

An Overview of Fungal Keratitis and Case Report on Trichophyton Keratitis

Ivana Mravičić¹, Iva Dekaris¹, Nikica Gabrić¹,
Ivana Romac¹, Vlade Glavota¹ and Emilija Mlinarić- Missoni²
¹University Department of Ophthalmology, Eye hospital „Svjetlost“, Zagreb,
²Croatian National Institute of Public Health, Zagreb,
Croatia

1. Introduction

1.1 Keratitis

Keratitis represents corneal inflammation from various causes and clinical manifestations. (Table 1.) It might affect populations of all ages, both males and females with variable incidence. The cornea has a few different defensive mechanisms because it is constantly exposed to external pathogens and environmental influences:

- reflexive eye closing
- flushing effect of tearing
- epithelium diffusion barrier
- very quick regeneration ability

Due to impaired defensive mechanisms caused by injuries or little epithelial defects, different types of pathogens or environmental influences might induce corneal inflammation (keratitis). The form of corneal inflammation called superficial keratitis involves just the corneal surface (epithelium). If the inflammation involves corneal stroma it is called stromal or interstitial keratitis. Keratitis might be mild, moderate or severe and may involve other parts of the eye. It might be acute or chronic, infectious or noninfectious. All conditions that lead to epithelial break are possible risk factors to induce keratitis. Microorganisms cannot invade an intact, healthy cornea and infection rarely occurs in the normal eye because the human cornea is naturally resistant to infection.

Keratitis	
Noninfectious	Infectious
Superficial punctate keratitis	Bacterial keratitis
Exposure keratitis	Viral keratitis
Neuroparalytic keratitis	Fungal keratitis
	Protozoal keratitis

Table 1. Types of keratitis

1.1.1 Noninfectious keratitis

Noninfectious keratitis represents corneal inflammation with no known infectious cause. There is a wide spectrum of eye disorders that might be the very reason for this frequent corneal manifestation causing defects of corneal epithelium. This includes:

- tear film disturbances
- eyelid anomalies and inflammations
- physical or chemical trauma
- allergies
- problems with contact lens wearing
- facial neuropathy

Persisting epithelial defects are typically accompanied by this form of keratitis. Pain, tearing, redness, photophobia and decreased visual acuity are the most common clinical symptoms. Alongside symptomatic therapy, treatment also depends on the specific cause and it is aimed at promoting corneal healing.

1.1.2 Infectious keratitis

Infectious keratitis (microbial keratitis) as the most frequent cause of keratitis is a sight threatening process characterized by defects of corneal epithelium with inflammation of underlying corneal stroma. Bacteria, viruses, fungi and parasitic organisms are all possible causes of this medical emergency condition. The most common predisposing risk factors to develop infectious keratitis include overnight or extended contact lens wear, inadequate disinfection of contact lenses (contamination of the contact lens storage case or contact lens solution), trauma, previous ocular and eyelid surgery, especially corneal surgery (refractive surgery and keratoplasty), chronic ocular surface disease (tear film deficiencies, corneal exposure due to abnormalities of eyelid anatomy and function, systemic diseases (diabetes mellitus, immunocompromised status), extended use of topical corticosteroids. In about 10% of patients with infectious keratitis none of these risk factors was recognized. Clinical presentation varies and depends on the type of causative agent. Patients usually present with redness, tearing, rapid onset of pain and blurred vision. Varied physical findings can be revealed using slit lamp biomicroscopy and external examination will reveal: eyelid edema, conjunctival hyperemia, corneal ulceration, corneal infiltrates, stromal inflammation of the cornea, anterior chamber reaction with or without hypopyon, Descemet folds, endothelial inflammatory plaques, posterior synechiae.

Infectious keratitis as a serious and possible eye threatening medical emergency requires prompt and adequate treatment. Treatment options include local and systemic antibacterial, antifungal and antiviral medications that depend on the underlying cause and severity of disease.

1.2 Fungal keratitis

Fungal keratitis or keratomycosis refers to an infective process of the cornea caused by any fungal species capable of invading the ocular surface. It is a result of fungal colonization or epithelial infiltration and/or invasion of the corneal stroma. It is most typically a slow, relentless disease that must be differentiated from other types of corneal conditions with similar presentation; especially its bacterial counterpart.

Fungal keratitis is a very serious, potentially sight-threatening corneal infection which most commonly develops in patients after trauma or those with a compromised corneal surface.

