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## OPHTHALMIC INJURIES IN SAILORS AND SEA WORKERS – PATHOMECHANISM AND TREATMENT

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#### ABSTRACT

The purpose of the article is to do a literature review and present own experience regarding the main causes of ophthalmic injuries in sailors and crew workers. Sailors and sea workers often use heavy equipment when working on a vessel, offshore platform or other. Using these types of tools often carries high risk of injury. They are also exposed to various chemicals, many of which are eye irritants. Ophthalmic injuries are common but rarely fatal. They can lead to vision loss, reduce the quality of life and inability to continue work. The categorized types of these injuries and included chemical, mechanical, electrical, diving related barotrauma and infections. We present the most common cause of these types of injury, situations in which they can occur, pathomechamism of eye damage, recommend a prevention method, recommend the possible first aid and present cases in which specialized treatment in a reference hospital is necessary.

Keywords: ophthalmic injuries, sea workers

#### **INTRODUCTION**

Ocular trauma can account for 2-3% of emergency room visits [1]. It is estimated that every year 1.5-2 million people worldwide suffer from monocular vision loss following ocular trauma [2]. Due to the sometimes unpredictable nature of their work, sailors and sea workers are generally more exposed to a number dangerous injuries. Ships and oil rigs are hazardous environment with a high injury and mortality rate when compared to offshore workers. This type of work requires using heavy equipment and tools that carries increased risk of injury, including injuries involving the eyes. Ophthalmic injuries are more common in these groups and can account for up to 3.6% of all trauma [3]. Ocular trauma is a common reason for hospital admission [1]. Although not always life threatening they may be a cause of temporary inability to work or permanent vision loss and lowering the quality of life. The purpose of this article is to acquaint the reader with most common injuries that working on a vessel or offshore can lead to. We show the pathomechanism behind the injury, instruct on the first aid that should be provided and describe the specialist treatment.

For the purpose of this article we have divided the injuries into categories.

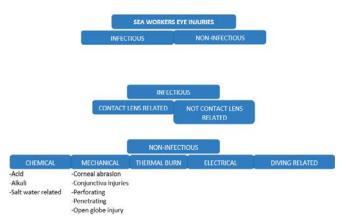


Fig. 1. Sailors and sea workers ophthalmic injuries divided into categories

#### INFECTIOUS

Injuries caused by ophthalmic exposure to water are often described as water related ocular diseases (WORDs) [4]. Infectious injuries occur when there is exposure to contaminated water, usually after a splash of water on the patients face. Depending on the amount of water, the pathogens present, patients medical history, wearing contact lenses during the incident and removing them after, time before eye rinsing and time to an ophthalmology consult the symptoms and complications can vary from mild irritation to corneal ulcer which can lead to corneal perforation.

The most dangerous and vision threatening infections are caused by Acanthamoeba, Pseudomonas aeruginosa, Giardia lamblia, Toxoplasma gondi, Gnathostoma spp, Coenurus cerebralis, Burkholderia pseudomallei, Leptospira spp, Toxocara cani, Toxocara cati, Adenoviruses [4]. Most dangerous infections are usually contact lens related.

### ACANTHAMOEBA

Five species of these free-living amoebae have been reported to cause keratitis. These are: A. polyphaga, A. castellani, A. hatchetti, A. culbertsoni and A. rhysodes [4]. Acanthamoeba can be found in most fresh and salty water tanks and soil [5]. It can also be found in artificial water reservoirs, humidifiers, air purifiers and air conditioning systems. The main risk factor for developing Acanthamoeba keratitis is poor contact-lens hygiene [4, 5]. Removing contact lenses after ocular exposure to contaminated wated is crucial to minimise risk of infection.

Amoeba enters the eye through microscopic corneal abrasions (damaged epithelium, most anterior part of the cornea), most commonly present due to contact lens wearing and damages the cornea, penetrating through corneal layers. Acanthamoeba infections are very painful and quickly lead to deterioration of visual acuity. Patients usually seek medical attention at early staged of the infection due to severe symptoms.



