npj | microgravity

Article

Published in cooperation with the Biodesign Institute at Arizona State University, with the support of NASA

https://doi.org/10.1038/s41526-025-00462-3

Management of corneal injuries in spaceflight and recommendations for planetary missions

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In February 1968, NASA purchased 400 antigravity ballpoint pens from the Fisher Pen Company for the Apollo Program to prevent potential harm to astronauts and equipment. Mechanical pencils previously used in microgravity posed risks like eye injuries from floating fragments penetrating the cornea. The cornea is vulnerable to abrasions, perforations, and chemical burns in such environments, affecting crewmembers aboard the International Space Station (ISS). While they undergo extensive training for emergency situations, there are inherent complexities when faced with eye injuries. In this challenging context, adapting available medications and leveraging emergency medical training is critical for addressing ocular injuries in a high-stakes environment. This paper explores ISS medications and management strategies for corneal injuries, highlighting the need to include effective medications and countermeasures in future ISS medical kits.

In February 1968, NASA purchased 400 antigravity ballpoint pens for the Apollo Program from the Fisher Pen Company with a primary goal in mind: to reduce potential harm to astronauts and equipment[1]. Previously used mechanical pencils in a microgravity environment could pose a threat to the human eye if small floating fragments were to penetrate the cornea. The cornea is a highly innervated transparent curved layer of tissue that plays a critical role in focusing light onto the retina. The tissue is particularly susceptible to damage due to its exposed location in the front of the eye and lack of blood vessels for nourishment and repair[2]. Therefore, the pressurized ink cartridge of the AG7 Space Pen thus contributed to a safer environment for astronauts aboard the International Space Station (ISS).

The cornea is subject to damage from abrasions, perforations, and chemical burns. On Earth, approximately 3% of emergency department visits are due to ocular trauma, with 80% involving corneal abrasions or foreign bodies[3]. Moreover, 11.5–22.1% of all ocular injuries presented to the emergency department are due to ocular chemical burns[4]. Medications and interventions must be deployed to reduce injury and infection after inciting events as well as increase speed of recovery[5]. For example, in the setting of a mild corneal abrasion, prophylactic antibiotics may be administered to prevent bacterial superinfection[6]. However, in the context of spaceflight, ocular health concerns become exponentially more sensitive. The unique environment of space poses risks beyond what may be expected in a terrestrial setting, thus warranting additional safety precautions and medical preparations[7]. Moreover, seeking professional healthcare following ocular injuries becomes exceptionally challenging, especially when return to Earth in a timely manner is not feasible.

Aside from such special protocols for ocular injury, supplies are severely limited on the ISS[8,9]. First and foremost, the cost of launching supplies to low Earth orbit is exorbitantly high at around $5000 to $25,000 per kilogram[10]. Limited supply space on the ISS further compounds the issue, necessitating efficient and effective utilization of available cargo space. Many medications require specific conditions of storage (e.g., controlled temperatures, humidity), which can be challenging to maintain in the strict space station environment[11]. Extended missions or delays in resupply missions can also potentially lead to expired or ineffective medications. Consequently, a meticulous selection and management of medications and supplies is necessary to ensure the vital support and well-being of ISS astronauts[12].

Some materials in the medical kit checklist may also not have the primary function as an "eye" medication. Cyanoacrylate glue, for example, may have a dual purpose for the management of corneal perforations[13]. In this paper, we aim to explore the relevant eye medications aboard the ISS

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and routes of management for treatment of corneal injuries. Moreover, this paper may bring to light medications and countermeasures that may be beneficial for corneal injuries and should be included in future medical kits onboard the ISS (Table 1)[14].

Results and discussion

Classification, staging, and terrestrial management of corneal injuries

Corneal injuries encompass a diverse spectrum of conditions, necessitating unique approaches for classification, staging, and terrestrial management. This section will expound upon three distinct categories of corneal injuries: corneal abrasions, corneal perforations, and chemical corneal burns. Understanding the management of corneal injuries in a terrestrial setting not only enhances the ability to address ocular health challenges on Earth but also paves the way for potentially paralleling and adapting treatment options to injuries that astronauts may sustain during spaceflight.

Corneal abrasion

Corneal abrasion pertains to the disruption of the corneal epithelium. Injury often results from foreign body entry or traumatic contact (e.g., scratches or minor impact). 2% of primary care visits pertain to eye complaints, 8% of which are due to foreign bodies[15]. Of all the ocular symptoms obtained from the Lifetime Surveillance of Astronaut Health (LSAH), eye abrasions secondary to a foreign body were by far the most accounted-for events[16]. During the Space Shuttle Program and ISS through Expedition 13 in 2006, eye abrasions secondary to a foreign body were 70 of 104 (67.3%) documented ophthalmic medical conditions and symptoms. Eye debris was accounted for in 4 (3.8%) additional events[16].

Pain, foreign body sensation, tearing, photophobia, and blurred vision may result from corneal abrasion. To examine the eye, an eye care professional may apply topical anesthetics and then use fluorescein staining, which will illuminate the corneal abrasion under blue light[17]. Permanent scarring and vision loss may result from a lack of intervention of a corneal foreign body. Irrigation with saline is often successful, but more persistent foreign bodies may be removed with a topical anesthetic (e.g., ophthalmic proparacaine hydrochloride 0.5% or tetracaine hydrochloride 0.5%) and gentle sweeping over the cornea with a cotton swab. If unsuccessful, a trained professional should steady their hand on the patient's zygomatic arch and utilize an eye spud or 25-gauge needle to remove the foreign body. It is important to note that while topical anesthetics can be utilized to facilitate ocular examinations, they are not routinely prescribed on Earth due to the potential risk of corneal damage. In an extraterrestrial setting, however, temporary use of topical anesthetics may be justified for immediate pain management, especially in scenarios where other forms of care are limited or unavailable. These anesthetics can provide crucial relief prior to the escalation of medical interventions or during the interim period before evacuation back to Earth if evacuation is feasible. Despite their short-term benefits, the prolonged use of topical anesthetics is strongly discouraged due to the significant risk of exacerbating ocular injuries over the long term. Continuous application can impair corneal healing, increase susceptibility

