

Acanthamoeba Keratitis

An Important Consideration When Evaluating Ocular Complaints in Contact Lens Wearers

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Over 23 million Americans wear contact lenses, and the percentage of those who use soft or extended-wear contact lenses has gradually increased from the time of their introduction nearly a decade ago. Since that time evidence has mounted that the use of these lenses increases the risk of microbial corneal infection.¹⁻⁵ This heightened risk may be the result of increased bacterial adherence to soft lenses as compared with hard lenses.⁶

Additional risk factors include patient compliance problems, the common practice of using unpreserved saline solutions, and the increased degree of difficulty in sterilizing soft lenses.^{2,4,5,7,8} The most common organisms cultured in contact lens-related corneal ulcers, from most to least common, are *Pseudomonas aeruginosa*, *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Streptococcus pneumoniae*, β -hemolytic streptococcus, and *Serratia marcescens*.⁹

A relatively rare but potentially devastating cause of keratitis is the amoeba. The *Acanthamoeba* is a genus found in virtually all fresh water and has been isolated in brackish and sea water as well.⁹ It exists in nature as a uninucleated, mobile trophozoite or, during unfavorable conditions for the organism, may change to a double-walled cyst that is highly resistant to environmental insult. The amoeba in the trophozoite form may enter the body through contact with ground water; in the cyst form, it may exist in chlorinated pools or hot tubs or may be inhaled in dry environments.¹⁰

The first reports in the ophthalmic literature concerning the parasite were as a cause of chronic keratitis after minor

corneal trauma.¹¹⁻¹³ More recently the organism has been shown to be a cause of acute and chronic stromal keratitis in people who wear contact lenses, particularly soft lenses.^{14,15} Those who would appear to be at greatest risk wear soft lenses and have a history of minor corneal trauma and poor lens-cleaning habits.¹⁶ The use of home-made saline solution for storage and cleaning has recently been linked to *Acanthamoeba* infections.¹⁷

CASE REPORT

An 18-year-old man with a four-year history of soft contact lens use was referred to the Ophthalmology Clinic at the University of Utah Health Sciences Center with a two-year history of mild, intermittent eye discomfort. Increasing pain in the left eye prompted this referral by his general ophthalmologist. For the first two years of soft contact use, lens care followed a regular, manufacturer-recommended regimen, and the patient reported no significant problems. For the last two years, however, he had prepared his own lens solution from salt tablets and distilled water. During that time the patient reported that his eyes were often sore and inflamed. He also related frequent exposure to dust and grit while tilling the soil on the family farm as being responsible for some minor ocular abrasions.

His initial visit on October 15, 1986, revealed an uncorrected visual acuity of 20/200 in the right eye, and finger counting at three feet in the left eye. He was very light sensitive and in moderate distress, making further visual testing difficult. The right eye showed mild conjunctival injection and was otherwise unremarkable. The left eye showed inflammation around the corneal nerves, with a diffuse area of central edema and dendritiform pattern of irregular epithelium that was otherwise intact. Corneal sensation was decreased in this eye with trace cell and flare. No subepithelial infiltrate was seen. The picture

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References: 1. Newton RE, et al. A review of the side effect profile of buspirone. *Am J Med* 1986; 80(3B):17-21. 2. Moskowitz H and Smiley A: Effects of chronically administered buspirone and diazepam on driving-related skills performance. *J Clin Psychiatry* 1982; 43(12, Sec 2):45-55. 3. Lader M: Assessing the potential for buspirone dependence or abuse and effects of its withdrawal. *Am J Med* 1987; 82(5A):20-26.

Contraindications: Hypersensitivity to buspirone.

Warnings: The administration of BuSpar to a patient taking a monoamine oxidase inhibitor (MAOI) may pose a hazard. Since blood pressure has become elevated when BuSpar was administered concomitantly with an MAOI, such concomitant use is not recommended. BuSpar should not be employed in lieu of appropriate antipsychotic treatment.

