The Neglected Eye: Ophthalmological Issues in the Intensive Care Unit

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Abstract

Background: The eye is not an organ immune to insults as a result of impairments to normal function or illnesses. In those patients that are intubated and/or sedated, the protective blink reflex is often not working properly, or not working at all. This paper will review some of the conditions of the eye most often encountered in the intensive care unit (ICU).

Methods: PubMed was searched using the keywords ophthalmological problems, ICU, ophthalmology, eye, keratitis, chemosis, candidemia, infections to locate reports of ophthalmologic problems in the intensive care unit and literature about recommendations for the management of those ophthalmologic conditions.

Results: The present study is a review of the recent literature related to the diagnosis and management of ophthalmological issues in the ICU.

Conclusions: The eye is an important, and often under utilized, diagnostic indicator of disease. In the ICU the eye is vulnerable to the increased potential of insult. It is necessary to prevent eye damage by trying to preserve its protective layers integrity and regularly examined in ICU patients.

Key words: Ophthalmologic, intensive care units, ICU, eye, vision, corneal abrasion, keratitis.

Introduction

Patients in the intensive care unit (ICU), present physicians with new challenges in diagnosis and management on a daily basis. A typical ICU patient may present with multiple organ involvement with a diverse amalgam of signs and symptoms that give

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Joseph Varon, MD, FACP, FCCP, FCCM 2219 Dorrington Street Houston, Texas 77030, USA Tel: +1-713-669-1670 Fax: +1-713-669-1671 Email: Joseph.Varon@uth.tmc.edu the practitioner hints into making a correct diagnosis. Ophthalmologic symptoms are as important to making an appropriate diagnosis as a patient's cough, nausea, or edema.

To neglect examination of the eye in the course of attempting to make a correct diagnosis would be a mistake, as it would disregard valuable information about the patient, but also because the practitioner may overlook an important aspect in the overall treatment of the patient.

The eye is a very specialized, highly vascular organ that is not only susceptible to complications from concomitant pathologies, but it is also vulnerable to infections, abrasions and other exogenous processes in the critically ill patient. Ophthalmological issues arising in the ICU can be seen with presentations that

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range from corneal abrasions and keratitis to more serious processes like endophthalmitis, glaucoma, autoimmune disease, and vascular collagen illnesses [1,2].

Examination of the eye yields important information necessary for making accurate differential diagnosis; hence, ocular examination should always be considered an important element of the patient's examination [3]. A funduscopic examination may give insight into a process such as an increased intracranial pressure with the presence of papilledema. If examination of the eye is overlooked when treating a critical patient, it may increase the possibility of error in making an accurate diagnosis. Even if the patient's condition indicates a poor prognosis, or high mortality rate, permanent visual acuity defects can be devastating. If the purpose of treating a patient is to improve the patient's quality of life, this improvement may be compromised if the eye is neglected.

Corneal exposure

The eye's natural protection is composed of the upper and lower lids, lacrimal film, and the conjunctiva. The eyelids and tears help flush organisms and abrasive particles from the eye with each blink [4]. The conjunctiva has lymphoid tissue that provides the eye with immediate immune response [4]. If any of these protective mechanisms are disrupted, the eye's natural protection will be compromised.

The use of sedatives and neuromuscular blockers are quite common in the ICU and in the management of patients on mechanical ventilation. Ophthalmologic complications when using these agents must be taken into consideration, in order to prevent further ocular damage, which in some cases become irreversible [4]. Both sedatives and neuromuscular blockers produce lagophthalmos(incomplete eye closure) by reducing the muscular tone and contraction of the orbicularis muscle [4]. Studies have found that up to 75% of the patients who are heavily sedated develop lagophthalmos [5]. When incomplete eyelid closure occurs in the heavily sedated, 2 things happen: 1) the lacrimal fluid looses

its properties and is significantly reduced in quantity and quality with severe dry eye syndrome and 2) Bell's phenomenon disappears, leaving the anterior part of the eye unprotected by the suppression of the eye's natural rotation, while closing the eyelids, during sleep [2]. The presence of lagophthalmos may induce drying of the epithelium, which can progress to exposure keratopathy and a subsequent corneal ulcer [4].

