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EDITORIAL

The Second Congress of the Romanian Society of Cataract and Refractive Surgery, connected to The Annual Conference of the Romanian Retina Society took place in the middle of June at the seaside, in Eforie Nord.

The conjunction of these two conferences was an experiment that wanted to solve an older issue of the Romanian Society of Ophthalmology: the increasing number of congresses and the limited time to attend them all.

I think this association was a great success, with a numerous audience of more than six hundred ophthalmologists from Romania and also from abroad.

The event started on Thursday with a very interesting session of the Annual Conference of The Romanian Retina Society about anti-VEGF therapy in retinal diseases. Ophthalmologists famous for their interest in this field presented an update regarding the possibilities and limitations of this therapy that has had such a dynamic development.

Fig. 1 Florian Balta, MD., President of the Romanian Retina Society

The following day began with a session addressed both to anterior and posterior pole surgeons: Combined pathology of the anterior segment-posterior segment. Modalities to solve complications of the anterior segment surgery, by using different techniques of posterior vitrectomy were shown.

The last session of this congress demonstrated the high level of competence of Romanian posterior segment surgeons in solving traumatic pathology.

In the same afternoon, the Congress of the Romanian Association of Cataract and Refractive Surgery began.

The first session was dedicated to cornea and corneal transplantation. During this session, Thierry Chazalon, MD., (Nantes, France), a friend of the Romanian Society of Ophthalmology, shared his experience in modern techniques of corneal transplantation, especially DSAEK, with his Romanian colleagues. All these were followed by a very informative symposium on corneal cross-linking.
Although Saturday was a day with a very dense schedule, exciting topics were approached: complications of cataract surgery, refractive surgery of the lens, special cases in cataract surgery, which managed to keep a vivid interest and to incite to active participation from the audience.

A very special event that I wish to point out was the launching of the new format of our journal, “Oftalmologia”. Calin Tataru, MD., the President of the Romanian Association of Cataract and Refractive Surgery and Vice President of the Romanian Society of Ophthalmology made a short, but comprehensive presentation of the reasons why this had to happen. Our review will have a new name: “Romanian Journal of Ophthalmology”, a new graphic format, and it will be printed by another publisher. Times of great changes require us to deliver great things!
Finally, the last day of the congress was entirely reserved to refractive surgery, a modern field with a spectacular development.

The international participation was even greater than mentioned previously, with interesting presentations from: Thierry Chazalon, MD., on corneal transplantation and refractive surgery, Rhonda Waldron, MD., (USA), on special techniques of biometry, P. Gomez, MD., (Mexico), on epidemiology of diabetic retinopathy and also others. A special mention goes to the course on ocular ultrasound examination (for beginners and advanced users) held by Tatiana Kisseleva, MD., (Russia).

Taking into consideration the duration of the congress, the dense schedule and the high number of participants, I can also say that all the organizing details were carefully managed; from choosing the Conference Center to planning the social events, in order to provide ample space and adequate conditions for presentations, and also to create a relaxing and friendly environment for the participants, by the beautiful pool side in the evenings.

As a long time member of different Organizing Committees of many congresses, I would like to congratulate my colleagues: Florian Balta, MD., Calin Tataru, MD., Horia Stanca, MD., Constantin Mihai, MD., and others, for the great success of this congress.

Overall, this congress managed to show that with great effort and good organizing skills, we could manage to address the issue of lesser time and increasing number of congresses successfully. I can only hope that next year’s congress will rise to the level of this one, and so, a great tradition will continue.