Precautions: General—Interference with cognitive and motor performance: Although buspirone is less sedating than other anxiolytics and does not produce significant functional impairment, its CNS effects in a given patient may not be predictable; therefore, patients should be cautioned about operating an automobile or using complex machinery until they are reasonably certain that buspirone does not affect them adversely. Although buspirone has not been shown to increase alcohol-induced impairment in motor and mental performance, it is prudent to avoid concomitant use with alcohol.

Potential for withdrawal reactions in sedative/hypnotic/anticholinergic drug dependent patients: Because buspirone will not block the withdrawal syndrome often seen with cessation of therapy with benzodiazepines and other common sedative/hypnotic drugs, before starting buspirone withdraw patients gradually from their prior treatment, especially those who used a CNS depressant chronically. Rebound or withdrawal symptoms may occur over varying time periods, depending in part on the type of drug and its elimination half-life. The withdrawal syndrome can appear as any combination of irritability, anxiety, agitation, insomnia, tremor, abdominal cramps, muscle cramps, vomiting, sweating, flu-like symptoms without fever, and occasionally, even as seizures.

Possible concerns related to buspirone's binding to dopamine receptors: Because buspirone can bind to central dopamine receptors, a question has been raised about its potential to cause acute and chronic changes in dopamine mediated neurological function (e.g., dystonia, pseudoparkinsonism, akathisia, and tardive dyskinesia). Clinical experience in controlled trials has failed to identify any significant neuroleptic-like activity; however, a syndrome of restlessness, appearing shortly after initiation of treatment, has been reported; the syndrome may be due to increased central noradrenergic activity or may be attributable to dopaminergic effects (ie, represent akathisia).

Information for Patients—Patients should be instructed to inform their physician about any medications, prescription or non-prescription, alcohol or drugs they are now taking or plan to take during treatment with buspirone; to inform their physician if they are pregnant, are planning to become pregnant, or become pregnant while taking buspirone; to inform their physician if they are breast feeding; and not to drive a car or operate potentially dangerous machinery until they experience how this medication affects them.

Drug Interactions—Concomitant use with other CNS active drugs should be approached with caution (see **Warnings**). Concomitant use with trazodone may have caused 3- to 6-fold elevations on SGPT (ALT) in a few patients. Buspirone does not displace tightly bound drugs like phenytoin, propranolol, and warfarin from serum proteins, but may displace less firmly bound drugs like digoxin.

Carcinogenesis, Mutagenesis, Impairment of Fertility—No evidence of carcinogenic potential was observed in rats or mice; buspirone did not induce point mutations, nor was DNA damage observed; chromosomal aberrations or abnormalities did not occur.

Pregnancy: Teratogenic Effects—Pregnancy Category B: Should be used during pregnancy only if clearly needed.

Nursing Mothers—Administration to nursing women should be avoided if clinically possible.

Pediatric Use—The safety and effectiveness have not been determined in individuals below 18 years of age. **Use in the Elderly—**No unusual, adverse, age-related phenomena have been identified in elderly patients receiving a total, modal daily dose of 15 mg.

Use in Patients with Impaired Hepatic or Renal Function—Since buspirone is metabolized by the liver and excreted by the kidneys, it is not recommended in severe hepatic or renal impairment.

Adverse Reactions (See also Precautions): Commonly Observed—The more commonly observed untoward events include dizziness, nausea, headache, nervousness, lightheadedness, and excitement.

Associated with Discontinuation of Treatment—The more common events causing discontinuation included: central nervous system disturbances (3.4%), primarily dizziness, insomnia, nervousness, drowsiness, lightheaded feeling; gastrointestinal disturbances (1.2%), primarily nausea; miscellaneous disturbances (1.1%), primarily headache and fatigue. In addition, 3.4% of patients had multiple complaints, none of which could be characterized as primary.

Incidence in Controlled Clinical Trials—Adverse events reported by 1% or more of 477 patients who received buspirone in four-week, controlled trials: **Cardiovascular:** tachycardia/palpitations 1%, CNS: Dizziness 12%, drowsiness 10%, nervousness 5%, insomnia 3%, lightheadedness 3%, decreased concentration 2%, excitement 2%, anger/hostility 2%, confusion 2%, depression 2%. **EENT:** Blurred vision 2%. **Gastrointestinal:** Nausea 8%, dry mouth 3%, abdominal/gastric distress 2%, diarrhea 2%, constipation 1%, vomiting 1%. **Musculoskeletal:** muscle aches/pains 1%. **Neurological:** Numbness 2%, paresthesia 1%, incoordination 1%, tremor 1%. **Skin:** Skin rash 1%. **Miscellaneous:** Headache 6%, fatigue 4%, weakness 2%, sweating/clamminess 1%.