Table 1 | Relevant eye medications and tools on the ISS[14]

Medication/diagnostic tool	Application	Corneal injury
Tetracaine (0.5%, 15 mL)	Eye (topical)	Ulcer, abrasion, perforation, chemical burn
Erythromycin ointment (0.5%, 3.5 g)	Eye (topical)	Ulcer, abrasion, perforation, chemical burn
Moxifloxacin (Vigamox) 0.5% 3 mL	Eye (topical)	Ulcer, abrasion, perforation, chemical burn
Tobramycin and dexamethasone (Tobradex) 0.3%; 0.1%, 10 mL	Eye (topical)	Ulcer, abrasion, perforation, chemical burn
Cyclopentolate (Cyclogyl) 1%, 15 mL	Eye (topical)	Ulcer, abrasion, perforation, chemical burn
Fluorescein strip 1 mg	Eye (topical)	Abrasion, perforation, herpes keratitis
Tropicamide (Mydriacyl) 1%, 15 mL	Eye (topical)	Ulcer, abrasion, perforation, chemical burn
Olopatadine (Pataday) 0.2%, 2.5 mL	Eye (topical)	Abrasion, irritants
Carboxymethylcellulose (Refresh Plus) 0.5%, 0.4 mL	Eye (topical)	Ulcer, abrasion, perforation, chemical burn
Hypromellose (Nature's Tears) 0.4%, 15 mL	Eye (topical)	Ulcer, abrasion, perforation, chemical burn
Mineral oil and white petrolatum (Refresh PM) 42.5%; 57.3%, 3.5 g	Eye (topical)	Ulcer, abrasion, perforation, chemical burn
Cyanoacrylate glueA (Dermabond)	Eye (topical)	Corneal perforation
Saline	Eye (topical)	Chemical corneal burn
Eugenol (1 mL)	Topical	Fungal keratitis
Levofloxacin	Oral	Ulcer, abrasion, perforation, chemical burn
Azithromycin	Oral	Ulcer, abrasion, perforation, chemical burn
Clindamycin	Oral	Ulcer, abrasion, perforation, chemical burn
Sulfamethoxazole and trimethoprim (Bactrim DS)	Oral	Ulcer, abrasion, perforation, chemical burn
Amoxicillin (Amoxil) 500 mg	Oral	Streptococcal keratitis ulcer
Fluconazole (Diflucan) 150 mg	Oral	Fungal keratitis
Prednisone	Oral	Non-infectious corneal inflammation
Valacyclovir (1 g)	Oral	Herpes keratitis
Acetaminophen (Tylenol) 325 mg	Oral	Corneal abrasion, corneal ulcer, corneal perforation
Aspirin 325 mg	Oral	Corneal abrasion, corneal ulcer, corneal perforation
Ibuprofen (Motrin) 400 mg	Oral	Corneal abrasion, corneal ulcer, corneal perforation
Ketorolac (Toradol) 30 mg/mL, 2 mL	Intramuscular	Corneal abrasion, corneal ulcer, corneal perforation
Ceftriaxone (Rocephin) 1 g	Intramuscular	Streptococcal keratitis ulcer
Urine chemstrips 0.5 mL	Eye (surface)	Chemical corneal burn
Eyewash	Eye (surface)	Abrasion, chemical burn

to infections, and potentially lead to further complications, thus it is essential to use these agents judiciously and under strict medical supervision in space environments.

Broad-spectrum topical antibiotics should be started after removal of the offending body. Erythromycin ointment four times a day for five days or antibiotic drops (e.g., sulfacetamide 10%, polymyxin/trimethoprim, ciprofloxacin, or ofloxacin) have been demonstrated to be effective at reducing infection. Contact lens users should be started on antipseudomonal antibiotics (e.g., fluoroquinolones or aminoglycosides), and careful monitoring should be carried out to detect signs of corneal ulcers[18]. A therapeutic bandage contact lens may provide some short-term comfort as it serves as a barrier from the shearing forces of the eyelids against the cornea surface. However, it is important to consider that a bandage contact lens may increase the risk of infection, so it is not recommended for contact lens users. Oral or topical NSAIDS (e.g., ibuprofen, acetaminophen) and short-acting topical cycloplegic drops (atropine sulfate, homatropine hydrobromide, cyclopentolate hydrochloride, and tropicamide)[19] may alleviate the discomfort[20].

Despite the availability of topical medications on the ISS, their efficacy may be compromised due to altered fluid dynamics within the bottle and increased risks of contamination. These challenges exacerbate the potential for corneal abrasions. Unlike terrestrial settings, the transmission of topical drugs in microgravity involves unique difficulties. Crewmembers must rely on surface tension forces to create a globule of topical medication and then make direct contact with the dropper bottle to "wick" the solution into the eye. This maneuver increases the likelihood of eye contact with contaminants, raising the risk of corneal abrasions.

Corneal abrasions, dry eye, and contact lens misuse predispose individuals to bacterial, viral, and fungal cultivation, which may result in corneal ulcers[21]. The primary differences between the non-surgical treatment of corneal ulcers and corneal abrasions lie in the complexity and aggressiveness of the treatment required for ulcers. Corneal ulcers may necessitate cultures with specific and potent medications to target the underlying infection, along with close and careful monitoring to prevent serious complications that could lead to vision loss. On the other hand, corneal abrasions generally require simpler, prophylactic measures to prevent infection and manage pain, with follow-up focused on ensuring proper healing. More severe ulcerations may require surgical interventions such as debridement and corneal transplantation. Close monitoring and prompt medical attention are critical for managing corneal ulcers effectively, as long-term complications and corneal perforation may result if left untreated[21].