It is relatively rare. However, with the increasing and extensive use of antibiotics and corticosteroids there has been an increase in the incidence of fungal keratitis over the past 20 years. Worldwide, the reported incidence of fungal keratitis is 17% to 36%. Despite advances in diagnosis and medical treatment of keratomycosis, 15% to 27% of patients require surgical intervention such as keratoplasty, enucleation, or evisceration because of either failed medical treatment or advanced disease at presentation.

1.2.1 Etiology

Fungi are eukaryotic organisms that have rigid walls and multiple chromosomes containing both DNA and RNA.

They are either saprophytic, free organisms living out of decaying organic matter or pathological, those that need a living host for perpetuation. At least 35 genera of fungi have been reported and are associated with corneal infection, the more common among which are *Candida*, *Fusarium*, *Cephalosporium* and *Aspergillus*.

Keratomycosis can be caused by moulds (filamentous multicellular fungi that produce tubular projections known as hyphae): hyalohyphomycete (from any of the 30 genera with over 55 species) and pheohyphomycete (from 19 genera and over 30 species), or yeasts (unicellular fungi that reproduce by budding and may occasionally form hyphae or pseudo-hyphae) (from 7 genera, over 18 species).(Table 2).

Moulds		Yeasts
Hyalohyphomycetes	Pheohyphomycetes	
<i>Fusarium</i> spp.	<i>Alternaria</i> spp.	<i>Candida</i> spp.
<i>Aspergillus</i> spp.	<i>Curvularia</i> spp.	<i>Cryptococcus</i> spp.
<i>Acremonium</i> spp.	<i>Bipolaris</i> spp.	<i>Geotrichum</i> spp.
<i>Paecilomyces</i> spp.	<i>Cladosporium</i> spp.	<i>Malassezia</i> spp.
<i>Penicillium</i> spp.	<i>Lecytophora</i> spp.	<i>Rhodotorula</i> spp.
<i>Pseudallescheria boydii</i>	<i>Phialophora</i> spp.	<i>Torulopsis</i> spp.
<i>Verticillium</i> spp.	<i>Phoma</i> spp.	<i>Trichosporon</i> spp.
<i>Rhizopus</i> spp.	<i>Aureobasidium</i> spp.	<i>Cryptococcus</i> spp.

Table 2. Most common agents of keratomycosis

The most common type of keratomycosis is **keratohyalohyphomycosis** caused by moulds of the *Fusarium* and *Aspergillus* genera. Some studies into the etiology of keratohyalohyphomycosis in the USA proved that species of the *Fusarium* genus (*F. solani* and *F. oxysporum*, in particular) were the causative agents in 64% of the cases. Species of *Aspergillus* genus (e.g. *A. fumigatus*, *A. flavus*, *A. niger*) rank second most frequent agents of keratomycosis. Other less common agents of keratohyalohyphomycosis belong to the

following genera: *Acremonium*, *Cylindrocarpon*, *Paecilomyces*, *Penicillium*, *Pseudallescheria* and *Scopulariopsis*. *Zygomycete* moulds (genera *Absidia*, *Apophysomyces*, *Rhizopus*) are also documented agents of keratomycosis.

Keratopneohyphomycosis is a less common fungal infection of the cornea, more prevalent in tropical and subtropical regions, mostly caused by species of the genera *Curvularia*, *Alternaria*, *Bipolaris*, *Drechslera*, *Exserohilum* and *Phialophora*.

Moulds are responsible for most cases of fungal keratitis in tropical climates.

Yeasts rarely cause keramycosis, mostly species of the *Candida* genus. Risk factors for contracting **keratocandidosis** is a chronic disease of the cornea. Yeasts are responsible for most cases of fungal keratitis in temperate climates.

Causative agents of keratomycosis documented over the last five years by the Ministry of Health and Social Welfare Referral Center for mycological diagnostics or systemic and disseminated infections at the Croatian National Institute of Public Health, Zagreb, are species from the *Fusarium*, *Verticilium* and *Acremonium* genera. Extremely rare causative agents are primary pathogenic species of dermatophytic moulds eg. *Trichophyton* spp.

1.2.2 Pathogenesis

Fungal keratitis is more common in males than in females. Risk factors are previous history of ocular trauma (especially if organic matter is involved), agricultural occupations, age, pre-existing ocular disease, exposure keratopathy, chronic keratitis, hydrophilic contact lenses, chronic use of steroids, diabetes, systemic immunosuppressive disease.