Fig 2. Patient suffering from acanthamoeba keratitis (green arrow)

All cases of Acanthamoeba keratitis requires urgent ophthalmology consult. The treatment is difficult and should be provide in ophthalmology department with the highest degree of referentiality. The prognosis is uncertain in most cases. Acanthamoeba keratitis can cause corneal perforation in 11.3-27.3% of cases [6, 7]. Acanthamoeba keratitis is commonly treated with cationic antiseptics (e.g. 0.02% chlorhexidine), 0.02% propamidine isethionate (Brolene), imidazoles (e.g. 1% clotrimazole, 2% fluconazole). There is no gold standard of care. Propamidine isethionate is likely the best therapeutic option available. Some cases might require penetrating keratoplasty (full corneal transplant).



Fig 3. Patient with Acanthamoeba keratitis after penetrating keratoplasty

#### **PSEUDOMONAS AERUGINOSA**

Pseudomonas aeruginosa is a common Gram-negative, aerobic bacteria. It is very common in various types of environment throughout the world. Ocular infections caused by P. aeruginosa are severe and mainly acquired by exposure to water while wearing contact lenses [4]. The bacteria infiltrates the eye as a result of damage to the surface of the cornea [8]. In most cases the damage is caused by wearing contact lenses or corneal erosion due to foreign body. Other risk factors include: history of refractive surgery, ocular trauma, immunosupression and systemic diseases such as diabetes. The initial treatment is empirical. Topical and systemic fluroquinolones are usually the first choice while waiting for the result of inoculation and sensitivity results [9]. Targeted antimicrobial therapy is always the best therapeutic option.

#### CONJUNCTIVITIS

Viral conjunctivitis is the most common cause of conjunctivitis. Is is usually a mild, self-limiting infection most often caused by adenoviruses [10]. Some conjunctiva infections can be sparsely symptomatic or asymptomatic. Symptomatic infections are usually self-limiting and resolve spontaneously after 1-2 weeks [11]. Viral conjunctivitis is very contagious.

The main method to preventing spreading of the infection is through increased hygiene: frequent hand washing, avoiding touching the face and eyelids and avoiding human contacts. Patients should be warned to keep their infected towels, soap, bedding, away from other family members. Towels and bedding used by the infected individual should be washed often during and after the infection. Antiviral therapy, moisturizing eyedrops and corticosteroids are used in the treatment of this types ocular infection.

#### **PREVENTION OF INFECTIONS**

When unknown water splashes over the patients eyes the first aid should be to remove contact lenses if he is wearing any and to profusely rinse eyes with 0.9% NaCl solution over 15-20 minutes. If that is not available tap water is a possible alternative. Some cases might require specialized ophthalmology treatment. If there was no contact lenses during the incident, the contact with contaminated water was brief, the patient does not present ophthalmology consult is not necessary. Mild irritation should resolve spontaneously after 3-5 days. It is advised to use lubricating eye drops 4-6 times a day for 1-2 weeks after the incident.

#### NON INFECTIOUS

#### CHEMICAL

Chemical related injuries make up approximately 11.5%-22.1% of all ocular trauma [12, 13]. That percentage is probably higher in sailors and sea workers due to contact with dangerous substances in the workplace. Chemical related eye injuries can be divided into acid related, akali related and salt water related.

Acid	Chemical formula	Component and uses
Acetic acid	СН3СООН	inks, paints, coatings, solvent, food industry
Hydrobromic acid	HBr	production of inorganic bromides
Hydrochloric acid	HCl	pickling of steel, production of inorganic compounds, leather processing
Hydrofluoric acid	HF	semiconductor industry, oil refining, organofluorine compounds
Hydroiodic acid	HI	co-catalyst for the production of acetic acid
Nitric acid	HNO3	rocket propellant, metal processing, nuclear fuel reprocessing, woodworking, cleaning agent
Perchloric acid	HClO4	rocket fuel production, ion- exchange chromatography
Sulfuric acid	H2SO4	batteries, pigments, detergents, petroleum refining, metalurgy
Sulfurous acid	H2SO3	bleach, refrigerant, disinfectants

Fig 5. Common acids in the industrial workplace

Alkali	Chemical formula	Component and uses
Ammonia	NH3	solvent, solution of metals, fertilizer, cleaning agent, antimicrobial, fuel, hydrogen carrier, refrigerant
Lime	CaOH2	flocculant in water and sewage treatment, mortar, cement, white wash
Magnesium Hydroxide	MgOH2	medical use, food additive
Potassium Hydroxide	КОН	soft soaps, electrolyte, food industry
Sodium Hydroxite	NaOH	soap, tissue digestion, cleaning solution, food preservation

Fig 5. Common alkali in the industrial workplace

A chemical eye related injury occurs when chemical substance comes in contact with the eyelids, or ocular surface - cornea or conjunctiva. Most commonly it occurs when the substance splashes over the patients face or when the patient rubs their face after working with chemicals. Depending on the substance, its amount and the time of exposure the injury can vary in how dangerous it is from small irritation to complete vision loss. When working with chemicals it is advised to always wear eye protection in the form of goggles or full face mask and gloves.