Corneal perforation

Corneal perforation is characterized by a rupture of the corneal tissue, a critical and sight-threatening condition. Perforations may result from trauma (chemical injury, surgical, penetration[22]), infections (e.g., *Pseudomonas aeruginosa*, *Herpes zoster)*, inflammation (e.g., Polyarteritis nodosa, Rheumatoid arthritis), or other pre-existing conditions (e.g., keratoconjunctivitis sicca, Sjogren syndrome, ulcerative keratitis, etc.), leading to severe ocular pain, rapid vision loss, and excess tear production[23]. The stringent astronaut selection process significantly reduces the likelihood of such pre-existing condition. However, this process does not apply to space tourists or participants, raising potential concerns regarding ocular health and predisposition to corneal injuries in the space environment[24]. While no open globe injuries have been documented in space thus far, the absence of such reports does not eliminate the possibility of their occurrence.

The Seidel test may be employed to detect the presence and rate of flow of aqueous humor leakage[25]. A perforation is confirmed if a sterile saturated fluorescein strip with saline placed over the suspected perforation becomes diluted. Prompt assessment is vital for determining the need for emergent surgical repair (e.g., corneal suturing, tissue grafts). Adjuvant medical therapy is similar to the aforementioned options for corneal abrasions and ulcers. In the setting of impending corneal perforation or corneal ulceration secondary to aqueous deficient dry eye, punctual occlusion (blocking tear drainage) and tarsorrhaphy (procedure partially or completely joining the upper and lower eyelids) may promote corneal re-epithelization[26]. Topical or systemic antibiotics are also indicated for prophylaxis of infection. Systemic tetracyclines may also serve as means for inhibiting matrix metalloproteinases, which reduce collagen breakdown and promote corneal healing[27]. Topical steroids may be beneficial for corneal ulcers by blocking the entry of polymorphonuclear lymphocytes and reducing collagenases; however, a randomized control trial reported variable improvement[28]. Topical aqueous suppressant medications (beta-blockers, carbonic anhydrase inhibitors, alpha-2 agonists) may encourage healing by decreasing outflow of aqueous humor through reduction of intraocular pressure[29]. Oral and topical vitamin C can also stimulate collagen production and be used as an adjuvant therapy[30].

A bandage contact lens in the setting of small perforations can serve as a barrier from the friction of eyelid blinking and eye movements, thus promoting corneal healing and providing therapeutic comfort[31]. Dry eye cases related to aqueous deficiency may also benefit from a bandage contact lens. Cases of corneal penetration can close leaks by employing a soft, hydrophilic bandage contact lens for four to seven days[32]. Topical or systemic antibiotics should be used in conjunction to reduce the risk of infection.

In severe cases or unsuccessful medical therapy, surgical intervention may be indicated. Cyanoacrylate and fibrin glues are adhesive interventions for small (<3 mm), concave perforations away from the limbus. Cyanoacrylate glue, an ester derivative of cyanacrylic acid, undergoes polymerization and hardening when introduced to water or weak bases[13]. Alternatively, fibrin glue is a biological product containing fibrinogen and thrombin. Cyanoacrylate glue has reported success rates of up to 86%, and fibrin glue has reported success rates ranging from 44 to 79%[13]. The application techniques of cyanoacrylate glue vary, but one method would be attaching an applicator to the vial of glue to connect a 23-gauge catheter for precise administration at the perforation site. The corneal patch technique may also be implemented, where the glue is first placed on a corneal patch and then directly placed over the perforation. The cyanoacrylate may polymerize and solidify in a rough manner, so a bandage contact lens may be placed superficially to prevent glue dislodgement and provide comfort.

Terrestrially, amniotic membrane transplantation (AMT) is an adjuvant therapy to fibrin glue or 10-0 polyglactin sutures[33]. It is often used in cases with peripheral defects and when medical treatment has been unsuccessful. The amniotic membrane has been found to have fibroblastic growth factor, hepatocyte growth factor, and transforming growth factor β, which promote tissue repair, epithelialization, and reduction in inflammation. The AMT may be sutured in a single-layer graft or in a multilayered fashion[34,35]. AMT has had a reported 70 to 90% success rate, with a mean epithelial healing time of three to four weeks[36]. In very severe cases with full thickness penetration and large corneal perforations (>3 mm), corneal transplantation (i.e., corneal keratoplasty) may be indicated[37].

Chemical corneal burns

Chemical corneal burns are typically a result of exposure to corrosive substances, such as acids, alkalis, or other hazardous chemicals. During an Apollo-Soyuz Test Project in July 1975, combustion products and propellant (hydrazine, nitrogen oxide, nitrogen tetroxide) entered the cabin[38]. Nine incidents from STS (Space Transportation System)-35 to STS-55 have also reported thermodegradation of spacegraft polymers into formaldehyde, ammonia, benzene, acetaldehyde, and dimethyl sulfides within the cabin, further emphasizing the limitless possible scenarios for ocular toxicity[39,40]. Three cases of eye burning secondary to anti-fog substance sprayed into the space visor/helmet during an EVA have also been documented[41].

During chemical burns to the cornea, rapid and severe damage to the tissues leads to intense pain, redness, vision impairment, and in severe cases, conjunctival blanching. Subsequently, corneal melt, limbal stem cell deficiency, and glaucoma may develop in the long term[4]. Acid burns from chemicals less than pH of 4 (e.g., hydrochloric acid, sulfuric acid) tend to denature, coagulate, and precipitate corneal proteins on contact. The innate acidic reaction tends to create a barrier and results in shallower penetration relative to alkali burns. Contrarily, alkali chemicals (e.g., sodium hydroxide,

Table 2 | Roper-Hall classification of chemical eye injury[82] and recommended treatment