Corneal trauma is the most frequent and major risk factor for fungal keratitis. There should be a high level of suspicion if a patient presents with a history of corneal trauma, particularly with plant or soil matter. Previous corneal trauma was documented in 26-100% of keratomycosis patients.

Fungal keratitis frequently occurs in farmers and outdoor workers after ocular injuries (sometimes trivial) involving some type of vegetable matter. It would appear that the fungus is inoculated into the cornea by the injuring material rather than by subsequent contamination of the epithelial defect by environmental organisms in most of the cases reported.

The trauma that accompanies contact lens wear is miniscule. Contact lenses are not a common risk factor of fungal keratitis. *Candida* is the principal cause of keratitis associated with therapeutic contact lens wear and filamentous fungi are the ones associated with refractive contact lens wear.

Environmental conditions including temperature, annual rainfall, windy seasons and the harvest period have a significant role in increasing the incidence. The incidence of fungal infections is higher in tropical and semitropical areas and is much more frequent in developing countries. In some hot and humid regions it accounts for 50% of cases.

Fungal keratitis is an important ophthalmic problem in all parts of the world, because it leads to corneal blindness and sometimes to loss of the eye.

Normal conjunctival microbiota usually does not consist of fungi. In some specific life or work circumstances, however, individuals are exposed to corneal trauma and thus become more prone to develop mycotic infection.

Corneal epithelium is firmly built and resistant to prospective invasion of microorganisms. The infection probably starts when the epithelial integrity is broken either due to trauma or ocular surface disease and fungi gain access into the tissue, proliferate and elicit a severe inflammatory response that can cause stromal necrosis and melting. Proteases, collagenases, and phospholipases, extracellular enzymes of moulds and yeasts facilitate their penetration into corneal stroma. These enzymes, fungal antigens and toxins liberated into the cornea can result with necrosis and damage of its architecture thus compromising the eye integrity and function. Once in the anterior chamber, the infection is very difficult to eradicate and aggressive surgery is usually required. Wearing safety glasses while gardening will diminish the risk of ocular trauma, also general hygiene, proper contact lens care and avoidance of nonessential steroid use should diminish the probability of mycotic infection.

Fungal keratitis was first described by Theodor Leber in 1879 in a farmer who had his cornea injured by wheat blades. The causative agent was *Aspergillus glaucus species*. Since then and until the middle of the last century, individual cases of keratomycosis caused by species of the *Aspergillus genus*, occurring through an injury of the cornea, were documented, mostly in the tropical regions. Whilst this entity is not a common cause of corneal infection, it certainly represents one of the major causes of infectious keratitis in tropical areas of the world.

The incidence of fungal keratitis has increased over the past 30 years as a result of the frequent use of ocular corticosteroids; a rise in the number of patients who are immunocompromised, and the availability of laboratory diagnostic techniques that aid in its diagnosis.

Fungal keratitis, if not diagnosed and treated with celerity, can be rapidly destructive to the integrity of the eye, resulting in devastating ocular damage. Unfortunately, delayed diagnosis is common, primarily because of the lack of suspicion and even if the diagnosis is made accurately, management remains a challenge. Poor corneal penetration and limited commercial availability of antifungal drugs further exacerbate the management problem.

1.2.3 Clinical manifestations

Symptoms of fungal keratitis are similar to any corneal infection and include unilateral red eye, pain, foreign body sensation, photophobia, tearing, decreased vision and discharge. Pain and photophobia are initially mild, but become severe relative to the clinical signs.

The clinical appearance of fungal keratitis varies greatly depending on the duration and severity of infection.

Patients often have a history of trauma, chronic ocular surface disease or corticosteroid eye drop usage.

Signs vary with the infectious agent. In early disease there tends to be less redness and lid swelling than with bacterial infection. The corneal surface typically appears grey with a dry rough texture.

Non specific signs of fungal keratitis include conjunctival injection; epithelial defect; suppuration;stromal infiltration; anterior chamber reaction; hypopyon; aqueous flare and corneal neovascularization.

Specific signs of fungal keratitis include infiltrates with feathery margins, rough texture, raised borders, brown pigmentation, associated endothelial plaque, and satellite lesions; deep stromal infiltrates with an intact epithelium; dull grey appearance of the cornea with possible heaping of epithelium.