#### ACID AND ALKALI

Alkali agents are lipophilic and therefore penetrate tissues more rapidly and easily than acids. They saponify the fatty acids of cell cell membranes, penetrate the corneal stroma and destroy proteoglycan ground substance and collagen bundles. The damaged tissues then secrete proteolytic enzymes, which lead to further damage. Exposing the human cornea to strongly alkaline substances for as short as one second can cause irreversible tissue damage.

Acids are generally less harmful than alkali substances. They cause damage by denaturing and precipitating proteins in contacted tissue. The coagulated proteins act as a barrier to prevent further penetration (unlike alkali injuries).The one exception to this is hydrofluoric acid, where the fluoride ion rapidly penetrates the thickness of the cornea and causes significant anterior segment destruction.

Depending on the area affected by the substance, time of exposure and time before first aid the prognosis can vary. There are classifications that can help predict the final visual outcome such as Modification of classification of ocular chemical injuries [14].

Modified classification of ocular chemical injuries							
Grade	Cornea	Limbal ischaemia		Conjunctival involvement	Prognosis		
I	Clear: epithelial damage only	None		None	Good		
п	Clear: epithelial damage only	<1/3		<1/3	Good		
ш	Hazy cornea	>1/3	OR	>1/3	Guarded		

Fig 6. Modified classification of ocular chemical injuries by Harus S [14]

#### SALT WATER

NaCl amounts to about 77.8% of all substances dissolved in salt water. Salt water is a hypertonic solution. Human cornea when exposed to salt water acts as a semi-permeable membrane which can cause water to move outside the cornea. This causes Descemet membrane folds, irregular astigmatism, corneal abrasion and epithelial haze. This leads to light aberrations and consequently blurry vision. These are usually minor damage that can resolve spontaneously after a couple of days.

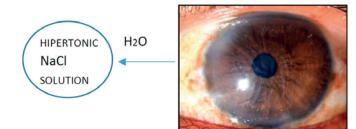


Fig 7. Cornea when exposed to salt water solution

When exposed to chemical substances the symptoms may include: redness, tearing, eyelid swelling, pain, burning sensation, feeling of a foreign body, blurry vision. As with other similar cases first aid should be to remove contact lenses and start eye rinsing with 0.9% NaCl solution over an extended period of time.

#### **MECHANICAL**

Mechanical eye injuries are the most common type of eye injuries. Studies show most eye injuries occur at work [15]. Vision loss following eye trauma is a serious health problem worldwide. Any of the ocular structures can be damaged after an eye injury. Classifications such as the Birmingham Eye Trauma Terminology System help to standardize terminology for mechanical eye trauma [16]. It is a simple, unambiguous and consistent system.

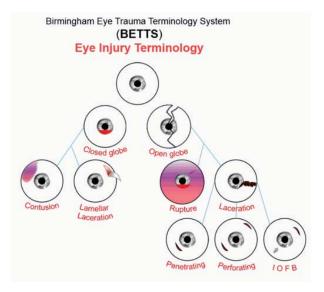


Fig 8. Birmingham Eye Trauma Terminology System (BETTS) [16]

Systems such as Ocular Trauma Score [17] provide a reliable method of predicting the visual outcome of eye injury based on clinical findings after the injury.

Every mechanical eye trauma should be consulted with an ophthalmologist. While most don't result in permanent vision deterioration or loss, some patients may require urgent surgery.

#### **THERMAL BURNS**

Ocular burns are a relatively uncommon injury. These types of ocular injuries constitute about 7-18% of injuries [18, 19]. The majority of thermal burns victims are young. Most cases of these type of injuries are work related or at home. The blink reflex causes the eyes to close when exposed to a thermal stimulus and prevents or limits corneal and conjunctival exposure and damage. Because of this eyelids thermal burns are significantly more common than other parts of the eye. First aid should be to rinse profusely with sterile isotonic saline solution and apply antibiotic ointment three to four times a day for seven days. Some cases may require skin transplant with tarsal plate reconstruction.