Grade	Clinical findings	Limbus	Prognosis	Recommended treatment
I	Corneal epithelial damage	No limbal ischemia	Good	-Topical antibiotic ointment (e.g., erythromycin) 4x/day -Prednisolone acetate 1% four times a day -Preservative free artificial tears prn -Short-acting cycloplegic (e.g., cyclopentolate) 3x/day for pain
II	Corneal haze, iris details visible	<1/3 limbal ischemia	Good	-As grade I -Topical antibiotic (e.g., fluoroquinolone) 4x a day -Long-acting cycloplegic (e.g., atropine) -Oral vitamin C, 2 grams 4/day -Doxycycline 100 mg 2x/day -Sodium ascorbate drops (10%) hourly -Debridement of necrotic epithelium and application of tissue adhesive
III	Total epithelial loss, stromal haze, iris details obscured	1/3–½ limbal ischemia	Guarded	-As Grade II -Consider amniotic membrane transplant
IV	Cornea opaque, iris and pupil obscured	>1/2 limbal ischemia	Poor	-As Grade II and III -Surgery; Tenonplasty may reestablish limbal vascularity; Amniotic membrane transplant

ammonia, calcium hydroxide, etc.) have lipophilic properties that saponify membrane lipids and penetrate deep into the collagen matrix of the cornea[42]. Inflammatory release of proteolytic enzymes can cascade and result in liquefactive necrosis, further exacerbating tissue destruction[43,44].

Destruction of conjunctival goblet cells from direct chemical damage can result in irreparable dry eye conditions. Limbal stem cell deficiency is another condition that can lead to significant complications in the eye, including corneal opacification and neovascularization. This condition arises from the loss or dysfunction of corneal epithelial progenitor cells, which are essential for the maintenance and regeneration of the corneal epithelium. When these progenitor cells are depleted or impaired, the corneal surface becomes unstable and vulnerable to damage. Glaucoma is an additional complication that may develop from damage to the trabecular meshwork, contraction of structures in the anterior globe, and inflammatory damage to ganglion cells[5]. The Roper-Hall and Dua classifications are two graded schemes that divide chemical eye injuries from least to worst severity and prognosis[44]. Table 2 displays the Roper-Hall classification as well as the recommended treatment modalities for each grade.

Immediately after the offending agent is removed, irrigation with copious amounts of neutral saline or water for at least 30 min is critical for diluting the chemicals and irrigating the eye to return the pH to 7.0 to 7.2. Thereafter, the pH of both eyes should be measured, even if only one eye was affected[5]. Litmus paper strips are a practical method for determining if the inciting agent is acidic or basic. If pH papers are not available, urine dipstick reagent strips may be trimmed accordingly to estimate the pH of the eye[45]. Amphoteric chelating agents (e.g., ethylenediamine tetraacetic acid (EDTA), Diphoterine®, hexafluorine, and Cederroth Eye Wash) may also be used to reduce tissue necrosis[44]. It is important to consider that over-irrigation can result in corneal edema[46]. After irrigation is stopped, the pH should be checked after at least 5 min and a physical exam of the eyes should assess the degree of damage and estimate prognosis. Wet sterile cotton-tipped applicators may be used to inspect and remove foreign bodies from under the eyelids and conjunctival fornixes. Intraocular pressure (IOP) may also be altered, so tonometer or Tonopen devices may measure IOP if epithelial damage is not severe[47].

Mild burns (Roper-Hall Grade I) generally have a good prognosis with topical medical treatment options; however, severe burns often require more extensive therapies and surgical interventions. As outlined in Table 2, topical antibiotic ointment therapy (e.g., erythromycin ointment) is used as prophylaxis in reducing the progression of necrotic tissue and reducing local infection. Mydriatic and cycloplegic agents (e.g., atropine, cyclopentolate), oral pain medications, and lubricating eye drops (e.g., artificial tears) may provide some therapeutic comfort[48]. Oral tetracyclines (e.g., doxycycline) can inhibit matrix metalloproteinases and reduce signs of corneal melting. Due to the high levels of ascorbic acid normally present in the aqueous humor, oral and topical administration of vitamin C has been found to prevent or delay ulceration[30]. However, it is important to note that in the context of a chemical corneal injury, the levels of ascorbic acid in the aqueous humor are significantly diminished. This depletion is critical because vitamin C plays a crucial role in collagen synthesis and wound healing, providing antioxidant protection to the corneal tissue. Multiple studies have described following a chemical corneal injury, the natural reserves of ascorbic acid are reduced, compromising the eye's ability to effectively repair and protect itself. Consequently, the administration of vitamin C, both topically and systemically, becomes particularly beneficial in this scenario. The supplementation helps to restore the diminished levels of ascorbic acid, thereby enhancing collagen production, reducing oxidative stress, and promoting more effective healing of the corneal epithelium[3,30,42,44]. Topical steroids (e.g., prednisolone) may also be effective in reducing further corneal breakdown and reducing inflammation but should be utilized modestly and tapered accordingly to balance collagen synthesis and breakdown[49].

In cases of severe chemical corneal burns, early removal of necrotic epithelium through debridement can aid in the re-epithelization process. Furthermore, AMT is a costly procedure that has the potential to enhance patient comfort by reducing eyelid friction while promoting improved neovascularization and epithelial growth. While there have been reported cases of enhanced visual acuity compared to those receiving medical therapy alone, it is important to note that conclusive evidence in this regard remains elusive[50].

Ocular medications on the ISS and routes of management with ISS medications

Crewmembers aboard the ISS are not immune to medical emergencies, especially corneal abrasions, perforations, and chemical burns. While they undergo extensive training for emergency situations, there are inherent complexities when faced with eye injuries. Although some astronauts are trained for ocular experiments, more intricate ophthalmic procedures, like the removal of a foreign body with a 25-gauge needle, may exceed their scope of training. Moreover, the ISS operates with limited pharmaceutical resources, necessitating the use of medications and materials for a variety of potential problems[14]. According to NASA's Space Medicine Operations Division, no changes have been made to the ocular medications since the publication of the 2015 medical kit list (https://www.nasa.gov/wp-content/uploads/2015/03/medical_kit_checklist_-_full_release.pdf), with the sole exception of a reduction in Cylogyl (Cyclopentolate) concentration from 2 to 1%. The microgravity environment also adds another layer of difficulty to ocular injury management, as a trained eye care professional is unlikely to be present on the ISS, although some crewmembers may hold medical qualifications[51,52]. In this challenging context, adapting available medications and leveraging emergency medical training is critical for addressing ocular injuries in a high-stakes environment[16].