Other Events Observed During the Entire Pre-marketing Evaluation—The relative frequency of all other undesirable events reasonably associated with the use of buspirone in approximately 3000 subjects who took multiple doses of the drug under well-controlled, open, and uncontrolled conditions is defined as follows: Frequent are those occurring in at least 1/100 patients; infrequent are those occurring in 1/100 to 1/1000 patients; and rare are those occurring in less than 1/1000 patients. **Cardiovascular—**frequent: non-specific chest pain; infrequent: syncope, hypotension, hypertension; rare: cerebrovascular accident, congestive heart failure, myocardial infarction, cardiomyopathy, bradycardia. **Central Nervous System—**frequent: dream disturbances; infrequent: depersonalization, dysphoria, noise intolerance, euphoria, akathisia, fearfulness, loss of interest, disassociative reaction, hallucinations, suicidal ideation, seizures; rare: feelings of claustrophobia, cold intolerance, stupor, slurred speech, psychosis. **EENT—**frequent: tinnitus, sore throat, nasal congestion; infrequent: redness and itching of the eyes, altered taste, altered smell, conjunctivitis; rare: inner ear abnormality, eye pain, photophobia, pressure on eyes. **Endocrine—**rare: galactorrhea, thyroid abnormality. **Gastrointestinal—**infrequent: flatulence, anorexia, increased appetite, salivation, irritable colon, rectal bleeding; rare: burning of the tongue. **Genitourinary—**infrequent: urinary frequency, urinary hesitancy, menstrual irregularity and spotting, dysuria; rare: amenorrhea, pelvic inflammatory disease, enuresis, nocturia. **Musculoskeletal—**infrequent: muscle cramps, muscle spasms, rigid/stiff muscles, arthralgias. **Neurological—**infrequent: involuntary movements, slowed reaction time; rare: muscle weakness. **Respiratory—**infrequent: hyperventilation, shortness of breath, chest congestion; rare: epistaxis. **Sexual Function—**infrequent: decreased or increased libido; rare: delayed ejaculation, impotence. **Skin—**infrequent: edema, pruritus, flushing, easy bruising, hair loss, dry skin, facial edema, blisters; rare: acne, thinning of nails. **Clinical Laboratory—**infrequent: increases in hepatic aminotransferases (SGOT, SGPT); rare: eosinophilia, leukopenia, thrombocytopenia. **Miscellaneous—**infrequent: weight gain, fever, roaring sensation in the head, weight loss, malaise; rare: alcohol abuse, bleeding disturbance, loss of voice, hiccoughs.

Drug Abuse and Dependence: Controlled Substance Class—Not a controlled substance.

Physical and Psychological Dependence—Buspirone has shown no potential for abuse or diversion and there is no evidence that it causes tolerance, or either physical or psychological dependence. However, since it is difficult to predict from experiments the extent to which a CNS active drug will be misused, diverted, and/or abused once marketed, physicians should carefully evaluate patients for a history of drug abuse and follow such patients closely, observing them for signs of buspirone misuse or abuse (e.g., development of tolerance, incrementation of dose, drug-seeking behavior).

Overdosage: Signs and Symptoms—At doses approaching 375 mg/day the following symptoms were observed: nausea, vomiting, dizziness, drowsiness, miosis, and gastric distress. No deaths have been reported in humans either with deliberate or accidental overdosage.

Recommended Overdose Treatment—General symptomatic and supportive measures should be used along with immediate gastric lavage. No specific antidote is known and dialyzability of buspirone has not been determined.

For complete details, see Prescribing Information or consult your Mead Johnson Pharmaceuticals Representative.