Most thermal burns affecting the conjunctiva or cornea are mild and heal without complications. First aid should be to rinse conjunctival sav with sterile isotonic saline solution and apply ophthalmic antibiotic ointment three to four times a day until full recovery. Some cases may require conjunctival fornix massage using a glass rod and antibiotic ointment to prevent the formation of adhesions between palpebral and bulbar conjunctiva.

#### ELECTRICAL

The most common ocular complication following an electric shock is the development of cataract. Other less common ocular injuries may include retinal detachment, macular hole and Purtscher retinopathy [20].

While cataract formation following electric shock is common, it remains one of the less frequent causes of cataract. Cataract forms usually after 1-2 months, probably due to the coagulation of lens proteins and osmotic changes following damage to the subcapsular epithelium [21]. Electric cataract should and can be treated with normal phacoemulsification followed by foldable in the bag implantation of posteriorchamber intraocular lens. If no other vision affecting damage occurred following the electric shock, visual acuit post-surgery can be satisfactory.

Retinal detachment and macular hole following electric shock aren't common and every case should be consulted with retinal specialist. There is very limited data about these types of complications but the prognosis should be similar to other causes.

Purtscher retinopathy is a rare condition first described in 1910 by Otman Purtcher in a man who fell from a tree and suffered cranial trauma [22]. It is described as chorioretinopathy associated with non-ocular trauma. It is an occlusive microvasculopathy [23]. Purtschers retinopathy retinal findings are cotton-wool spots, retinal hemorrhages, optic disc oedema and Purtscher flecken - retina whitening. It can also be associated with acute pancreatitis as a result of trauma [24]. Currently there are no official evidence based guidelines for treatment of Purtscher retinopathy. A systematic review did not find any difference in the improvement of visual acuity when they compared treatment with steroid with observation [25]. Some reports suggest metyloprednisolone pulses followed by oral steroids. Purtscher retinopathy cases are very rare and each case should be considered individually based on other symptoms.

# PRESSURE RELATED OCULAR BAROTRAUMA WHILE DIVING

Mask squeeze or mask related barotrauma is a type of soft tissue facial barotrauma injury that occurs most commonly while self-contained underwater breathing apparatus diving or freediving [26]. It is the most common type of injury amongst divers. During diving pressure increases outside the goggles or mask but the pressure inside remains at atmospheric value, resulting in negative pressure. This negative pressure pulls the eyes and periorbital soft tissues into the goggles and can sometimes create tissue damage [27]. Diving at deeper depths increases this pressure gradient and the likelihood of soft tissue damage. Oscillating pressure parallel to respiration inside the mask can also cause tissue damage. These types of injuries are more common with inexperienced divers. The most common symptom is benign subconjunctival haemorrhage but in sereve cases subperiosteal hemorrhage is also possible [28]. Patients with ocular surgery history are probably more susceptible to these types of injuries. To prevent this type of injury it is advised to exhale from the nose into the mask while descending [29].

Central Serous Chorioretinopathy is a potentially severe, recurring ocular disease in which fluid accumulates under the retina causing a serous retinal detachment and vision loss. Depending on the recurrence rate, the amount and location of fluid this can be a mild of vision threatening disease. The physiology behind central serous chorioretinopathy is not fully understood. Exposure to corticosteroid drugs and type A personalities are commonly associated with the disease. Some studies suggest that up to 4% of cases of central serous chorioretinopathy can be associated with diving, however the physiology of that link is still poorly understood [30].

#### CONCLUSION

Eye injuries amongst sailors and crew workers are one of the most common types of injuries. Most eye injuries are easily preventable with eye or full face protection. It is very important for these professionals to know how to react in case of an ophthalmic injury and how to prevent further damage. Early first-aid and fast ophthalmic consult can reduce the chance of permanent vision impairment.

