th>Acanthamoeba</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Sensitivity %</td>
<td>Specificity %</td>
<td>Sensitivity %</td>
<td>Specificity %</td>
<td>Sensitivity %</td>
</tr>
<tr>
<td>Gram 3442</td>
<td>56.6</td>
<td>97.8</td>
<td>89.8</td>
<td>93.7</td>
<td>73.3</td>
</tr>
<tr>
<td>Giemsa 2774</td>
<td>ND</td>
<td>ND</td>
<td>85.2</td>
<td>96.1</td>
<td>72.2</td>
</tr>
<tr>
<td>KOH + CFW 2555</td>
<td>ND</td>
<td>ND</td>
<td>90.6</td>
<td>94.3</td>
<td>84.0</td>
</tr>
</tbody>
</table>

A – Sensitivity; B – Specificity; ND – Not Done; KOH+CFW – potassium hydroxide + calcofluor white, n* is different for each staining method as all procedures could not be done for all cases

Confocal Microscopy
a) Anterior stroma More cellular (1000/mm²), elongated nuclei, Activated keratocytes, Nerve fibers

b) Posterior stroma Less cellular (700/mm²)
Oval / bean shaped nuclei, Scanty nerves, Brighter background

c) Endothelium – Monolayer, Hexagonal / polygonal cells, Maximum intensity
Homogenous bright cell body
Dark borders, Nuclei: not seen

d) Subepithelial plexus - Beneath Bowman’s layer, 3 - 7 μ
Wavy Beaded appearance, Sub basal plexus - Above Bowmans layer
2 - 4 μ

e, f) Stromal Nerves- Anterior-mid stroma
Thicker (10 -15μ), Uniform thickness, Linear “Y-shaped” bifurcation.
Figure(a-e) Representative confocal photographs of patients with fungal keratitis – Fungal filaments appear as high reflective, double walled, septate filaments Size 3 - 8 μ, uniform width, irregular branching
**Figure(1)**- Bacterial keratitis is characterized, activated keratocytes, with infiltration of leucocytes, and Langerhans cells. Bacteria typically not visualized

**Figure(2)**- Acanthamoeba cysts present as highly reflective, double walled round particles 10–20 μm in diameter within the corneal epithelium and stroma. The inner wall has a hexagonal configuration

**Figure(3)**- Viral keratitis is characterized by ovoid dendritic cells at the level of sub epithelial cells which are an indicator of disease activity which is often over looked on slit lamp examination.
Question:
All are true for Confocal microscopy, except?

1. Tandem and Slit scanning techniques may be used to image the cornea
2. Useful to diagnose atypical keratides- fungus and acanthamoeba
3. Bacteria cannot be visualized
4. Unable to measure endothelial cell density and corneal pachymetry
Role of Confocal Microscopy in the Diagnosis of Fungal and Acanthamoeba Keratitis

Pravin K. Vaddavalli MD, Prashant Garg MD, Savitri Sharma MD, Virender S. Sangwan MD, Gullapalli N. Rao MD, Ravi Thomas MD

Results

We included 148 cases of infiltrative keratitis. Of the 103 microbiologically proven cases of Acanthamoeba or fungal keratitis, the confocal microscope was able to identify fungal filaments or Acanthamoeba cysts in 91 cases with either fungal or Acanthamoeba keratitis with a sensitivity of 88.3% (95% confidence interval [CI], 82.2–94.5) and a specificity of 91.1% (95% CI, 82.8–99.4). The interobserver agreement in interpreting the scans was good (kappa = 0.6; phi = 0.617). The intraobserver agreement was kappa = 0.795 and phi = 0.807.
Aetiology of suppurative corneal ulcers in Ghana and south India, and epidemiology of fungal keratitis


Br J Ophthalmol 2002;86:1211-1215

Attributable to a genuine change of bacterial flora within the geographical area, as influenced by climate and environment. Traditional diagnostic laboratory methods, including microscopy and culture may be negative despite a clear clinical presentation of suppurative keratitis. This was true in 50% and 31% of cases in Ghana and India, respectively. This may be due to difficulty in obtaining sufficient corneal material for conventional investigation. This applies particularly to large, late-stage ulcers, because of the risk of perforation and
Characteristic clinical features as an aid to the diagnosis of suppurative keratitis caused by filamentous fungi

P A Thomas, A K Leck, M Myatt

Table 1 Univariate analysis of clinical features occurring in fungal and bacterial keratitis