Corneal abrasions during spaceflight

Risk factors for corneal abrasions during spaceflight. Future planetary missions will likely involve crewmembers being exposed to celestial dust and other particles, increasing the risk of ocular foreign body entry or corneal abrasions. Moreover, microgravity conditions result in suspended particulate matter that can enter crewmembers' eyes through air currents within the aircraft[53,54]. Altered tear distributions may also contribute to eye dryness and increased susceptibility to abrasions. 2 out of 269 ocular complaints in the LSAH between 1961 and 2020 have been associated with tear film insufficiency[41].

During extravehicular activities (EVAs), crewmembers will explore beyond Earth's atmosphere (e.g., spacewalks, planetary surface missions) and be confined to the spacesuit. During which, crewmembers will not be able to manually remove (e.g., rub eyes) any potential debris entrapped in the spacesuit, subjecting the user to persistent eye irritation. EVAs on celestial bodies may allow dust caught on equipment and spacesuits to enter the spacecraft, which subsequently may float around the cabin in the microgravity environment. In a more recent study combining LSAH data with ISS expeditions 1 to 63 and STS Missions 1 to 135, 14 out of 269 (5.2%) of ocular complaints occurred during or immediately after EVAs, 10 of which resulted from particulates[41]. In the case of Apollo missions, lunar dust was also able to access the interior of the spacesuits and spacecraft, which may be concerning with special consideration of the Artemis Program's return to the moon[55,56].

Although ocular toxicity studies of lunar dust have demonstrated minimal irritation (slight redness and swelling of conjunctiva), no acute adverse effects on the cornea, iris, or conjunctiva have been reported. However, the effects of chronic lunar dust exposure and particles of other celestial bodies remain unknown and necessary precautions must still be employed. Windstorms and other environmental factors on the Martian surface may also potentiate the risk for ocular irritation or injury.

Qualitative data has been collected to determine common causes of ocular complaints related to eye irritation, foreign body sensation, and dry eye syndromes. Complaints of eye irritation (26.3% of total ocular complaints), foreign body sensation, and dry eye syndromes (21.3% of total ocular complaints) have been reported to be associated with air, sweat, irritants in the spacesuits, increased carbon dioxide levels, food particulates, lint particles, anti-fog treatment, salt crystals, lithium hydroxide dust, electrode paste, and aluminum particles in the air[41].

Limitations to managing corneal abrasions during spaceflight. Current corneal diagnostic equipment on the ISS is limited to an ophthalmoscope, which crewmembers are trained to use for primary ocular examinations. Fluorescein strips and a blue light filter are available for identifying corneal abrasions, but a slit lamp biomicroscope is not available for stronger visualization[57]. Aside from equipment limitations, microgravity-induced fluid dynamics alter the distribution of bodily fluids. Therefore, affected tear dynamics challenge the appropriate eye irrigation and effective administration of eye drops. Consequently, microgravity may hinder the accuracy, control, and precision of eye drops and ointments necessary to treat damaged corneal epithelium. Otherwise, the treatment approaches for corneal abrasions on the ISS closely mirror those employed in terrestrial management.

Treatment and countermeasures to corneal abrasions during spaceflight. Dry conditions disrupt the delicate tear film balance on the ocular surface, contributing to dry eye syndrome. Insufficient humidity increases tear evaporation, thus leading to increases in susceptibility to foreign body sensations, as the tear film struggles to shield the corneal epithelium from external irritants[58]. Reduced tear film elevates risks of corneal abrasions, making the cornea more susceptible to friction-induced microtraumas. Arid and compromising conditions to ocular health are counteracted on the ISS by maintaining a humidity level of approximately 60% by the Life Support Systems. The Temperature and Humidity Control (THC) subsystem circulates air, not only contributing to the complex water recycling technology but also helping with eye health aboard the ISS[59].

After any potential ocular injury, visual acuity for each eye can be measured with the available Eye Chart aboard the ISS[60]. In the setting of minor particle abrasions, artificial tears may be used to rinse the eye. If unsuccessful, a space eyewash apparatus currently aboard the ISS may be employed, which consists of flushing an eyewash solution through swimming goggles. The solution's input and output flow are contained within the goggles, which prevents loose water from floating around electrical equipment in a microgravity environment[61]. More persistent foreign bodies may be removed by applying the ISS's Tetracaine (0.5%) topical anesthetic and gently sweeping the surface of the cornea with a cotton swab[62]. In more emergent and complex cases, crewmembers may be trained to utilize an eye spud or 25-gauge needle to more precisely remove foreign bodies. Nevertheless, the microgravity environment of space poses challenges to stabilize and accurately maneuver the fine-tipped instruments.

Prophylactic broad-spectrum antibiotic ointment is indicated following the foreign body removal. On the ISS, topical Erythromycin ointment (0.5%) and Moxifloxacin (Vigamox, 0.5%) are appropriate options for reducing the incidence of infection. Tobramycin and Dexamethasone (Tobradex, 0.3%; 0.1%) are also available for prophylaxis, but topical corticosteroids may increase the risk of infection, delay healing, activate herpes keratitis, and increase IOP[63,64]. Crewmembers who use contact lenses should especially be started on antibiotics to prevent the risk of pseudomonal infections. The ISS does not currently have any therapeutic bandage contact lens aboard, so future adjustments to medical kits should consider adding them for non-contact lens users. Available cycloplegic drops (e.g., Cyclopentolate (Cyclogyl, 1%), Tropicamide (Mydriacyl, 1%)), oral NSAIDS (Acetaminophen (Tylenol) 325 mg, Aspirin 325 mg, Ibuprofen (Motrin) 400 mg) and artificial tears (Carboxymethylcellulose (Refresh Plus, 0.5%), Hypromellose (Nature's Tears, 0.4%)), Mineral Oil and White Petrolatum (Refresh PM, 42.5%; 57.3%, 3.5 g) may also provide therapeutic relief. In the presence of extraterrestrial particulate irritants, Olopatadine eye drops (Pataday, 0.2%) are included in the ISS medical kit, offering antihistamine symptomatic management.