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of corneal neuritis and dendritiform epithelial pattern was consistent with herpes simplex virus keratitis. The antiviral trifluridine five times per day, originally prescribed by his family ophthalmologist, was continued in the left eye, as the patient reported symptomatic improvement since beginning the treatment five days earlier. For control of anterior segment inflammation, 0.25 percent fluorometholone four times per day and homatropine two times per day were also prescribed. Culturing for herpes simplex virus did not appear indicated, since treatment with trifluridine was already started, and the clinical picture was atypical for Acanthamoeba. He was released to his general ophthalmologist for follow-up care.

The patient was seen again on November 14, 1986, because he had noted no significant improvement in vision or pain. There was conjunctival injection (2+) in the left eye, and he was severely photophobic. The epithelium remained intact with superficial stromal scarring, active white cell infiltrate, and peripheral corneal opacities. Complete corneal cultures were taken for amoeba, fungus, virus, and bacteria. In addition, corneal scrapings for cytologic examination were done, which resulted in a corneal epithelial defect. Trifluridine and fluorometholone were discontinued, and neomycin-polymyxin B-dexamethasone four times per day was started for bacterial coverage until the epithelial defect healed and because neomycin is an effective anti-amoebic agent.

Three days later the cultures were reported positive for Acanthamoeba castellanii. Treatment with neomycin-polymyxin B-dexamethasone was continued, and topical propamidate therapy four times per day, oral ketoconazole 200 mg four times per day, 1 percent prednisolone acetate four times per day, homatropine four times per day, and 5 percent sodium chloride ointment two times per day were added to the protocol. All other cultures remained negative.

On December 12, 1986, the patient was still photophobic, with only mild conjunctival injection in the left eye. The epithelium of the left cornea appeared intact, with central punctate staining indicating probable epithelial erosions overlying the defect. There was a 20-percent corneal stromal loss in the area of his nasal immune ring, decreased infiltrate around the nerves, and signs of improvement.

On January 13, 1987, the patient presented with severe pain and photophobia of the left eye. Uncorrected visual acuity on the left was finger counting at two feet. Ocular examination revealed a ring of corneal infiltrate and two areas of epithelial defect with 50 percent thinning. New Acanthamoeba cultures were sent to rule out active infection. The cultures were negative at 72 hours, and penetrating keratoplasty was performed three days later because of impending corneal perforation. Histopathology of the excised corneal button showed stromal degeneration as well as cysts typical of Acanthamoeba.

DISCUSSION

Routine laboratory procedures used to evaluate most patients with microbial keratitis may not reveal the typical *Acanthamoeba* trophozoite or cyst. To further complicate the clinical and laboratory picture, the *Acanthamoeba* can flourish in a substrate of gram-negative bacilli¹⁶ and be overlooked in a culture positive for *Pseudomonas*.

It is important to note that calcofluor white, a chemofluorescent dye with an affinity for the polysaccharide polymers of the amoebic cyst, is now being used. The calcofluor white method is currently the most sensitive test available for the diagnosis of amoebic keratitis, making an accurate, early diagnosis more likely. Most laboratories are not equipped to perform this test, however, which should be done under the direction of an ophthalmologist.

Using data from 74 cases of acanthamoebic keratitis, a mean interval of 22 weeks and a range of two to 68 weeks from onset of symptoms to diagnosis have been reported recently.¹⁶ The rarity of the disease, coupled with the difficulty in differentiating it from more common ocular problems, likely leads to delays in diagnosis. The most common misdiagnosis illustrated by this case is herpes simplex keratitis. As with most diseases, the more quickly acanthamoebic keratitis can be diagnosed and an appropriate treatment regimen started, the more favorable is the prognosis.

Corneal transplantation to prevent or treat perforations and to restore vision is required in over 90 percent of these cases. Medical cures at this time are rare. A high index of suspicion coupled with early ophthalmic referral is essential if corneal transplant is to be avoided.