The importance of preventing corneal exposure (**Figure 1**) is considerable in preventing more serious ophthalmological processes. Bacteria and viruses can only penetrate the corneal epithelium once it is damaged, such as in patient with poor lid closure [6]. Conditions such as corneal exposure in the ICU, are preventable [1] by addressing them in a timely manner, and by being cognizant of the development of new signs or symptoms of ophthalmic complications [4].

Suresh *et al* in 2000, showed that 42% of the patient in the ICU have ocular surface disease [4], including corneal exposure. The authors evaluated the effectiveness and efficiency of an algorithm they developed in the prevention of ocular surface disease in sedated and unconscious patients in the intensive care unit. They showed that with the correct use of their algorithm, the prevalence of ocular surface disease was as low as 8.7% [4]. Patients with lagophthalmos can be categorized into 4 groups: patients with lids closed, conjunctive exposure, and cornea exposed, and patients who were prone ventilated. There are different prevention measures which can be employed for patients in each of the 4 categories [4].

In 2005, Dawson *et al* [7] developed an algorithm for managing ophthalmic disorders in the ICU. They found a prevalence of incomplete lid closure of 20.8% in 31 patients [7]. Dawson's algorithm is more complete when compared to Suresh's algorithm, but it is also more complicated. An important aspect of Dawson's eye care guideline is that it emphasizes treatment and diagnosis of the patient's ocular disorder.

While factors like the Glasgow coma scale, intubation and length of stay within the ICU have shown to be good predictive markers for the development of ocular surface disorders, the most important predictive factor is incomplete eyelid closure [6]. Therefore the principal issue when trying to prevent exposure keratopathy is maintaining proper eyelid closure.

Corneal abrasion

Corneal abrasions in the ICU are often caused as a complication of lagophthalmos, which allows the cornea to dry and therefore jeopardizes the integrity of the eye's epithelium [2]. Likewise, the use of misplaced ventilation masks may rub against the eye, irritating it and further provoking a corneal abrasion [2]. Corneal abrasions present with severe pain, blurry vision and red eye [2,8]. Once the eye's epithelium is dry, an ulcer may develop (**Figure 2**), that can lead to compromising the integrity of the eye, resulting in irreversible visual loss [8].

The frequency of corneal abrasions, as well as other ocular surface disorders, in hospitalized patient increases with paralysis, sedation, and prolonged hospital stays [9]. In heavily sedated and paralyzed patients, lagophthalmos may result in drying of the cornea [8]. Concomitantly, drying of the cornea may lead to more severe pathologies such as keratitis or corneal perforation. Patients with continuous sedation have shown a 35% incidence rate of ocular surface disorders, and the incidence is higher (39%) in patients with continuous paralysis [9]. Moreover, conjunctival and corneal abnormalities may be associated with trauma, infections, coma, and mechanical ventilation [9]. All of these conditions may be encountered, or developed in the ICU.

The combination of corneal exposure and lagophthalmos decreases the natural defense of the eye, and the formation of corneal abrasion [9]. In 1997, Imanka *et al* showed in a prospective study that 60% of the patients, that were heavily sedated or on muscle relaxants present some degree of corneal erosion [9]. They demonstrated a positive correlation of incomplete lid closure and corneal erosion, with a 100% prevalence of corneal erosion in patients with lagophthalmos [9]. Several treatment options are available for the management of corneal abrasion;

however, there is no consensus of opinion on what is the most appropriate care plan. With the use of preventive measures in paralyzed or heavy sedated patients, such the use of passive closure of the eyes or artificial tear ointments, the prevalence of corneal abrasion can be significantly diminished [8]. The incidence of corneal abrasion in patients with passive eyelid closure alone has been reported as 18% in one eye, and 4% in both eves, with the application of eye lubricant every 4 hours no corneal abrasions presented [8]. When employing passive evelid closure, the evelids should be taped shut horizontally from the epicanthus to the eyelid angle, as vertical taping can injure the eye's epithelium instead of providing protection [4]. Compared to lubrication, the use of polyethylene covers and bandage contact lenses are more effective in preventing corneal exposure and corneal abrasion [7].