Sclerotic scatter can be used to highlight the density and scalloped borders of the fungal lesion. Many fungal ulcers demonstrate no striking morphological pattern, and often it is not possible to differentiate clinically between fungal keratitis and bacterial keratitis.

Filamentous keratitis is characterized by a grey-yellow stromal infiltrate with indistinct margins , a progressive infiltration, often surrounded by satellite lesions and hypopyon. Filamentous fungi classically grow in a feathery branching pattern, but may be very rapidly progressive and indistinguishable from bacterial keratitis. (Figure 1.)



Fig. 1. Fungal corneal ulcer

Candida keratitis is characterized by a yellow-white infiltrate associated with dense suppuration. *Candida* species produces a small ulcer with expanding infiltrate in a collar-stud configuration, often superimposed on a debilitating corneal condition. There may be an endothelial plaque under the lesion and satellite lesions at the edges. Suppurative keratitis, fibrinoid uveitis, hypopyon and elevated IOP may occur.

Several features of fungal keratitis are characteristic if not pathognomonic and may permit an immediate or early diagnosis. These features are:

1. The surface of the lesion is usually gray or dirty white with a dry rough texture.
2. Areas of the lesion may be raised above the plane of the uninvolved cornea.
3. The margins of the ulcer tend to be irregular.
4. There may be satellite lesions.
5. There may be a complete or partial white immune ring“ around the lesion. This is said to be formed by the fungal antigen and host antibody response.

1.2.4 Diagnostics

After establishing the patient's general condition the examiner should look for evidence of ocular surface disease. Determine the amount and type of secretions and lid swelling. The upper eyelid should be everted to exclude a retained foreign body. The examiner should measure the size and depth of the lesion as well as the presence of satellite lesions. Also the intraocular pressure should be ascertained. Anterior chamber reaction and evidence of hypopyon should be recorded. Vitreous reaction if present may suggest intraocular spread of the disease.

Under the slit lamp, early in the evolution, the lesion might look like an unhealed corneal abrasion with scanty infiltrates and no secretions. With time the ulcer develops thicker infiltrates and fuzzy margins. The presence of satellite lesions strongly suggests a fungal infection. Redness and periocular edema are also common. This combined with a history of trauma, especially with vegetable matter, ocular surface disease or chronic use of topical steroids should alert about the possibility of a mycotic etiology.

We should ask the patient about ocular or systemic disease: keratocandidosis is commonest in debilitated patients or those with preexisting corneal disease. Ocular trauma is associated with filamentous fungi, e.g. *Aspergillus* or *Fusarium spp.*

A diagnosis of fungal keratitis is based on a matrix of the following:

1. Case history
2. Clinical signs
3. Confirmation from cytology and/or culture results.

The most important step in the initial management of suspected fungal keratitis is to obtain corneal material for direct smears and inoculation of media. It is important to scrape multiple sites in the ulcer crater, particularly at the margins, to enhance recovery of the organisms. Corneal scrapings are taken from deep into the lesion with a surgical blade or sterile spatula. To perform a corneal biopsy a dermatological 2 mm punch can be used.

Laboratory diagnostics should be performed before starting antifungal therapy. Filamentous fungi tend to proliferate anterior to Descemet membrane and a deep stromal biopsy may be required (similar in technique to performing a trabeculectomy-the excised deep tissue is sent for culture). Sometimes the diagnosis can only be confirmed following anterior chamber tap or excisional keratoplasty.

Direct microscopy of corneal smears can be performed with special methods such as KOH, calcofluor white, Gram or/and Giemsa staining.. Gram stain may identify the yeast forms of *Candida*, and Giemsa stain is more likely to detect filamentous fungus.(Fig. 2)

Cultivation of causative agents can be done on Sabouraud's dextrose agar, although most fungi will also grow on blood agar or in enrichment media at 27 deg celcius or at room temperature within 3 days. PCR with pan fungal primers are used as an adjunct to culture.

Antifungal susceptibility testing can be performed in reference laboratories but the relevance of these results to clinical effectiveness is uncertain.

Histology involving periodic acid-Schiff(PAS) stain and Grocott silver stain of corneal tissue are the most sensitive.