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AGE-RELATED MACULAR DEGENERATION

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Abstract
Objectives: The objective of our study was to review the current knowledge on Age-Related Macular Degeneration, including pathogenesis, ocular manifestations, diagnosis and ancillary testing.
Systematic review methodology: Relevant publications on Age-Related Macular Degeneration that were published until 2014.
Conclusions: Age-related macular degeneration (AMD) is a common macular disease affecting elderly people in the Western world. It is characterized by the appearance of drusen in the macula, accompanied by choroidal neovascularization (CNV) or geographic atrophy.
Keywords: choroidal neovascularization, geographic atrophy, age related macular degeneration

Introduction
Age-related macular degeneration is a common, chronic, progressive degenerative disorder of the macula that affects older individuals and features loss of central vision as a result of abnormalities in the photoreceptor/retinal pigment epithelium/Bruch’s membrane/choroidal complex often resulting in geographic atrophy and/or neovascularization. Advanced AMD can be classified broadly into two types: dry and wet. Although dry AMD accounts for the majority of all diagnosed cases, wet AMD is responsible for the majority of the severe vision loss and it usually occurs over weeks to months. Although neovascularization has been the most common cause of severe vision loss, geographic atrophy, the most advanced form of dry AMD, can cause a significant loss of vision as well.

Epidemiology
Globally, AMD ranks third as a cause of blindness after cataract and glaucoma. Most of the affected individuals live in developed countries. In general, advanced AMD is rare before the age of 55, and more common in persons of 75 years and older. The prevalence of neovascular AMD and geographic atrophy appears to vary in different ethnic and racial groups throughout the world. The prevalence of advanced AMD increases with each decade after the age of 50 with the highest prevalence occurring after the age of 80.

Risk factors
Risk factors for AMD may be broadly classified into personal or environmental factors (e.g., smoking, sunlight exposure, and nutritional
factors including micronutrients, dietary fish intake, and alcohol consumption).

Personal factors may be further subdivided into sociodemographic (e.g., age, sex, race/ethnicity, heredity, and socioeconomic status), ocular (e.g. iris color, macular pigment optical density, cataract and its surgery, refractive error, and cup/disc ratio), and systemic factors (e.g., cardiovascular disease and its risk factors, reproductive and related factors, dermal elastotic degeneration, and antioxidant enzymes).

Risk factors for progression to choroidal neovascularization. Presence of five or more drusen, hyperpigmentation, systemic hypertension, one or more large drusen (> 63 µm in greatest linear dimension), white race, and smoking.

Pathogenesis

The cause of AMD is currently being elucidated through the molecular dissection of histopathologic specimens and genetic linkage analyses by using different populations. Early in the disease process, lipids are deposited in Bruch's membrane, possibly from failure of the RPE to process cellular debris associated with outer segment turnover. Only later in the disease process are drusen visible. The appearance of drusen is the earliest visible clinical sign of AMD.

Analysis of drusen reveal that they contain lipid, amyloid, complement factors, and additional cellular components [1,2].

The appearance of drusen is preceded by or concomitant with the thickening of the Bruch's membrane collagenous layers, degeneration of elastin and collagen within Bruch's membrane with calcification of the membrane, increased levels of advanced glycation end products, and accumulation of lipids as well as exogenous proteins [3]. These changes may serve as a hydrophobic barrier to impede the passage of fluid and nutrients between the choroid and outer retina resulting in relative ischemia. Subsequent ingrowth of neovascularization from the choriocapillaris may then occur through fractures in Bruch's membrane [4].

Ocular manifestation

Dry Age-Related Macular Degeneration

Drusen are one of the earliest signs in AMD. Clinically, typical drusen appear as focal, whitish yellow excrescences deep to the retina. Typical drusen deposits are located beneath the retinal pigment epithelium and Bruch's membrane and vary widely in number, shape size, and distribution. Most drusen are 20-100 µm and are characterized as hard or soft.

Hard drusen, which appear as round, discrete yellow-white spots are commonly identified in many populations. They are not age-related and do not carry an increased risk for the development of neovascularization [5,6]. In contrast, soft drusen are ill defined, with non-discrete borders, measuring 63 µm or greater. Different studies and trials have indicated that large, soft, confluent drusen are age-related and associated with a higher risk for the development of advanced AMD with neovascularization [6,7].