Keratitis

In the ICU, the organism most commonly responsible for the development of bacterial keratitis is *Pseudomonas* aeruginosa, which produces a rapid and severe infection and may result in corneal perforation [3]. Pseudomonas keratitis and respiratory colonization by Pseudomonas are often seen concomitantly. It has even been suggested that colonization of the conjunctivae is produced by the suction of secretions from intubated patients in the ICU [3]. Parkin et al found that the incidence of pseudomonal ocular isolation in critically ill patients decreased if eye protection was practiced, even when respiratory tract colonization remained high [3]. The combination of lagophthalmos and nosocomial contamination of the eye are the conditions that bacteria such as Pseudomonas require to produce corneal infections.

Parkin *et al* conducted a 2 phase study from 1988 to 1995. In the first phase he developed a guideline to prevent *pseudomonas* keratitis in patients in the ICU [3]. During this phase, the only ophthalmologic care patients received was the application of a polyacrylamide gel [3]. In the second phase of his study he executed treatment guidelines developed in phase 1 to test efficacy. The results demonstrated the

isolation of *Pseudomonas* in the eye decreased from 0.8% to 0.05% (p < 0.001) in patients in the ICU, once the guidelines had been followed [3].

Chemosis

Chemosis is edema of the conjunctiva. Patients with cirrhosis, malnutrition and nephrotic syndrome, commonly encountered in the critically ill, tend to have decreased oncotic pressure due to protein loss (Figure 3). When a patient's oncotic pressure is low and there are concomitant limitations in movement; extended periods of time in supine position provoke the accumulation of liquid on their face that may lead to conjunctival edema (i.e., chemosis) [2]. The sclera and conjunctiva are united by fibers of connective tissue, creating a virtual space between them where fluid accumulates causing swelling of the conjunctiva, making it protrude. In some cases [9] the swelling is so severe that eyelid closure is not possible [2].

Patients in the ICU often experience fluid overload, electrolyte problems, and increased permeability. All of these are situations may potentially lead to the conjunctival edema [9]. Likewise, patients with renal disease and cardiovascular disease are at greater risk for developing chemosis. When these patients are placed on mechanical ventilation, the fluid retention increases, precipitating the risk of developing chemosis [3]. Venous pressure increases due to positive pressure in mechanical ventilation; this decreases blood drainage from the ocular vessels, hence causing chemosis [9]. Once chemosis has developed repair of the cell damage is slow, particularly in patients with multiple organ failure whose condition prevents them from having an adequate response to tissue damage [9]. This condition leaves the eye exposed to damage and infection [3].

Suresh and colleagues reported a high incidence of chemosis in the ICU (60%) [4]. In some cases the degree of chemosis may be so severe that closure of the eyelids can only be obtained with the use of a frost suture [4]. Both preventive and treatment measures should be taken into consideration as chemosis is a predisposing factor to other disorders such as corneal abrasion [3]. The use of ophthalmologic gel and gauze are recommended, as well as Saran wrap covering the chemotic area; however, caution must be taken in order to prevent the gel from drying, as gauze alone can provoke corneal abrasion [3].

Acute angle closure glaucoma

Anticholinergic drugs are often used in the ICU. One of their effects is to dilate the pupil. In susceptible patients this can lead to acute angle closure glaucoma [2] which can present with signs of a painful red eye with a non reactive pupil that is mildly dilated and symptoms such as severe ocular pain with concomitant confusion and emesis [2]. Topiramate is an antiepileptic drug used not only in the treatment of epilepsy but in the treatment of depression, migraine, and neuropathic pain, as well as other psychiatric disorders [10]. The use of topiramate has been known to cause acute secondary glaucoma, being bilateral in most of the patients [10]. The typical presentation time for topiramate induced glaucoma is an approximately 2 weeks, although it may occur within hours if the dose is high [10]. The physician should be mindful of the possibility that drug induced acute glaucoma may occur when using topiramate. The primary treatment for topiramate induced glaucoma is based on stopping topiramate and applying oral and topical aqueous suppressants [10]. Drug induced glaucoma is not necessarily related to chronic glaucoma.