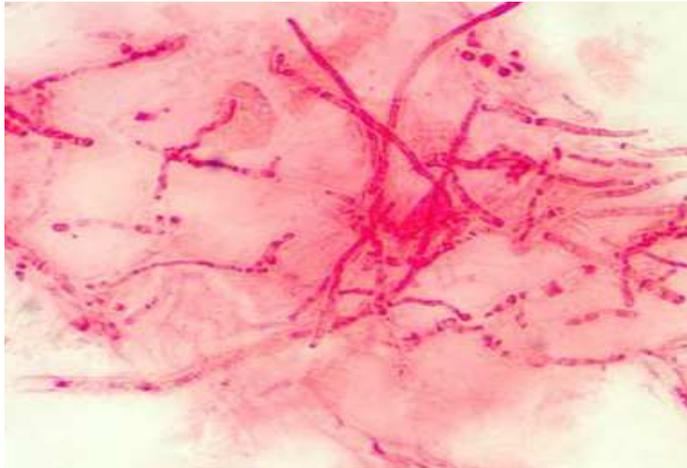


Fig. 2. Gram stain of corneal smear revealing hyphae

The drawback is that not all laboratories can handle those, so, again we might need to rely on the patient's evolution and the physician's clinical acumen. If all laboratory results are negative we should consider a corneal biopsy.

If available, in vivo confocal microscopy may be diagnostic.

1.2.5 Differential diagnosis

Fungal keratitis should be considered in the differential diagnosis of herpetic, acanthamoeba and atypical bacterial keratitis e.g. *Nocardia*, *Mycobacterium*, *Propionibacterium*; that does not respond to conventional treatment or has an unusual history or suspicious appearance.

1.2.6 Treatment

Antifungal therapy should be limited to cases with positive fungal smears or cultures. In general, management consists of medical therapy with the use of topical and or systemic anti-fungal medications alone or in combination with surgical treatment.

Antifungal agents are classified into the following groups:

- **Polyenes** include natamycin, nystatin, and amphotericin B. Polyenes disrupt the cell by binding to fungal cell wall ergosterol and are effective against both filamentous and yeast forms. Amphotericin B is the drug of choice to treat patients with fungal keratitis caused by yeasts. Although polyenes penetrate ocular tissue poorly, amphotericin B is the drug of choice for treatment of fungal keratitis caused by *Candida*. In addition, it has efficacy against many filamentous fungi. Administration is every 30 minutes for the first 24 hours, every hour for the second 24 hours, and then is slowly tapered according to the clinical response. Natamycin has a broad-spectrum of activity against filamentous organisms. The penetration of topically applied amphotericin B is found to be less than that of topically applied natamycin through the intact corneal epithelium. Natamycin is the only commercially available topical ophthalmic antifungal preparation. It is

effective against filamentous fungi, particularly for infections caused by *Fusarium*. However, because of poor ocular penetration, it has primarily been useful in cases with superficial corneal infection.

- **Azoles** (imidazoles and triazoles) include ketoconazole, miconazole, fluconazole, itraconazole, econazole, and clotrimazole. Azoles inhibit ergosterol synthesis at low concentrations, and, at higher concentrations, they appear to cause direct damage to cell walls. Oral fluconazole and ketoconazole are absorbed systemically with good levels in the anterior chamber and the cornea; therefore, they should be considered in the management of deep fungal keratitis. Imidazoles and triazoles are synthetic chemical antifungal agents. High cornea levels of ketoconazole and fluconazole have been demonstrated in animal studies. Because of excellent penetration in ocular tissue, these medications, given systemically, are the preferred treatment of keratitis caused by filamentous fungi and yeast. The adult dose of ketoconazole is 200-400 mg/d, which can be increased to 800 mg/d. However, because of the secondary effects, increasing the dose should be done carefully. Gynecomastia, oligospermia and decreased libido have been reported in 5-15% of patients who have been taking 400 mg/d for a long period. The potential role of itraconazole in treatment of fungal keratitis is still unclear. However, it may be a helpful adjunctive agent in fungal keratitis. An oral antifungal (e.g. ketoconazole, fluconazole) should be considered for patients with deep stromal infection. Antifungal therapy usually is maintained for 12 weeks, and patients are monitored closely. Fluconazole has been shown to penetrate better into the cornea after systemic administration compared to other azoles and may be associated with fewer adverse effects.
- **Fluorinated pyrimidines**, such as flucytosine, are other antifungal agents. Flucytosine is converted into a thymidine analog that blocks fungal thymidine synthesis. It is usually administered in combination with an azole or amphotericin B; it is synergistic with these medications. Otherwise, if flucytosine is the only drug used in therapy for candidal infections, emergence of resistance rapidly develops. Therefore, flucytosine should never be used alone. Treatment should be instituted promptly with topical fortified antifungal drops, initially every hour during the day and every 2 hours over night. Subconjunctival injections may be used in patients with severe keratitis or keratoscleritis. They also can be used when poor patient compliance exists.