#### REFERENCES

- M. R. Wilson, F. Wooten, and J. Williams, "Frequency and characteristics of ocular trauma in an urban population," Journal of the National Medical Association, vol. 83, no. 8, pp. 697–702, Aug. 1991, Accessed: Sep. 20, 2022. [Online]. Available: https://pubmed.ncbi.nlm.nih.gov/1956080/
- J. P. Whitcher, M. Srinivasan, and M. P. Upadhyay, "Corneal blindness: a global perspective," Bulletin of the World Health Organization, vol. 79, no. 3, pp. 214–221, 2001, [Online]. Available: https://pubmed.ncbi.nlm.nih. gov/11285665/
- 3. S. Ka, S. Pk, S. Ka, and S. Pk, "Occupational eye traumatism of members of vessel's crews of the Northern Water's

Basin," Journal of Clinical Research and Ophthalmology, vol. 6, no. 1, pp. 021–024, Jun. 2019, Accessed: Sep. 20, 2022. [Online]. Available: https://www.peertechzpublications. com/articles/JCRO-6-158.php

- 4. S. S. Ahmad, "Water related ocular diseases," Saudi Journal of Ophthalmology, vol. 32, no. 3, pp. 227–233, Jul. 2018, doi: 10.1016/j.sjopt.2017.10.009.
- M. Reyes-Batlle, I. Sifaoui, R. L. Rodríguez-Expósito, J. E. Piñero, and J. Lorenzo-Morales, "New Insights in Acanthamoeba," Pathogens, vol. 11, no. 5, p. 609, May 2022, doi: 10.3390/pathogens11050609.
- M. H. Nasef, S. Y. El Emam, M. S. ElShorbagy, and W. A. Allam, "Acanthamoeba Keratitis in Egypt: Characteristics and Treatment Outcomes," Clinical Ophthalmology (Auckland, N.Z.), vol. 15, pp. 1339–1347, 2021, doi: 10.2147/ OPTH.S301903.
- K. Megha, A. Thakur, S. Khurana, R. Sehgal, and A. Gupta, "Acanthamoeba keratitis: A 4-year review from a tertiary care hospital in North India," Nepalese Journal of Ophthalmology, vol. 12, no. 1, pp. 83–90, Jul. 2020, doi: 10.3126/nepjoph.v12i1.24769.
- Y. Hilliam, S. Kaye, and C. Winstanley, "Pseudomonas aeruginosa and microbial keratitis," Journal of Medical Microbiology, vol. 69, no. 1, pp. 3–13, Jan. 2020, doi: 10.1099/jmm.0.001110.
- D. Subedi, A. K. Vijay, and M. Willcox, "Overview of mechanisms of antibiotic resistance in Pseudomonas aeruginosa : an ocular perspective," Clinical and Experimental Optometry, vol. 101, no. 2, pp. 162–171, Oct. 2017, doi: 10.1111/cxo.12621.
- T. P. O'Brien, B. H. Jeng, M. McDonald, and M. B. Raizman, "Acute conjunctivitis: truth and misconceptions," Current Medical Research and Opinion, vol. 25, no. 8, pp. 1953– 1961, Jun. 2009, doi: 10.1185/03007990903038269.
- 11. A. A. Azari and N. P. Barney, "Conjunctivitis," JAMA, vol. 310, no. 16, p. 1721, Oct. 2013, doi: 10.1001/jama.2013.280318.
- 12. T. Y. Wong, B. E. K. Klein, and R. Klein, "The prevalence and 5-year incidence of ocular traumal1The authors have no proprietary interest in the methods or materials described in this paper.," Ophthalmology, vol. 107, no. 12, pp. 2196– 2202, Dec. 2000, doi: 10.1016/s0161-6420(00)00390-0.
- 13. S. C. Loon, W. T. Tay, S. M. Saw, J. J. Wang, and T. Y. Wong, "Prevalence and risk factors of ocular trauma in an urban south-east Asian population: the Singapore Malay Eye Study," Clinical & Experimental Ophthalmology, vol. 37, no. 4, pp. 362–367, May 2009, doi: 10.1111/j.1442-9071.2009.02035.x.