Ophthalmological issues in the diabetic patients in the intensive care unit

Diabetic patients have ophthalmological illnesses including diabetic retinopathy, vascular events including arterial and vein occlusions, cranial nerve palsies, and proneness to opportunistic eye infections [11]. Many of these complications can occur as in patients, while being treated in an ICU. Vascular events such as central retinal artery occlusion, central retinal vein occlusion may be emergencies that must be addressed within a short period of time, to better improve the outcome of the patient [11].

Central retinal artery occlusion

Whenever a patient presents with new onset of painless and near complete monocular vision loss, occlusion of the central retinal artery must be considered [11,12] Central retinal artery occlusion is usually caused by an embolus (Figure 4), produced elsewhere in the vascular system that travels to the retinal artery impeding the regular flow of blood [11]. Patients with diabetes develop vascular sclerotic changes faster then non diabetic patients [13]. When a diabetic patient has arterial hypertension, the risk of developing retinal artery occlusion significantly increases [11]. When a sudden loss of vision develops, a funduscopic examination must be performed in order to evaluate the vascular changes in the eye. Two hours after the event there is segmentation of the vessels blood column [11]. In some instances the plaque or embolism (such as Hollenhorst plaque) may be visualized as refractile, and are usually bigger then the vessel [11]. If a funduscopic examination is performed 24 hours after the event has attenuated arteries and pallor of the fundus caused by retinal edema is typically observed [11].

In most cases vision loss is permanent within 2 hours of the event; however, if an anterior chamber paracentesis can be performed to reduce ocular pressure and restore blood flow within 2 hours of the event, vision may be partially restored [11]. The use of fibrinolytic therapy may be a useful treatment, and there are reports of vision being restored up to 12 hours after the artery occlusion [11]. Other treatment methods include breathing into a paper bag, lowering the eye pressure medically, and the use of hyperbaric oxygen.

Central retinal vein occlusion

Central retinal vein occlusion is not only associated with diabetes mellitus, but also with other clinical conditions that are common among ICU patients such as arterial hypertension, glaucoma, atrial fibrillation, and the use of medications such as angiotensin-converting enzyme inhibitors, aspirin, and warfarin [14]. When the central retinal vein is occluded the symptoms are somewhat similar but less dramatic than those seen with central retinal artery occlusion [11]. It is a common finding to note hemorrhages, exudates, and retinal tortuous veins starting at the obstruction during a funduscopic examination and sometimes even macular edema. [11]. Treatment includes intravitreal steroids when there is risk of ischemic changes or severe macular edema [15]. In addition, there is recent evidence, that intravitreal Bevacizumab can improve the outcome for patients with central retinal vein occlusion [16].

Ocular Motor Nerve Palsies

All 3 cranial nerves (CN) that provide motor function to the eye movement (i.e., III, IV and VI) can be compromised in a diabetic patient causing diplopia. The most common nerve involved in motor nerve palsies is CN III [11]. Clinically, motor nerve palsies present with mild ocular pain, diplopia, and ptosis with normal pupil. In contrast, palsies produced by aneurysmal compression have a fixed dilated pupil [11]. If CN III palsy includes pupillary involvement, both a brain magnetic resonance imaging and either magnetic resonance angiography or a computed tomographic arteriogram if available should be performed. In addition, cerebral angiography is also recommended prior to treatment via coiling [11]. When the pupil is normal, there is typically no need for neuroimaging. Motor nerve palsies in the diabetic patient are often benign, resolving within 3 months; however, it should be noted that patients with a history of nerve palsies are at increased risk for reoccurrences [11].