In vitro antifungal susceptibility testing is often performed to assess resistance patterns of the fungal isolate. However, *in vitro* susceptibility testing may not correspond with *in vivo* clinical response because of host factors, corneal penetration of the antifungal drug and difficulty in standardization of antifungal sensitivities. Therefore, they should be performed in a standardized method at a reference laboratory.

The promotion of fungal growth by corticosteroid treatment is well recognized; therefore, corticosteroid drops should not be used in the treatment of fungal keratitis until after 2 weeks of antifungal treatment and clear clinical evidence of infection control. Steroids should only be used when the active inflammation is believed to be causing significant damage to the structure of the cornea and/or vision. The steroid is always used in conjunction with the topical antifungal. Therapy may be modified. Decisions about alternate therapy must be based on the biomicroscopic signs and on the tolerance of the topical medications. Improvement in clinical signs may be difficult to detect during the initial days of antifungal therapy. However, some of the biomicroscopic signs that may be helpful to evaluate efficacy are as follows:

- Blunting of the perimeters of the infiltrate
- Reduction of the density of the suppuration
- Reduction in cellular infiltrate and edema in the surrounding stroma
- Reduction in anterior chamber inflammation
- Progressive reepithelization
- Loss of the feathery perimeter of the stromal inflammation

Successful antifungal therapy for fungal keratitis requires frequent drug administration for prolonged periods (ie, at least 12 wk). Some corneal manifestations of toxicity are as follows:

- Protracted epithelial ulceration
- Punctuate corneal epithelial erosion
- Diffuse stromal haze

Surgical therapy may be required not only for complications of acute infectious processes, but also if medical management fails.

Debridement

Debridement is the simplest form of surgical intervention. The organisms and necrotizing material is removed and the penetration of antifungal medications is enhanced by the removal of the epithelium, which is a barrier for the topical antifungals. Debridement is recommended only in cases when necrotic tissue unables healing of the corneal ulcer.

Biopsy

A biopsy is indicated for the direction of diagnostic and/or therapeutic treatment.

Conjunctival flaps

Conjunctival flaps have been advocated for nonhealing ulcers and are often effective, although fungal organisms have been found to persist under a conjunctival flap.

Penetrating keratoplasty (PK)

Penetrating keratoplasty should be performed sooner rather than later in cases not responding to aggressive antifungal therapy. If the infectious process progresses and the fungus reaches the limbus or sclera, it will be too late for keratoplasty to rid the eye of viable fungus, and the eye will be destroyed by the fungal infection.

Lamellar keratoplasty

Lamellar keratoplasty may be ineffective in treating fungal keratitis because of the inability to remove the infectious agent. If the area of infection can be completely encompassed by the penetrating graft, and if there has been an inadequate response to medical treatment, the corneal graft may be an effective cure.

Typically, diagnosis occurs late, as many practitioners frequently misdiagnose fungal keratitis as bacterial keratitis. Fungal keratitis is considered only after a presumed bacterial keratitis worsens during antibiotic therapy. Fungal keratitis is difficult to treat for various reasons. Few antifungal medications have good corneal penetration, and most are merely fungistatic hence requiring an intact immune system and a prolonged therapeutic course. Except for natamycin 5%, all antifungal medications must be adapted for ophthalmic use from systemic drugs. The result is considerable ophthalmic toxicity.

The three major goals for treating fungal keratitis are:

1. Eradicate the fungal infection
2. Prevent secondary bacterial infection
3. Control ocular pain

Analgesic therapy includes cycloplegics and nonsteroidal anti-inflammatory drugs. Atropine 1% ophthalmic solution or ointment should be applied topically, as frequently as is necessary, to maintain pupillary dilation. It not only blocks painful ciliary spasm but also minimizes the development of synechiae. Ocular pain may also be controlled by the systemic administration of non-steroidal anti-inflammatory drugs. Secondary glaucoma may require oral carbonic anhydrase inhibitors or hyperosmotic agents. Additional antibacterial therapy for individual cases should be guided by culture and sensitivity testing results. Because secondary bacterial invasion is likely, topical antibiotics should be included in the therapeutic regimen. Initial antibacterial therapy should be directed against both gram-positive and gram-negative organisms. Medical treatment can be effective, provided that suitable drugs are administered appropriately. Combinations of surgical and medical treatment usually reduce the duration of therapy, although surgical treatment can produce more scarring. Surgery is often chosen because of the shorter recovery time and potential better prognosis.