- 14. S. Harun, "Modification of classification of ocular chemical injuries," British Journal of Ophthalmology, vol. 88, no. 10, pp. 1353–1355, Oct. 2004, doi: 10.1136/ bjo.2004.046797/047308.
- 15. T. AlMahmoud, S. M. Al Hadhrami, M. Elhanan, H. N. Alshamsi, and F. M. Abu-Zidan, "Epidemiology of eye injuries in a high-income developing country," Medicine, vol. 98, no. 26, p. e16083, Jun. 2019, doi: 10.1097/ md.000000000016083.
- F. Kuhn, R. Morris, C. D. Witherspoon, and V. Mester, "The Birmingham Eye Trauma Terminology system (BETT)," Journal Francais D'ophtalmologie, vol. 27, no. 2, pp. 206– 210, Feb. 2004, doi: 10.1016/s0181-5512(04)96122-0.
- F. Kuhn, R. Maisiak, L. Mann, V. Mester, R. Morris, and C. D. Witherspoon, "The Ocular Trauma Score (OTS)," Ophthalmology Clinics of North America, vol. 15, no. 2, pp. 163–165, vi, Jun. 2002, doi: 10.1016/s0896-1549(02)00007-x.
- S. Bawany, T. Macintosh, and L. Ganti, "Ocular Thermal Burn Injury in the Emergency Department," Cureus, Feb. 2020, doi: 10.7759/cureus.7137.
- E. Masson, "Brûlures oculaires," EM-Consulte. https:// www.em-consulte.com/article/186598/brulures-oculaires (accessed Sep. 20, 2022), doi: 10.1016/s0181-5512(08)74391-2.
- AA. Sharma, Y. C. V. G. Reddy, A. P. Shetty, and S. M. A. Kader, "Electric shock induced Purtscher-like retinopathy," Indian Journal of Ophthalmology, vol. 67, no. 9, pp. 1497– 1500, Sep. 2019, doi: 10.4103/ijo.IJO\_1737\_18.
- 21. J. R. Saffle, A. Crandall, and G. D. Warden, "Cataracts: a long-term complication of electrical injury," The Journal of Trauma, vol. 25, no. 1, pp. 17–21, Jan. 1985, Accessed: Sep. 20, 2022. [Online]. Available: https://pubmed.ncbi. nlm.nih.gov/3965734/
- 22. "Purtscher, O. (1910) Noch Unbekannte Befunde Nach Schadeltrauma. Bericht Uber Die Zusammenkunft Der Deutschen Ophthalmologischen Gesellschaft, 36, 294-301.
  References - Scientific Research Publishing," www.scirp. org. https://www.scirp.org/(S(i43dyn45teexjx455qlt3d2q))/ reference/ReferencesPapers.aspx?ReferenceID=1346756 (accessed Sep. 20, 2022).
- K. Tripathy and B. C. Patel, "Purtscher Retinopathy," PubMed, 2022. https://www.ncbi.nlm.nih.gov/books/ NBK542167/ (accessed Sep. 20, 2022).
- 24. J. B. Alsberge, J. J. Chen, and H. R. McDonald, "Purtscherlike retinopathy in a patient with milk-alkali syndrome and pancreatitis," Retinal Cases & Brief Reports, Apr. 2021, doi: 10.1097/ICB.00000000001157.

- 25. A. I. M. Miguel, F. Henriques, L. F. R. Azevedo, A. J. R. Loureiro, and D. A. L. Maberley, "Systematic review of Purtscher's and Purtscher-like retinopathies," Eye, vol. 27, no. 1, pp. 1–13, Nov. 2012, doi: 10.1038/eye.2012.222.
- 26. J. C. Bowman and W. Gossman, "Diving Mask Squeeze," PubMed, 2022. https://www.ncbi.nlm.nih.gov/books/ NBK545224/
- 27. S. Ergözen, "Preventable Diving-related Ocular Barotrauma: A Case Report," Türk Oftalmoloji Dergisi, vol. 47, no. 5, pp. 296–297, Oct. 2017, doi: 10.4274/tjo.67503.
- C. Rosenberry, M. Angelidis, and D. Devita, "Orbital Subperiosteal Hematoma From Scuba Diving," Wilderness & Environmental Medicine, vol. 21, no. 3, pp. 250–252, Sep. 2010, doi: 10.1016/j.wem.2010.06.003.
- 29. C. Edmonds, B. Mckenzie, and R. Thomas, Diving medicine for scuba divers. 5th ed. Carnegie, Vic.: Jl Publications, 2013.
- 30. L. Deleu, J. Catherine, L. Postelmans, and C. Balestra, "Effect of SCUBA Diving on Ophthalmic Parameters," Medicina, vol. 58, no. 3, p. 408, Mar. 2022, doi: 10.3390/ medicina58030408.