Rhino orbital cerebral Mucormycosis

Mucormycosis is an opportunistic fungal infection found in immunocompromised patients with uncontrolled diabetes [17]. When it mucormycosis involves the eye and its orbit it is known as rhino orbital cerebral mucormycosis (ROCM). Although it is not a common illness (a prevalence of 0.15% within the diabetic population) [11], diabetes is the most common predisposing factor leading to ROCM (60 81%) [18]. When ROCM presents, it is a very aggressive infection. Proptosis, ophthalmoplegia, chemosis, and vision loss from central retinal artery occlusion occurs in 80%, 89%, 74% and 80% of the patients, respectively [18]. Diabetic ketoacidosis is also a common finding in ROCM. In a retrospective interventional analysis of the medical records, Bhansali et al found that approximately one half of the patients with mucormycosis had concomitant diabetic ketosis/ ketoacidosis [18].

Proptosis and ophthalmoplegia are due to the invasion of the orbit, and vision loss is generally caused by cavernous sinus thrombosis [18]. Other causes for vision loss in patients with mucormycosis are central retinal artery occlusion, endophthalmitis and vascular involvement [18].

Diagnosis of mucormycosis is made based physical and histopathological findings under direct microscopy, and cultures on Sobroud's agar [18]. Treatment of ROCM with amphotericin B alone has limited efficacy, and surgical debridement should be added [17,18]. Other treatments such as the use of hyperbaric oxygen may also be useful. Exenteration is the most radical treatment for ROCM. While this treatment severely decreases quality of life, it may prove to be life saving and should be considered in only the most severe cases [12]. Hargrove et al found that patients with ROCM who had fever where most likely to die, and it was in these patients that exenteration made a significant survival difference [17].

Endophthalmitis

Endophthalmitis is the inflammation of all of the eye's cavities. In the ICU patient endophthalmitis most commonly caused by *Candida* (i.e., invasive candidemia) that frequently involves ocular infection within 15 days after the onset of fungemia [19,20]. Allison and colleagues have reported that 17% of patients with candidemia present with endophthalmitis, but incidences as high as 37% have been reported in the literature [21]. The incidence of bilateral endophthalmitis has been reported to be as high as 62% [21]. The percentage of patients treated for endophthalmitis in the ICU is ~77% with a mortality of 80% and a 6 month survival rate of 15% [21]. The

<u>mere</u> presence of endophthalmitis is an indicator of <u>poor prognosis and high mortality</u> in patients with candidemia [21].

The most common of the Candida organisms to cause endogenous endophthalmitis is *Candida albicans* followed by *Aspergillus sp.* [2]. Endogenous endophthalmitis includes both chorioretinitis and vitreitis processes [20]. These organisms infect the choroid and the vitreous cavity via vascular dissemination [2].

Candidemia is often the result of a nosocomial infection. Patients with intravenous access lines are at increased risk of developing fungemia with endophthalmitis as the microorganism tends to infect the blood stream via the access line [2]. Endophthalmitis secondary to Candida can be seen in immunocompromised patients that may or may not have candidemia. The initial symptoms experienced by patients with endophthalmitis are floaters, ocular pain and decreased vision [2]. The percentage of patients receiving treatment for endophthalmitis in the ICU is ~77% with an 80% mortality; and an overall mortality of 70% [2]. Treatment for endophthalmitis produced by *Candida albicans* is long and has a poor prognosis for maintaining the same vision as prior to infection, but if treatment is instituted some degree of visual acuity can be preserved in most cases with an average survival of 6 months with adequate treatment [2]. The prognosis is even more dismal in patients with infections caused by *Aspergillus* [2]. A routine ophthalmologic examination can help treat endophthalmitis in an opportune fashion, confirm diagnosis of candidemia in otherwise asymptomatic patients, and be a prognostic marker for patients already diagnosed with fungemia.

Ophthalmologic manifestations of systemic disease

The physician should be cognizant of the importance of a complete eye examination and exploration. Ocular examination may provide valuable clues in aiding the physician to make an accurate diagnosis. Both autoimmune and collagen vascular diseases often have ocular manifestations. Ocular examination may also be used to determine the severity of a disease process or the state of its progression [22].