If the smear and cultures are negative at 48 to 72 hr in a patient with strong suspicion of having fungal infection, and the patient is not improving on the initial, broad- spectrum antibacterial therapy chosen, a corneal biopsy is required. If the corneal biopsy is still negative, the destructive corneal process is progressing, and hypopyon exists; anterior chamber paracentesis or excisional biopsy (keratoplasty) should be performed.

Adverse results range from mild to severe corneal scarring, corneal perforation, anterior segment disruption and glaucoma up to endophthalmitis resulting in evisceration. The aftermath of fungal keratitis can be dreadful. There is severe visual loss in 26% to 63% of patients. Fifteen to twenty percent may need evisceration. Penetrating keratoplasty is performed in 31 to 38%.

2. Case report

We present a 22 year-old female who developed a corneal ulcer after contact lens wearing. The patient was treated with topical antibiotics, the conjunctival swab was sterile but the patient developed corneal melting syndrome. She was continually treated with topical and systemic antibiotics for two weeks but then developed descemetocella with spontaneous corneal perforation and complicated cataract of the left eye as a complication of keratitis.

At that stage of the disease the patient was examined in our clinic for a second opinion (Figure 3). Immediately after she was admitted to our clinic, a conjunctival swab, a piece of corneal tissue and a sample from the anterior chamber were sent to the microbiology department for analysis. During the procedure, a lavage of the anterior chamber with cefuroxime and vancomycin was performed. Therapeutic urgent perforating keratoplasty (PK) was performed 48 hours after she was admitted into our clinic by placing the graft onto a healthy recipient part of the cornea together with extracapsular cataract extraction and the implantation of the intraocular lens in the posterior chamber (figure 4). Intraoperatively we

found a melted cornea, descemetocella with central perforation, white-yellow snow balls in the anterior chamber with a thick pupillary membrane. The patient was treated with 400 mg i.v. ciprofloxacin and 50 mg diflucan, dexamethasone, atropine (subconjunctival application) and chlorhexidine, brolene, levofloxacin, polymyxin B, and dexamethasone/neomycin drops. Antibiotics were used because the results of culture and biopsy of corneal tissue and a sample from the anterior chamber were inconclusive. Use of antibiotics to prevent secondary bacterial infection in case of fungal keratitis is not generally advised unless the result of antibacterial swab is inconclusive. After the repeated swabs showed no bacterial ingrowth, systemic antibiotics were stopped.

Microbiological evaluation was performed following excisional biopsy of the intracameral portion of the lesion. The presence of *Trichophyton spp.* was confirmed. According to the infectologist's advice, 100 mg bid itraconazole was included in the systemic therapy. The corneal graft was clear for 17 days and then started to opacify and was rejected in the following 10 days. In spite of local and systemic therapy, microorganisms invaded the vitreous and caused endophthalmitis. Pars plana vitrectomy was performed in order to take fresh samples and decrease the quantity of microorganisms. In the postoperative period antifungal treatment was continued intensively. Despite the intensive therapy, the corneal graft gradually melted and the anterior chamber was again filled with inflammation masses. Anterior chamber washout with cefuroxim was done once again and samples were taken and sent to evaluation. *Trichophyton spp.* was confirmed but in decreased quantity. Due to progression of corneal melting, an amniotic membrane was transplanted to prevent perforation. In spite of systemic and local therapy, the patient developed endophthalmitis again and lost light sensation. Few months afterwards she developed phthisis. Evisceration with a drainage system was performed and a silicon prosthesis was implanted.

The patient had no macroscopic signs of mycotic infection in nails, foot or skin so the samples from this areas were not sent on microbiological evaluation. This patient worked in nursing home so she might had been in contact with patients who had dermatophytosis.

