The clinical characteristics, diagnostic methods, and treatment of 33 patients with keratomycosis are reported. In 17 patients, there was a history of injury with vegetable matter, and in 8, the control injury had been treated with steroids and antibiotics. Of the 17 treated medically, five required subsequent surgical treatment. The 22 treated surgically underwent one or more of the following procedures: keratectomy, conjunctival flap, and penetrating keratoplasty.

The frequency and distribution of corneal mycotic infections has increased since the development and use of topically applied steroids. Although certain climates favor fungal development, any corneal injury contaminated with soil or vegetable matter is a potential site for mycotic infection. Fungal infections may also occur following steroid or steroid-antibiotic therapy for intraocular surgery, chronic ocular inflammation, trauma with nonvegetable matter, or foreign body removal. For example, only three of 16 cases reported by Haggerty and Zimmerman had a history of corneal injury with vegetable matter.

Because of favorable climate for fungal development, and a large agricultural population, corneal mycoses are frequent in Florida. This situation has enabled us to study keratomycosis in several stages of development and evaluate its medical and surgical treatment.

Review of Cases and Results

This study comprises 33 cases of corneal infections due to several types of fungi, with all but one being identified and treated at the University of Florida from January 1969 to July 1970 (Table 1 and 2). Except in one case, all were adults, 25 were men and eight women. Four patients, with no history of trauma, had previous corneal disease. In 17 cases, the initial trauma was caused by injury with vegetable matter. In another 14 cases, there was a history of trauma with a variety of foreign bodies (metal, sand, stone, etc). In one case, a fingernail scratch precipitated an ulcer. In eight patients, the early lesion was erroneously diagnosed as either bacterial or herpetic and treated with antibiotics or idoxuridine and steroids.

Clinical Diagnosis.—During the first 24 hours after an injury, only the history of the initial trauma may suggest possible fungal infection; however, once the lesion has started to grow, several clinical findings help in diagnosis. These have been previously described by Wood and one of us (H.E.K.), the most useful being the appearance of an ulcer with raised borders, radiating lines of infiltrate from the margin and satellite lesions.

Laboratory Diagnosis.—Scrapings from the ulcer were smeared on several glass slides. At least two were stained with the Gridley stain (a modified PAS stain, specific for fungus), one was used for a potassium hydroxide wet preparation, one for gram stain and one for Giemsa stain. Cultures were made on blood agar plates and special Sabouraud's media without inhibitors (ordinary Sabouraud's media, in most hospital laboratories, contains inhibitors which prevent the growth of the common ocular pathogens). When negative slides were obtained from typical lesions with hypopyon, a diagnostic anterior chamber tap with aqueous aspiration for smears and cultures was done. If these two procedures were negative, a biopsy of the edge of the lesion for frozen sections was made (Fig 1).
Identification of the fungus was considered correct only after growth occurred in culture media. Except in one patient, fungus was identified from all infections and classified as follows: *Fusarium*, 15 cases; *Cephalosporum*, 11 cases; *Aspergillus*, two cases; *Candida*, two cases; *Tetraploa*, one case; and *Curvularia*, one case.

**Treatment.**—Initially all lesions were scraped and curetted to eliminate most of the necrotic tissue. The importance of this procedure has been previously reported by Fine and Anderson and Chick. In some of our cases, the curettage produced a clear cornea in the site previously occupied by the whitish, necrotic lesion. In such cases where the curettage could not remove the necrotic tissue, a superficial keratectomy was performed and the eye treated medically thereafter. Classification of cases by initial and subsequent therapy is as follows:

**Medical.**—Of 17 cases treated, five required subsequent surgery.

**Surgical.**—Seventeen cases were treated originally, an additional five treated after medical therapy. In two cases, the antifungal treatment apparently improved the degree of infection and ocular inflammation prior to surgery (cases 2 and 4).

In medical therapy, the following antifungal drugs were used topically: nystatin (50,000 units), 0.5% amphotericin B suspension, 1% potassium iodide, and 5% pimaricin alone or combined with 1% potassium iodide.

Initially, the selected antifungal was used every one or two hours, with frequency decreased as the infection improved. In most cases, the treatment was continued for four to six weeks (color Fig 1).

Classification of cases by drug used is as follows: (a) pimaricin with potassium iodide, six cases; (b) pimaricin alone, five cases; (c) amphotericin B and potassium iodide, three cases; and (d) nystatin and amphotericin B, one case. Table 1 summarizes all medically treated cases, some of which were reported previously by Newmark et al.

Nystatin has an effect only against Candida (a rare pathogen among our cases). It is not effective in most keratomycotic infections, and probably penetrates the cornea very poorly. Amphotericin B is very irritat-
keratoplasty was performed in small, deep corneal ulcers (less than 5 mm), or in large infections, which could be safely enclosed in a 7 to 8 mm graft. It was the treatment of choice in cases having slight anterior chamber reaction and rapidly growing ulcers (color Fig 4 and 5).

In one case (small graft), a superior peripheral iridectomy was done through a limbal incision. In other cases (larger grafts), two or more iridectomies or iridotomies were done through the trephined cornea. Postoperatively, patients received acetazolamide or glycerol orally as needed. In three cases, the lens was removed intraocularly at the time of surgery. In one patient, an extracapsular extraction was performed without postoperative reinfection (case 19).