Dry eye can present in a wide range of collagen diseases like Sjögren's disease and rheumatoid arthritis [22]. Keratitis is most commonly caused by a viral or bacterial infection but it may also be seen in pathologies such as rheumatoid arthritis and Wegener's granulomatosis [22]. Conjunctivitis is sometimes caused by Wegener's granulomatosis, Steven-Johnson syndrome, and Crohn's disease [22].

Uveitis, defined as inflammation of the iris, choroid and ciliary body, may be present with diseases such as AIDS, tuberculosis, Sjögren's syndrome, rheumatoid arthritis, and Wegener's granulomatosis [22]. Suspicion of anterior uveitis comes when decreased vision and photophobia present concomitantly. Anterior uveitis is uncommon and usually presents with less pain, and considerably more compromised visual acuity [22]. Treatment for anterior uveitis must be urgent and the use of cycloplegics is indicated, rare cases of viral uveitis must be excluded before using steroids [22].

Blurry vision can be caused by many disorders located in any part of the ocular globe. A <u>common cause of</u> <u>blurry vision is hyperglycemia in the diabetic patient</u> [22]. The <u>concentration of glucose within the eyes</u> <u>fluids causes this distortion of sight.</u> The treatment includes adequate glycemic control.

Bleeding diathesis such as hemophilia and von Willebrand disease presents with abnormal bleeding and ecchymosis. Subconjunctival hemorrhages are most likely to be caused by a traumatic event, but in some cases they might be suggestive of a bleeding disorder such as those mentioned above [22].

Ptosis is manifested in several illnesses. Pancoast tumors can present with pain in the arm and ipsilateral Horner's syndrome [22]. Both aneurysms and neuromuscular disorders such as myasthenia gravis can also present initially with ptosis and diplopia. The former involved the pupil and the latter spares it [22].

Ophthalmologic infections caused by methicillin-resistant *Staphylococcus aureus*

One of the most serious infections of the eye that the ICU patient may encounter is caused by methicillinresistant Staphylococcus aureus (MRSA), which can present in 4 ways: 1) asymptomatic, 2) conjunctivitis, 3) intraepithelial infiltrations, and 4) superficial or severe keratitis [20]. The predisposing factors for these patients are prolonged use of antibiotics, prolonged hospitalization, and immunological depression [20]. The incidence of MRSA infections has increased in the past 6 years from 4.1% to 16.7% [21]. Approximately 40% to 70% of the nosocomial infections in the ICU have been reported to be caused by MRSA [23]. The suggested treatment is based on antibiotic therapy with ofloxacin and vancomycin (with 100% sensitivity) [21]. The use of prophylactic vancomycin ointments for patients with high ophthalmological risk is controversial [24].

Conclusions

Vision is extremely valuable as a quality of life factor and should not be overlooked during any patient examination in the ICU setting. Patients who are sedated or unconscious are at greater risk for corneal insults and infections than those that are able to blink. Adequate eye care should include frequent assessment from both physicians and nursing personnel, and should be considered the standard of care in the ICU. Figure 5 represents an algorithm (i.e., guide) of care for the eyes of those patients in the ICU. During assessment the patient should be inspected from a parallel point of view, as opposed to a perpendicular point of view to ensure adequate closure in those patients sedated or unconscious. The use of ointments instead of liquid lubricants may be of greater benefit in retaining static moisture on the eye surface that does not have adequate tear protection. When suctioning a patient, the nurse should always cover the eye of the side that she is suctioning with a gauze, to prevent ocular contamination from the oral flora. Likewise, oral care should be maintained in the patient to prevent oral bacterial or fungal colonization that may spread to,