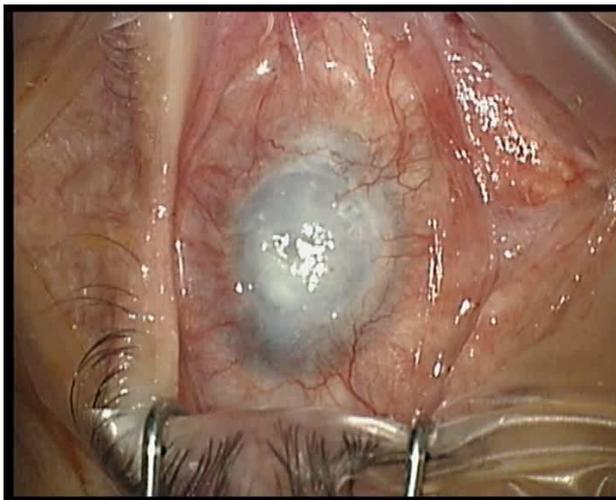


Fig. 3. Corneal ulcer developed after contact

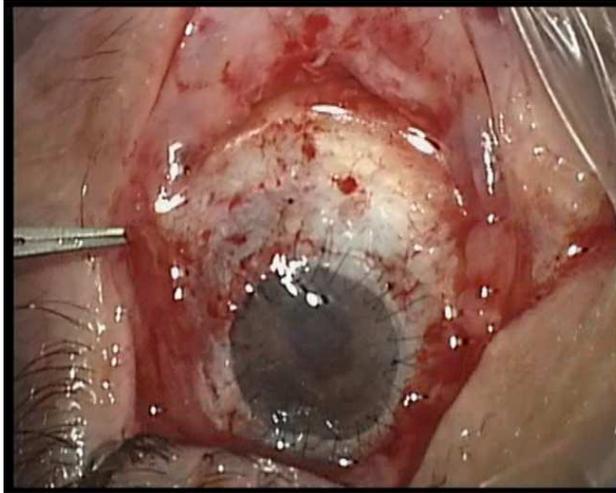


Fig. 4. Corneal graft after perforating keratoplasty lens wearing

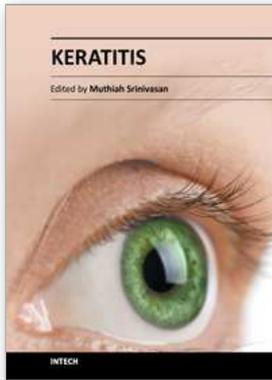
3. Conclusion

Trichophyton spp. is a rare cause of fungal keratitis which can be associated with progressive keratolysis and corneal perforation. Severe disease of the anterior eye segment can extend to the posterior pole with endophthalmitis and consequentially can often end with the loss of vision or even the entire eye. Treatment can be medicamentous or surgical. There are several guidelines for the antifungal medicamentous treatment, but efficacy of currently available antifungal agents is limited and there is a relatively high medical treatment failure rate. Daily „debridment“ with a spatula or blade can be performed due to removal of necrotic tissue which unables healing of the corneal ulcer, although it is not recommended if it is not necessary. Excimer laser **Phototherapeutic Keratectomy** (PTK) can be used for treating superficial infections. The most common surgical procedure is therapeutic penetrating keratoplasty. Keratoplasty is a method of choice when medical treatment fails or in the case of recurrent infection. It is wise to perform keratoplasty before infectious processes progress into the anterior chamber or before limbus or sclera are involved. The size of trephination should be planned to leave at least a 1 to 1.5 mm clear zone of clinically uninvolved cornea. Interrupted sutures should be used. Every affected intraocular structure (lens, iris, vitreous) should be excised and irrigation performed. If endophthalmitis is suspected antifungal agents should be injected intraocularly. After perforating keratoplasty topical antifungal agents should be continued in combination with systemic antifungal therapy. Prompt diagnosis and treatment of fungal infection (in our case *Trichophyton* keratitis) is crucial for preservation of an eye for a good visual outcome.

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The 4 chapters in this book focus on investigation, basic and advanced clinical aspects and management of frequently encountered corneal disorders. The authors have covered keratitis theory and practice. Onchocerciasis, even though found on one continent, has its impact on population, epidemiologists, ophthalmologists, NGOs, public health planners and care providers. The goal of this book is to provide information on ancient eye diseases; their investigation and management to prevent corneal blindness. I acknowledge the great help rendered by Publishing Process Manager and Editor Relations Consultant.

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University Campus STeP Ri
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Unit 405, Office Block, Hotel Equatorial Shanghai
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Phone: +86-21-62489820
Fax: +86-21-62489821

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