Optical keratoplasty was generally performed 10 to

<table>
<thead>
<tr>
<th>Patient No.</th>
<th>Fungus</th>
<th>History of Trauma</th>
<th>Ulcer Localization</th>
<th>Treatment†</th>
<th>Result</th>
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<tr>
<td>2</td>
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<td>+</td>
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</table>

* Seventeen patients received antifungal medication. The first six patients required additional treatment in the form of penetrating graft or conjunctival flap. Case 22 showed fungus in smears, but cultures were negative.

† Drugs used were the following: pimaricin, 5%; amphotericin B, 0.3%; and nystatin, 50,000 units.

** Table includes six patients who were previously treated with antifungals.
†† Where not specified; grafts were penetrating.
‡‡ LP indicates light perception.

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Fig 1.—Three types of Fusarium keratomycoses before and after four to six weeks of treatment with pimaricin.
Fig 2.—Deep corneal ulcer due to Cephalosporium.

Fig 3.—Same eye one month after a conjunctival flap.

Fig 4.—Cephalosporium keratomycosis during treatment with pimaricin.

Fig 5.—Seven months after penetrating keratoplasty.

Fig 6.—Conjunctival flap for large Fusarium ulcer.

Fig 7.—Same eye after removal of flap and one year after penetrating keratoplasty.
12 months after conjunctival flap or several months after the ulcer healed. The conjunctival flap was dissected from the cornea at the time of surgery, or a peritomy was done some days prior to keratoplasty to blanche the cornea and reveal the extent of corneal scarring (color Fig 6 and 7).

Superficial keratectomies in conjunction with thin conjunctival flaps were performed in six patients, and in one case, it was performed after removing the flap. Three underwent penetrating keratoplasty at a later date. In all, 16 patients had penetrating keratoplasties varying in size from 6.5 to 8.0 mm, and 8 obtained vision of 20/60 or better.

We feel that lamellar keratoplasty is contraindicated in cases where there is a suspicion of active fungal infection because most fungus tends to grow rapidly in the graft interface. Three cases in our series (cases 5, 14, and 15) demonstrate the poor results obtained with this treatment. Conjunctival flaps seem the best treatment in lesions too large to be grafted, ulcers resistant to, or too large for medical treatment and residual infection after keratectomy.

Comment

A review of our clinical histories indicates a tendency to misdiagnose early fungal infections as bacterial or herpetic, probably because there is a minimal epithelial lesion with little infiltration or discharge at the first visit. Several patients who had no evidence of herpes were treated almost from the beginning with idoxuridine and then with steroids when an obvious stromal keratitis appeared; four to ten days later, the full-blown picture of a mycotic keratitis appeared. To avoid this situation, it is recommended that any corneal injury with vegetable matter or any dirt-contaminated object should be observed for a period of 24 hours (after scraping if necessary), avoiding the use of antibiotics or steroids. Once the fungal etiology of the ulcer has been established, medical or surgical treatment can be selected.

Most referred patients, however, had their conditions diagnosed correctly on clinical grounds from the start. In these cases, the history, as well as the examination, was important in making a presumptive diagnosis of corneal mycosis which was confirmed by laboratory studies.

Ulcers which are not too extensive (5 to 6 mm), not involving more than the superficial third of the cornea, or near the limbus, seem to do well with medical treatment. Larger or deeper lesions may require combined medical-surgical treatment. In our experience, lesions too large for good medical control were improved to some extent with antifungal therapy for a few days so that corneal graff-
ing could be done in a less inflamed eye. However, in three instances, eyes that were apparently responding to antifungal treatment with pimaricin or amphotericin B therapy suddenly developed more inflammation, hypopyon and corneal clouding in previously clear zones, even though histological findings of corneal tissue after keratoplasty showed no fungus present. The cause of this inflammatory reaction is unknown but may be due to the liberation of antigens as the fungus dies (the polynye antibiotic cause rupture of the fungal wall membrane). Identification of the causative fungus is important because it will help to choose the most adequate medical or surgical treatment. For example, Candida infections tend to remain localized, whereas Fusarium ulcers grow rapidly and cause stromal lysis.

Opacification of the graft resulted in light perception in ten cases, demonstrating that the prognosis for good visual results is unsatisfactory in eyes with active ocular inflammation. A similar observation has been made by Sanders in a series of penetrating keratoplasties in active fungal keratitis.

Except in two very advanced infections, all eyes receiving surgical therapy were saved, even though in several cases there was evidence of fungus remaining in the cornea or in the anterior chamber. Seven of the ten eyes with light perception had glaucoma after flaps or keratoplasty. Attempts to control the glaucoma may eventually prove successful in some eyes so that a keratoplasty can be attempted. Good visual results were obtained in eyes grafted when the acute inflammation had been reduced to some extent by the topical use of antifungals, curettage, or conjunctival flap. These treatments are therefore recommended prior to penetrating keratoplasty.

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Key Words.—Fungal infection; keratomycosis; mycokeratitis; corneal ulcer; conjunctival flap; keratoplasty.

Nonproprietary and Trade Names of Drugs


References


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