Corneal abrasions are common precursors to ulcers, which can escalate to more severe conditions, including bacterial, viral, and fungal keratitis. 1 case of severe keratitis and 1 case of a corneal ulcer have been reported on the ISS from 1961 to 2020. However, with longer-duration missions planned for the near future (e.g., Mars), simple corneal abrasions may become exacerbated to keratitis or ulcers if not appropriately managed. Prognosis is largely dependent on the severity and latency of treatment. The available topical erythromycin ointment (0.5%) and moxifloxacin (Vigamox, 0.5%) on the ISS can treat a broad spectrum of bacterial keratitis via significant aqueous humor penetration. However, in the setting of more complicated infections, systemic options aboard the ISS (e.g., doxycycline, ampicillin, etc.) may also be employed if the eye ointments are ineffective. For example, doxycycline (Vibramycin, 100 mg) has a high lipid solubility, which may allow stronger penetration in the aqueous humor and cornea[65]. The antibiotic paired with vitamin C supplementations also has healing properties that can accelerate recovery of deep corneal ulcers[65–67]. Penicillin (e.g., ampicillin (Amoxil, 500 mg)) and cephalosporins (e.g., Ceftriaxone (Rocephin, 1 g)) may be effective for streptococcal keratitis if the bacteria are resistant to the topical moxifloxacin. Other oral antibiotics aboard the ISS (e.g., levofloxacin, azithromycin, clindamycin, Sulfamethoxazole and Trimethoprim (Bactrim DS)) have variable ocular penetration, limiting efficacy for resistant bacterial keratitis. However, as ocular drug delivery systems and research on dosage forms for topical eye drops continue to develop, future space missions may stock alternative antibiotics[68–70].

If herpes keratitis is suspected through observation of the classic dendrite fluorescein staining or other clinical manifestations (e.g., corneal opacity), prompt treatment with the available oral valacyclovir (1 g) must be administered[71]. Tobramycin and Dexamethasone (Tobradex, 0.3%; 0.1%), administration after vanquish of epithelial HSV may also provide benefit for stromal inflammation. In terms of antifungals, oral fluconazole (Diflucan,

150 mg) has demonstrated strong ocular structure penetration, serving as a useful treatment for fungal keratitis[72]. Alternatively, while topical eugenol may not have a primary use for ocular fungal infections, it may also provide utility as a treatment of fungal keratitis aboard the ISS. Eugenol in an ocular setting has been found to provide protection against *Candida*, *Aspergillus*, and other fungal keratitis sources[71,73]. Non-infectious ulcers may find relief through lubricating eye drops. However, severe ulcerations might require surgical debridement or even corneal transplantation, procedures that are unlikely to be feasible on the ISS due to the absence of specialized medical personnel. Therefore, early monitoring and timely medical intervention are of paramount importance for effectively managing corneal ulcers before they progress to severe complications such as corneal perforation and potential blindness.

Crewmembers may wear safety glasses while transversing through the cabin, although they may not be regularly worn at all times. These safety glasses offer an additional layer of protection against unexpected particle exposure and minor collisions with equipment or other surfaces. However, due to comfort, practicality, and the dynamic nature of daily activities aboard the ISS, crewmembers often forego wearing safety glasses continuously. Instead, they are typically donned during specific high-risk tasks or when moving through areas where particle exposure is more likely.

Corrective eyeglasses, which many astronauts wear for vision correction, may provide a slight barrier against particles. While they can offer some protection by deflecting small debris away from the eyes, their design is not optimized for safety, and thus, their protective efficacy is limited. The coverage area is smaller, and the material used in corrective lenses is not intended to withstand significant impacts or block hazardous substances. As a result, while corrective eyeglasses can offer minimal shielding, they do not replace the need for dedicated safety glasses or goggles, which are essential for ensuring comprehensive ocular protection in the unique environment of space.

Corneal perforations during spaceflight

Risk factors for corneal perforation during spaceflight. Risk factors for corneal perforation are similar to those mentioned for corneal abrasions (e.g., salt crystals, lithium hydroxide dust, aluminum particles). No events of corneal perforation have been documented in the LSAH, but the vision-threatening injury remains a potential outcome following traumatic impact or severe ulceration, reinforcing the critical importance of promptly and vigilantly addressing ocular abrasions and infections. Moreover, during splashdown to Earth, crewmembers may experience forces ranging from 3 to 5 G's, which can abruptly increase intraocular pressure. If a crewmember is returning with a severe perforating eye injury, these heightened pressures can further exacerbate the damage. The sudden increase in intraocular pressure can lead to additional complications, such as hemorrhage, retinal detachment, or worsening of the perforation, thereby posing significant risks to the already compromised ocular structures and potentially impacting the overall visual prognosis.

Limitations to managing corneal perforation during spaceflight. A primary obstacle to the precise diagnosis and monitoring of corneal perforations during spaceflight is the unavailability of a slit lamp biomicroscope. The absence impedes thorough examination of corneal injuries, limiting the ability to detect subtle nuances in perforation size and characteristics. Crucial resources (e.g., bandage contact lenses, amniotic membrane, corneal transplantation) are not available due to the constrained space and limited specialized medical personnel on board to address the corneal perforations comprehensively. Furthermore, delayed medical consultations due to communication latency pose a significant concern if corneal perforations were to occur, particularly for the extended and distant missions planned in the Artemis Program or future Mars expeditions. Such delays may exacerbate conditions, compromising the success of interventions.