<table>
<thead>
<tr>
<th>Clinical feature</th>
<th>Frequency (% fungal)</th>
<th>Frequency (% bacterial)</th>
<th>$\chi^2$</th>
<th>OR (CI)</th>
<th>p Value</th>
<th>Sens</th>
<th>Spec</th>
<th>PPV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serrated margins</td>
<td>180/228 (79%)</td>
<td>63/132 (48%)</td>
<td>37.14</td>
<td>4.09 (2.57 to 6.56)</td>
<td>0.00</td>
<td>0.79</td>
<td>0.52</td>
<td>0.74</td>
</tr>
<tr>
<td>Raised slough</td>
<td>135/228 (59%)</td>
<td>52/132 (39%)</td>
<td>13.50</td>
<td>2.23 (1.44 to 3.55)</td>
<td>0.00</td>
<td>0.59</td>
<td>0.61</td>
<td>0.72</td>
</tr>
<tr>
<td>Dry texture of slough</td>
<td>101/228 (44%)</td>
<td>37/132 (28%)</td>
<td>9.36</td>
<td>2.04 (1.29 to 3.26)</td>
<td>0.00</td>
<td>0.44</td>
<td>0.72</td>
<td>0.73</td>
</tr>
<tr>
<td>Satellite lesions</td>
<td>51/222 (23%)</td>
<td>17/132 (13%)</td>
<td>4.91</td>
<td>1.95 (1.08 to 3.61)</td>
<td>0.04</td>
<td>0.22</td>
<td>0.87</td>
<td>0.75</td>
</tr>
<tr>
<td>Hypopyon</td>
<td>105/219 (48%)</td>
<td>83/128 (65%)</td>
<td>9.29</td>
<td>0.50 (0.32 to 0.78)</td>
<td>0.00</td>
<td>0.48</td>
<td>0.35</td>
<td>0.56</td>
</tr>
<tr>
<td>Fibrin</td>
<td>21/210 (10%)</td>
<td>28/125 (22%)</td>
<td>9.65</td>
<td>0.38 (0.20 to 0.70)</td>
<td>0.00</td>
<td>0.10</td>
<td>0.78</td>
<td>0.43</td>
</tr>
<tr>
<td>Colour (not yellow)</td>
<td>213/228 (93%)</td>
<td>106/132 (80%)</td>
<td>14.26</td>
<td>3.47 (1.77 to 6.98)</td>
<td>0.00</td>
<td>0.93</td>
<td>0.20</td>
<td>0.67</td>
</tr>
</tbody>
</table>

PPV, positive predictive value.
Case 1

51/F S/P Failed graft in RE S/P TPK for fungal keratitis – 2 years ago
Graft infiltrate 1 day history
Scraping– Pseudomonas aeruginosa
Resolved with scarring
Managed on low potency steroids
Poor surface
Case 1

1 year FUP
Poor surface and small area of opacity
Do you think it is infection
Scraping—Pseudomonas aeruginosa
Resolved with scarring
Managed on low potency steroids
Poor surface
Case 1

1 year FUP

Poor surface and small area of opacity

Do you think it is infection
Poor surface
20
Case 1

1 year FUP

Poor surface and small area of opacity

Do you think it is infection

Scraping—Yeast

Resolved with Fluconazole
Title

Poor surface
### Clinical and Microbiological Characteristics of 29 *Candida* Keratitis Episodes

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Predisposing condition</strong></td>
<td></td>
</tr>
<tr>
<td>Ocular surface disorder, chronic keratopathy, or toxicity</td>
<td>17 (59%)</td>
</tr>
<tr>
<td>Corneal graft</td>
<td>9 (31%) *</td>
</tr>
<tr>
<td>Recent trauma</td>
<td>2 (7%)</td>
</tr>
<tr>
<td>Contact lens</td>
<td>5 (17%) **</td>
</tr>
<tr>
<td><strong>Recent treatment</strong></td>
<td></td>
</tr>
<tr>
<td>Corticosteroid and antibacterial agent</td>
<td>18 (62%)</td>
</tr>
<tr>
<td>Corticosteroid only</td>
<td>2 (7%)</td>
</tr>
<tr>
<td>Antibacterial agent only</td>
<td>3 (10%)</td>
</tr>
<tr>
<td><strong>Initial assessment</strong></td>
<td></td>
</tr>
<tr>
<td>Bacterial keratitis</td>
<td>22 (76%)</td>
</tr>
<tr>
<td>Fungal keratitis</td>
<td>2 (7%)</td>
</tr>
<tr>
<td>Herpetic keratitis</td>
<td>1 (3%)</td>
</tr>
<tr>
<td>Noninfectious keratopathy</td>
<td>4 (14%)</td>
</tr>
<tr>
<td><strong>Corneal isolate</strong></td>
<td></td>
</tr>
<tr>
<td><em>C. albicans</em></td>
<td>20 (69%)</td>
</tr>
<tr>
<td><em>C. parapsilosis</em></td>
<td>9 (31%)</td>
</tr>
</tbody>
</table>
Clinical Characteristics and Outcome of *Candida* Keratitis