Family physicians should be alert to the possibility of acanthamoebic infection in their workups on patients with seemingly common eye complaints, particularly those who wear soft contact lenses and those with a history of minor ocular trauma. The practice of making one's own saline and the use of intravenous saline solutions have become popular both because of lower cost and because many patients become allergic or sensitive to the preservative in some of the commercially prepared contact lens saline solutions. Since risk factor is significant, patient education for all those who wear soft contacts should reinforce the need for contact lens care and cleaning and discourage the use of homemade cleaning solutions.¹⁷ General advice and instructions to patients who wear contact lenses should include the following:

1. Do not use anything but commercially prepared preserved saline solution in the storage and cleansing of any contact lenses, unless your physician feels you have an allergy to the preservative. (Nonpreserved saline solutions, whether homemade or commercially obtained, must be refrigerated and discarded after one week. Nonpreserved saline solution in aerosol containers is considered sterile.)

2. Do not place lenses in your mouth for any reason.
3. Do not wear contact lenses while swimming or in hot tubs or saunas.
4. Do not handle contact lenses without first washing your hands.
5. Heat disinfection is the only reliable method of killing both forms of the amoeba; therefore, do not use nonpreserved saline (this includes salt tablets) with any contact lens that is not regularly heat disinfected.
6. Extended wear lenses cannot be heat disinfected, which puts the wearer at greater risk; therefore, do not use nonpreserved saline with extended wear polymers.
7. Of the soft lenses available, a daily wear soft lens used on a daily wear basis coupled with proper lens hygiene is safer than the extended wear lens.

References

1. Rosner M, Treister G, Blumenthal M: Corneal abscesses in silicone and soft contact wearers. *Ann Ophthalmol* 1983; 15:949-952
2. Wilson LA, Schlitzer RL, Ahearn DG: *Pseudomonas* corneal ulcers associated with soft contact lens wear. *Am J Ophthalmol* 1981; 92:546-554
3. Liesgang TJ, Forster RK: Spectrum of microbial keratitis in South Florida. *Am J Ophthalmol* 1980; 90:38-47
4. Krachmer JH, Purcell J Jr: Bacterial corneal ulcers in cosmetic soft contact wearers. *Arch Ophthalmol* 1978; 96:57-61
5. Cooper RL, Constable IJ: Infective keratitis in soft contact lens wearers. *Br J Ophthalmol* 1977; 61:250-254
6. Liotet S, Guillaumin D, Cochet P, et al: The genesis of organic deposits on soft contact lenses. *CLAO J* 1983; 9:49-56
7. Pitts RE, Krachmer JH: Evaluation of soft contact lens disinfection in the home environment. *Arch Ophthalmol* 1979; 97:470-472
8. Morgan JF: Complications associated with contact lens solutions. *Ophthalmology* 1979; 86:1107-1119
9. Ormerod LD, Smith RE: Contact lens-associated microbial keratitis. *Arch Ophthalmol* 1986; 104:79-83
10. Visvesvara GS: Free-living pathogenic amoebae. In Lennette EH (ed): *Manual of Clinical Microbiology*, ed 3. Washington DC, American Society of Microbiology, 1980, pp 704-708
11. Jones DB, Visvesvara GS, Robinson HM: *Acanthamoeba* polyphaga keratitis and *Acanthamoeba* uveitis associated with fatal meningoencephalitis. *Trans Ophthalmol Soc UK* 1975; 95:221-232
12. Lund OE, Stephani FH, Decant LO: Amoebic keratitis: A clinicopathologic case report. *Br J Ophthalmol* 1978; 62:373-375
13. Key SN III, Green WR, Willaert E, et al: Keratitis due to *Acanthamoeba castellanii*: A clinicopathologic case report. *Arch Ophthalmol* 1980; 98:475-479
14. Cohen EJ, Buchanan HW, Laughrea PA, et al: *Acanthamoeba* keratitis associated with soft contact lenses. *Am J Ophthalmol* 1985; 100:389-395
15. Moore MB, McCulley JP, Luckenbach M, et al: *Acanthamoeba* keratitis associated with soft contact lenses. *Am J Ophthalmol* 1985; 100:396-403
16. Jones DB: *Acanthamoeba*—The ultimate opportunist? *Am J Ophthalmol* 1986; 103:527-530
17. Public Health Note: Homemade Saline Solutions and *Acanthamoeba* Keratitis, publication No. 12084. San Francisco, American Academy of Ophthalmology, September 1, 1987