Treatment and countermeasures to corneal perforations during spaceflight. Recognizing inherent risk to the ocular health and safety of crewmembers is critical for preventing corneal injuries, especially in the context of engineering tasks and protocols. Meticulous protocols and safety equipment are devised to minimize the likelihood of accidents, such as rating toxicity hazards and implementing ventilated enclosures with High-Efficiency Particular Air (HEPA) filters[74]. Automatic safety devices are also designed to autonomously relieve pressure or inhibit power if overpressurization, overheating, or overcooling of a device poses a potential hazard, thus minimizing the occurrence of high-velocity particles from possibly impacting the eye. Furthermore, the utilization of specialized equipment, such as the Air Science® Purair FLEX Portable Isolator, serves as an effective countermeasure to corneal injuries during higher-risk experiments[75]. This lightweight apparatus functions as a portable method of containment, offering a cost-effective solution to shield crewmembers from potential bodily harm.

If a severe penetrating corneal injury were to occur, astronauts are instructed to refrain from disturbing the object causing the injury. Instead, they should delicately apply an eye pad to both the injured and unaffected eyes, followed by securing a metal eye shield over the injured eye. Covering both the injured and uninjured eyes after a penetrating eye injury minimizes eye movement, thereby reducing further trauma and pain, while also protecting the eyes from light, dust, and other contaminants. This practice helps prevent additional damage and provides psychological comfort to the patient. The injured crewmember may then be physically guided by fellow crewmembers while vision-impaired. Flight surgeons at mission control would then be contacted to coordinate a likely evacuation. With less apparent perforations, fluorescein testing with blue light may be used to diagnose penetrating foreign bodies or lacerations. Future missions should consider adding modified slit lamps to supply lists for stronger visualization of injuries. Management would be very similar to treatment options for corneal abrasions: artificial tears, antimicrobial prophylaxis, cycloplegic drops, pain management, and temporary use of topical anesthetics. Contact bandage lenses or collagen corneal shields should be incorporated into future missions to accelerate epithelial and stromal healing as well as enhanced topical drug delivery[76,77].

For more severe cases, cyanoacrylate or fibrin glues may be employed as a temporary solution before additional interventions are available. Cyanoacrylate glue is readily available on the ISS and serves as a viable option for managing smaller corneal perforations (<3 mm). While cyanoacrylate glue may offer improved visual outcomes, fibrin glue could be a valuable addition to the supply kits due to its higher biocompatibility, as it is derived from human plasma proteins, which can reduce the risk of foreign body reactions and minimize conjunctival and corneal inflammation. Bandage contact lenses, once more, should be considered for inclusion in supply kits for missions, as they can be applied over treated areas following glue application, offering an additional layer of protection, comfort, and support. If the mission allows, further escalation of treatment may be available upon return to Earth, such as amniotic membrane or corneal transplantation.

Chemical corneal burns during spaceflight

Risk factors for chemical corneal burns during spaceflight. Crewmembers conduct several laboratory experiments or maintenance tasks daily. During these procedures, the altered dynamics of liquids in the laboratory or even basic hygiene routines can inadvertently expose crewmembers to risky situations. The setting of microgravity may also lead to unpredicted splashing or drifting of liquid particles, increasing the chances of ocular exposure and, consequently, corneal chemical burns. Realistic scenarios, such as entry of propulsion propellant chemicals (Freon, hydrazines, nitrogen dioxide) into the airlock or crystallization on EVA suits, can pose threats to crewmembers at very low quantities[78]. In a review of ocular trauma during the NASA Space Shuttle Program and ISS through Expedition 13 in 2006, six chemical burns were documented[16]. Safety goggles are available aboard the ISS for higher-risk laboratory experiments, but exposure from unexpected reactions may occur that can inflict damage on crewmembers' eyes. While these goggles provide a significant level of protection, they cannot eliminate all risks,

particularly in the setting of unanticipated chemical reactions where harmful substances bypass protective barriers. Additionally, in the confined and complex environment of the ISS, the immediate response to such exposures may be challenging, further increasing the potential for injury. Therefore, despite the availability of safety equipment, the risk of corneal damage remains a critical concern for astronauts.

Although the ISS has the Environmental Control and Life Support System (ECLSS) to maintain airflow within the habitable space, local pockets of CO_2 may develop around the facial area, especially during sleep. Prolonged CO_2 exposure may lead to corneal epithelial damage to a minor degree[79]. Other chemical injuries may result from exposure (e.g., sulfuric acid, sulfurous acid, acetic acid, hydrofluoric acid, ammonia, potassium hydroxide, lye, magnesium hydroxide, Lime, etc.) that may leak from components of the ECLSS or from reagents of human research and biotechnology experiments[16].

Limitations to corneal chemical burn treatment during spaceflight. Corneal chemical burn treatment during spaceflight in a microgravity environment aboard the ISS encounters several limitations, exacerbated by the absence of necessary resources present on Earth. One principal constraint is the unavailability of traditional terrestrial eyewash stations on the ISS. This limitation arises from concerns related to the spread of water in microgravity environments, posing risks to electronic equipment and other critical systems. The lack of dedicated eyewash facilities complicates the immediate decontamination of the eyes following chemical irritant exposures, a crucial method of management for corneal chemical burns. The microgravity environment also alters the natural flow of fluids, impacting the rinsing process and may hinder the removal of chemical agents from the ocular surface. For more severe burns, the limited range of ophthalmic tools and medications available on the ISS may comprehensively restrict options for corneal chemical burn treatment (e.g., amniotic membrane and cornea transplantation).

Treatment and countermeasures to corneal chemical burns during spaceflight. In parallel to countermeasures employed for preventing corneal perforations, the approach to mitigating the risk of corneal chemical burns during spaceflight involves the implementation of similar specialized precautions and protocols. HEPA filters aboard the ISS are effective at removing components of reagents that may be present in the cabin from either scientific experiments or life support systems (e.g., Freon). The Air Science® Purair FLEX Portable Isolator also provides a puncture-resistant construction with solvent resistance across a range of chemicals to contain a dispersion of harmful substances that crewmembers may be exposed to during experimentation[75]. Chemical and biological samples are thoroughly evaluated and may only be used for the intended purpose when introduced to the pressurized habitable environment. This safety requirement protects crewmembers from chemically induced toxicity and contamination hazards[74].