Regina L. Sun, MD, Dan B. Jones, MD, and Kirk R. Wilhelmus, MD, PhD

- *Candida* species are opportunists that occasionally complicate chronic keratopathy and corneal grafts
- Immunosuppression and diabetes may predispose to candidiasis
- Often misdiagnosed and in spite of medical treatment may require keratoplasty
Peripheral ulcerative keratitis

Progressive crescentic ulceration of the peripheral cornea
Secondary infection—Epithelial defects overlying the area of melt predisposes to secondary microbial infections.
Case 2

66/M
10 days history of pain and redness
PUK
S/P Conj Resection+TA +BCL
On Topical steroids
Scraping- GNB
Culture: Pseudomonas aeruginosa
Sensitive to all
Ciprofloxacin 0.5% for 6 weeks
Infected PUK
Infectious vs Non-infectious

- Symptomatic
- Pus pointing
- Sometimes concomitant involvement of adjacent area
- Cellularity and infiltrate
- Anterior chamber reaction/Hypopyon
Case 3

44/M

H/O of fall of FB with watering and pain since 10 days
S/P topical moxifloxacin 0.5% hourly, ciprofloxacin e/ointment at bedtime
Case 3

44/M

H/O of fall of FB with watering and pain since 10 days
S/P topical moxifloxacin 0.5% hourly, ciprofloxacin e/o int at bedtime

Scraping- Septate hyaline fungal filaments
Culture Curvularia+ unidentified fungus
Question:
What is true in the management of dematiaceous fungus?

1. Responds well to medical management
2. Often needs surgical management
3. Poor visual prognosis
4. Voriconazole is the first line treatment
Keratomycosis: clinical and microbiologic experience with dematiaceous fungi

Prashant Garg, MS • Usha Gopinathan, MSc • Kushal Choudhary, MS • Gullapalli N Rao, MD

DOI: https://doi.org/10.1016/S0161-6420(99)00079-2

Comparative study on the incidence and outcomes of pigmented versus non pigmented keratomycosis

Sabyasachi Sengupta 1, Sanjeevani Rajan 1, Padmati Ravindranath Reddy 1, Krishnan Thiruvengadakrishnan 1, Ravilla D Ravindran 1, Prajna Lalitha 2, C Manivasagam Vaitilingam 3


Clinical characteristics, predisposing factors, and treatment outcome of Curvularia keratitis

Ashi Khurana 1, Sanjay Chanda 1, Preeti Bhagat 1, Swati Aggarwal 1, Mohit Sharma 2, Lokesh Chauhan 3
Table 6: Comparison of previous studies on pigmented keratitis with the present study