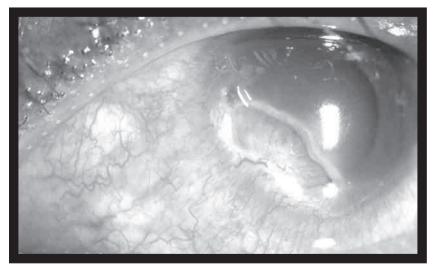
or contaminate, the eyes. Ocular examinations should be performed when new medications are added in the management of a patient's condition that carry risks of ocular involvement such as topiramate. Early detection of candidemia is also important to maintaining the good condition of the eye. When damage to cornea or conjunctiva arises despite the proper attention, swabs of the eye fluids and consulting with ophthalmologist should not be delayed. Similarly, high risk patients, such as those with diabetes or arterial hypertension, should closely be examined and monitored for the presence or development of ophthalmic conditions, particularly if the conscious patient reports vision lost or floaters.



Figure 1. CORNEAL EXPOSURE FROM LAGOPHTHALMOS

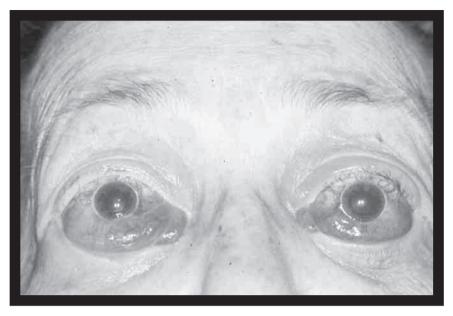
Corneal exposure produced by lagophthalmos can result into corneal exposure. This is commonly produced in the sedated patient, who does not have complete lid closure, leaving the cornea unprotected.

Figure 2. PERIPHERAL CORNEAL ULCER



Corneal ulcers are a step up the ladder on ICU ophthalmologic pathology. They can be very easily produced in patients whos eye care is overlooked.

Figure 3. SEVERE CHEMOSIS



Changes in oncotic pressure produce edema of the conjunctiva, chemosis. Severe chemosis can impede closure of the eyelid, further complicating the eye's illness.

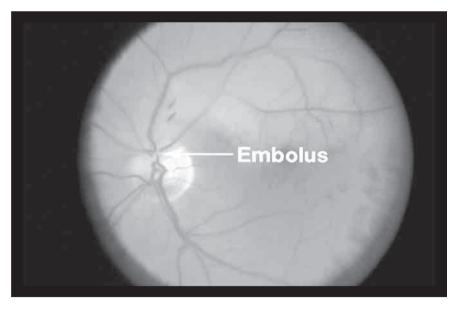
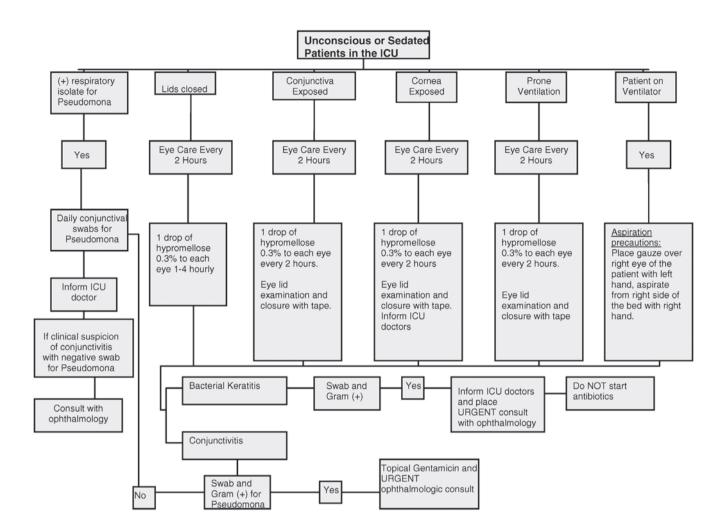


Figure 3. BRANCH RETINAL ARTERY OCCLUSION WITH RETINAL EDEMA

An embolus in the retinal artery will produce an occlusion in blood flow. Notice the embolus is refractile and bigger than the vessel.





Patient care following this guideline, facilitates diagnosis and adequate initial management in eye illness. The early and proper intervention in ophthalmological issues makes a difference in the patient outcome. This algorithm can serve as a guide in initial management.

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