Initial management of chemical burns requires measurement of the pH of the inciting substance followed by copious irrigation to dilute and neutralize the pH to near 7.0. Urine chemstrips aboard the ISS may be cut to measure the pH before and between irrigations[45]. The innovative space goggles can be applied for at least 30 min to continuously flush sterile ophthalmic solution while also containing the fluids to the apparatus. Thereafter, mild burns will follow a similar therapeutic treatment plan as corneal abrasions and perforations: temporary topical anesthetics, topical antibiotics, artificial eye drops, and cycloplegic eye drops. Tobramycin and Dexamethasone (Tobradex, 0.3%; 0.1%) may also be used sparingly and tapered down to reduce inflammation and prevent additional corneal breakdown. Vitamin C supplementation (oral) and doxycycline (oral) should also be employed to promote collagen healing and reduce the incidence of ulceration and corneal melting. Future missions should consider adding topical vitamin C to kits for more direct administration on the cornea.

In cases of severe chemical corneal burns, an imminent return to Earth for more professional treatment would be required. Surgical interventions such as tenonplasty or amniotic membrane transplantation may be utilized to promote neovascularization and epithelial growth of the cornea. However, even with early intervention and aggressive treatment, corneal burns often result in vision loss. Other complications (e.g., glaucoma, corneal perforation, cataracts, scarring, retinal detachment) may insidiously arise, challenging the crewmember's return to flight[80].

Takeaways

Management of corneal injuries (e.g., abrasion, perforation, chemical burns) in spaceflight is a complex endeavor, especially in the setting of unique microgravity environments and limited resources. Many medications currently available aboard the ISS provide a foundation for the treatment of ocular injuries; however, the expansion of the medical kit with other essential items (e.g., portable slit lamp, bandage contact lens, topical vitamin C) would enable more comprehensive approaches to treatment. Interestingly, though, some medications not primarily indicated for ocular injuries (e.g., cyanoacrylate glue, topical eugenol, oral doxycycline) present valuable treatment modalities for more unique circumstances. Nonetheless, interplanetary journeys with stringent constraints on mass and volume for medical resources will necessitate the meticulous selection of only essential supplies. It is of note that other ophthalmic pathologies have been documented in microgravity, including spaceflight-associated neuro-ocular syndrome (SANS). SANS findings include optic nerve edema, posterior globe flattening, hyperopic shift, and chorioretinal folds[81]. While SANS findings are primarily located in the posterior segment of the eye, it will be of utmost importance to take into consideration all the various factors that impact overall eye health in microgravity.

As NASA and other space agencies look ahead for future interplanetary travel, new challenges and ocular threats emerge. Lunar dust, for instance, may expose astronauts to irritants, especially when long-term human habitats of the Moon are constructed under the Artemis Program[78]. Similarly, the Martian surface's unpredictable and unknown weather patterns can endanger astronauts and their ocular health, warranting robust medical preparations. In the advent of commercial spaceflight programs, participants may not undergo the same rigorous medical evaluations as NASA astronauts, potentially putting them at higher risk of injury if pre-existing ocular conditions are present. Furthermore, as future missions become exponentially more complicated, the increased complexities of evacuation and mission abort emphasize a need for greater comprehensive medical preparedness. For example, the mission to Mars will last over two years, negating easy return to Earth for severe ocular injury treatment.

Communication latency will present a distinctive challenge in possible emergency scenarios, as flight surgeons and ophthalmologists will be unable to provide real-time guidance for the treatment of ocular injuries.

In light of these challenges, proactive protocols for corneal injuries aboard the ISS and interplanetary missions are beyond essential. Just as NASA purchased antigravity ballpoint pens to protect the well-being of astronauts, future missions will need to proactively address the expansive possibilities of corneal injuries. In the future, specialized medical kits will need compact and portable treatment modalities and diagnostic technologies. These advancements will not only propel the safety of crewmembers but also have the potential to eventually find applications in terrestrial medicine, particularly in resource-limited environments. Consequently, the collaborative efforts of NASA and the ophthalmology community will pave the way for humanity to evolve into an interplanetary species and cast its gaze toward a future among the cosmos.

Methods

Our search strategy consisted of using the PubMed and Google Scholar databases, combined with advanced search engines and keywords to review the available literature. January 1, 2024, keywords were searched independently or in conjunction including "Spaceflight," "Corneal Injuries," "Chemical Burns," "Corneal Abrasions," "Corneal Perforations," "Management," and "Neurodegenerative." Additional papers were added by searching through the references of each research paper. From the retrieved articles, relevant articles based on eligibility criteria as well as based on the presence of

keywords in the title or abstract were selected. Inclusion criteria were (1) related to the terrestrial management of corneal chemical burns, corneal abrasions, corneal perforations; (2) use of relevant management techniques (e.g., procedural, pharmaceutical, medications); and (3) corneal injuries in the in the context of spaceflight. A total of 240 papers were reviewed, and 88 were included in this paper. No limitations on the date of publication were used.

Data availability

The data supporting the conclusions of this article are available from the corresponding author upon reasonable request.

Received: 12 January 2024; Accepted: 23 February 2025;
Published online: 11 March 2025

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Author contributions

A.S. was responsible for the initial write up of the manuscript as well as the preliminary literature review for ocular injuries during spaceflight and terrestrial management of such injuries. A.S. reviewed the medications available on the International Space Station (ISS) and accordingly determined appropriate protocols for spaceflight treatment. J.O. was responsible for the development of the research idea and approval of the outline before the manuscript outline was created. J.O. reviewed the first rough draft for quality control before extending to the other authors. E.W. provided additional expert advice on current ophthalmology practices as well as providing preliminary edits before extending to other authors. J.B. is an expert on corneal injuries and provided insights and edits on the best step in management for terrestrial injuries. A.G.L. oversaw the project and provided extensive initial edits, which highlighted artificial intelligence and emergent evacuation. All authors contributed beneficial insights and edits to ensure the success of the manuscript.

Competing interests

Andrew G. Lee, MD, serves as a consultant for NASA. The other authors declare no competing interests.

Additional information

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