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Total number (N)</td>
<td>88</td>
<td>43</td>
<td>16</td>
<td>117</td>
</tr>
<tr>
<td>Study period (Years)</td>
<td>Jan 1991 – Dec 1996 (6 years)</td>
<td>1970 - 1999 (30 years)</td>
<td>NS</td>
<td>Jan 2006 – Aug 2008 (2.6 years)</td>
</tr>
<tr>
<td>Prevalence of pigmented keratitis</td>
<td>88/557 (15.7%)</td>
<td>NS</td>
<td>7/53 (11.1%)</td>
<td>117/373 (31.3%)</td>
</tr>
<tr>
<td>Mean size of the infiltrate</td>
<td>4.61 mm (max diameter)</td>
<td>7 mm² +/- 5 mm²</td>
<td>NS</td>
<td>10.5 mm²</td>
</tr>
<tr>
<td>Commonest fungus recovered</td>
<td>Curvularia</td>
<td>Curvularia</td>
<td>Curvularia</td>
<td>Curvularia</td>
</tr>
<tr>
<td>Macroscopical pigmentation</td>
<td>27%</td>
<td>6%</td>
<td>NS</td>
<td>14.5%</td>
</tr>
<tr>
<td>Hypopyon</td>
<td>53.4%</td>
<td>12.5%</td>
<td>NS</td>
<td>47%</td>
</tr>
<tr>
<td>VA at presentation</td>
<td>71% &lt; 20/400</td>
<td>NS</td>
<td>31%&lt;20/400</td>
<td>80% &lt; 20/400</td>
</tr>
<tr>
<td>Final VA</td>
<td>NS</td>
<td>&gt;20/40 (78%)</td>
<td>&gt;20/40 (44%)</td>
<td>&gt; 20/40 (16%)</td>
</tr>
<tr>
<td>First-line drug</td>
<td>Natamycin</td>
<td>Natamycin</td>
<td>Natamycin</td>
<td>Natamycin</td>
</tr>
<tr>
<td>Healed ulcers</td>
<td>72%</td>
<td>81%</td>
<td>NS *</td>
<td>48%</td>
</tr>
<tr>
<td>Penetrating keratoplasty</td>
<td>15.3%</td>
<td>9.3%</td>
<td>6%</td>
<td>8.6%</td>
</tr>
<tr>
<td>Superficial kerectomy</td>
<td>NS</td>
<td>9.3%</td>
<td>6%</td>
<td>7%</td>
</tr>
<tr>
<td>Evisceration</td>
<td>9%</td>
<td>None</td>
<td>None</td>
<td>11%</td>
</tr>
</tbody>
</table>

*NS-Not specified and outcome data not uniform
Smear – Septate Hyaline, Filamentous Fungi, GPC in pairs
Culture: Aspergillus Flavus, Streptococcus pyogenes

<table>
<thead>
<tr>
<th>Organism</th>
<th>Streptococcus Pyogenes</th>
</tr>
</thead>
</table>

**Streptococcus Pyogenes**

<table>
<thead>
<tr>
<th>Susceptible To</th>
<th>Intermediate To</th>
<th>Resistant To</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cefazolin = 0.25 µg/mL E Test</td>
<td>Ciprofloxacin = 20.00 mm Disk Diffusion</td>
<td>Levofoxin = 8.00 µg/mL AST</td>
</tr>
<tr>
<td>Ofloxacin = 20.00 mm Disk Diffusion</td>
<td>Gatifloxacin = 18.00 mm Disk Diffusion</td>
<td></td>
</tr>
<tr>
<td>Vancomycin = 24.00 mm Disk Diffusion</td>
<td>Moxifloxacin = 2.00 µg/mL AST</td>
<td></td>
</tr>
<tr>
<td>Ampicillin &lt;= 0.25 µg/mL AST</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cephoxime &lt;= 0.12 µg/mL AST</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ceftriazone &lt;= 0.12 µg/mL AST</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Linezolid &lt;= 2.00 µg/mL AST</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vancomycin = 0.50 µg/mL AST</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chloramphenicol = 4.00 µg/mL AST</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Co infection of Bacteria in fungal keratitis

Bacterial co infection of fungal keratitis may occur in 5-25%

Gram positive cocci were equally associated with yeast and filamentous fungi

Gram negative rods with yeast

Gram positive rods with filamentous fungi

Pate et al. 2006
Prevalence and spectrum of bacterial co-infection during fungal keratitis

J C Pate, D B Jones, K R Wilhelmus

Table 2  Clinical characteristics of fungal keratitis according to bacterial co-infection

Table 5  Joint associations of 65 principal and 24 additional bacterial co-isolates during polymicrobial keratomycosis

<table>
<thead>
<tr>
<th>Fungal corneal isolate</th>
<th>Bacterial co-isolates</th>
<th>Gram positive cocci</th>
<th>Gram positive rods</th>
<th>Gram negative rods</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Candida</em> sp</td>
<td>28</td>
<td>15</td>
<td>3</td>
<td>10</td>
</tr>
<tr>
<td>Other yeast</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td><em>Fusarium</em> sp</td>
<td>18</td>
<td>7</td>
<td>10</td>
<td>1</td>
</tr>
<tr>
<td><em>Aspergillus</em> sp</td>
<td>9</td>
<td>4</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td><em>Curvularia</em> sp</td>
<td>9</td>
<td>5</td>
<td>4</td>
<td>0</td>
</tr>
<tr>
<td>Other filamentous fungi</td>
<td>24</td>
<td>14</td>
<td>9</td>
<td>1</td>
</tr>
</tbody>
</table>
Question:
All are true of bacterial coinfection in fungal keratitis except?

1. Co infections occur rarely
2. Increase severity of keratitis
3. Demographics of co-infections are different
4. Adherence to fungal biofilm may assist co infection
Case 4

• 49/M, farmer, 5 month history of watering, pain and redness in LE,
Features of HSV immune stromal keratitis

• Primarily a clinical diagnosis
• H/O of waxing and waning
• Non specific history of long duration
• Exacerbation based on unknown triggers
• Presence of deep vascularization
• Foot print scars
• Abnormal corneal sensations
Case 4

• 49/M, farmer, 5 month history of watering, pain and redness in LE,

• Based on clinical picture advised anti viral, worsened with antivirals, history of trauma 5 years ago, Biopsy done, noted fungal filaments

• Taken for TPK
Corneal Biopsy
GMS Stain 40X

Grams Stain 100X
Prevalence of HSV

Nearly 100% individuals above the age of 60 and most middle aged persons harbor HSV in the Trigeminal Ganglion

Evidence-Based Treatment of Herpes Simplex Virus Keratitis: A Systematic Review

Scott Guess, MD, Donald U. Stone, MD, and James Chodosh, MD, MPH
PCR and IHC are both sensitive for the detection of HSV-1 in the cornea.

A combination of PCR and IHC increases the specificity for the diagnosis of HSK to 97%.

1. Quantitative Real Time PCR is faster and more sensitive and specific than conventional PCR for detection of HSV

2. qPCR determines virus load and distinguishes different types of HSV therefore helps in assessing response to treatment

3. Larger viral loads may suggest increasing disease severity and poorer prognosis

4. Dual infection with HSV 1 and 2 have been described. The one with lesser copy number is competed out

5. Co infection with fungi and bacteria are also reported and needs appropriate treatment
Case 5

38/F
Homemaker
10 days of watering, pain and redness
Case 5

38/F
Homemaker

10 days of watering, pain and redness

Smear and Culture: Pythium Insidiosum

Treatment: Linezolid and Azithromycin
Case 5
Case 5

Smear and Culture: Pythium Insidiosum

Treatment: Linezolid and Azithromycin

(Cornea 2015;34:438–442)
Leap forward in the treatment of *Pythium insidiosum* keratitis

Bhupesh Bagga, Savitri Sharma, Sai Jeevan Madhuri Guda, Ritu Nagpal, Joveeta Joseph, Kodiganti Manjulatha, Ashik Mohamed, Prashant Garg

1. Tentacle, dot like and plaque like presentation with a gutter
2. Scraping shows broad sparsely septate filaments and glabrous flat colony on CA, Zoospore formation and DNA sequencing to ITR of rDNA
3. Response is better to Antibacterial – such as TG, AZ, LZ, Macrolides
4. Consistent poor response to TPK with failed graft, evisceration, phthisis, recurrence

Case 6

55/M

Farmer

3 weeks history of watering, pain and redness

Scraping- negative

TA BCL applied

Broad spectrum antibiotics

AC exudates subjected to microbiology
Microbiology

AC Exudates
Septate fungal filaments
No growth in culture
Real Time PCR 8,239 copies/ml HSV 1 DNA

Treatment
Oral ACV 400mg/5times X 8 weeks
Hourly Natamycin 5%
1. Co-infection of Fungus and HSV is rare
2. Keep a possible index of suspicion
3. Clinical features may not be distinguishable
4. qPCR for HSV where available is confirmatory
5. Combination therapy with anti-fungals and anti-virals
6. Cautious use of topical steroids after ensuring that fungal infection has subsided
Case 7

61/F
Homemaker
RE 5 days – watering pain and redness
Scraping – Fungal filaments
Culture no Growth
Drug Toxicity with Antifungals

1. Decrease in cell viability
2. Increase in cellular permeability
3. Impaired Wound healing
4. Affected by dosage, concentration and preservatives
1. Clinical response of worsening after initial improvement
2. Mild to Intense forniceal congestion
3. Marked difference in redness in the upper and lower halves of bulbar conjunctiva

doi:10.1136/bjophthalmol-2012-301978

Harminder Singh Dua, Ahmad Muneer Otri,
Dalia Galal Said, Lana Akram Faraj

Department of Ophthalmology and Visual sciences,
Nottingham University Hospitals, University of Nottingham,
Nottingham, UK
Question: Ocular toxicity depends on all except

1. Concentration of drug
2. Duration of application
3. Frequency of instillation
4. Allergy to drug
Thank you!

LV Prasad Eye Institute

www.lvpei.org

Excellence • Equity • Efficiency
Case 5