Geographic atrophy is easily recognized clinically, as it appears as a well-demarcated area of decreased retinal thickness, compared to the surrounding retina, with a relative change in color that allows an increased visualization of the underlying choroidal vessels. Pigmentary alteration may be present, either hypopigmentation or hyperpigmentation, surrounding the macular atrophy.

If the foveal center is spared, good visual acuity may be preserved, although reading vision may remain poor because of a constricted central visual field [8].

Wet (neovascular) Age-Related Macular Degeneration

Wet AMD is characterized by the presence of neovascularization within the macula.

Choroidal neovascularization (CNV) is an ingrowth of new vessels from the choriocapillaris through a break in the outer aspect of Bruch's membrane into the subpigment epithelial space.

The clinical manifestations of neovascular AMD can include the following: subretinal fluid, intraretinal fluid, retinal, subretinal, or sub-RPE hemorrhage, lipid exudates, gray or yellow-green discoloration or plaque-like membrane, RPE detachment, RPE tear.

In the end-stage of the disease, the neovascularization results in a fibrovascular or atrophic macular scar (disciform scar), and subsequent permanent damage to the central vision [9-11].
**Pigment epithelial detachment** - a retinal pigment detachment (PED) may be caused by serous fluid, fibrovascular tissue, hemorrhage, or the coalescence of drusen beneath the RPE. Serous PED manifests as a dome shaped detachment of the RPE, exhibiting bright, diffuse hyperfluorescence with progressive pooling in a fixed space [12]. Hemorrhagic PED manifests as a dark elevation of the RPE due to underlying blood, showing blocked fluorescence throughout all phases of angiography [13].

**Diagnosis and ancillary testing**

Clinical examination is usually sufficient to establish a diagnosis of AMD, although subtle macular abnormalities are best detected with the help of ancillary tests such as fundus autofluorescence, optical coherence tomography, fluorescein angiography, and indocyanine green angiography.

**Optical coherence tomography** may be a useful ancillary test in any stage of AMD. In patients with dry AMD, the high definition B-scans are useful to assess the ultra-structure of drusen and to examine adjacent retinal layers that can be compromised by the disease process. The progression of early AMD to severe forms, such as geographic atrophy, can be monitored by OCT. The high definition B-scans can be used to identify some of the wet AMD features, such as the presence of intraretinal or subretinal fluid, presence of retinal PEDs, which can be classified in serous, fibrovascular, and hemorrhagic PEDs.

**Fundus autofluorescence** represents an imaging modality capable of reflecting the morphological changes associated with the metabolism of lipofuscin. Areas of geographic atrophy exhibit very low to extinguished fluorescence signals (dark) due to loss of RPE and lipofuscin, which leads to a region with a high contrast transition between the area of atrophy and perilesional retina.

Fluorescein angiography is usually performed to confirm the presence of neovascularization and identifies the characteristics of the lesion, including the location and composition of the neovascularization. Based on the angiographic patterns of fluorescence, the neovascular lesion may be categorized as either classic or occult. Classic CNV is characterized by bright, uniform, early hyperfluorescence exhibiting leakage in the late phase and obscuration of the lesion's boundaries.

Occult CNV is angiographically recognized by one of two patterns: fibrovascular PED or late leakage from an undetermined source. Fibrovascular PED is characterized by an area of irregular elevation of the RPE (which is neither as bright nor as discrete as in classic CNV), often with stippled hyperfluorescence present in the midphase of the angiogram and leakage or staining by the late phase [13].
Indocyanine green angiography was used to diagnose and guide treatment in patients with AMD. The dye’s characteristics enabled this mode of angiography to delineate the choroidal circulation better than fluorescein angiography.

In patients with dry AMD, indocyanine green angiography might help identify plaques representative of asymptomatic choroidal neovascularization, which may represent areas of occult CNV, or watershed zones that may be predictive of future exudative transformation.

Indocyanine green angiography is of a particular value in the following circumstances:
- Occult or poorly defined CNV
- CNV associated with overlying hemorrhage fluid or exudate
- Distinguishing serous from vascularized portions of a fibrovascular PED [14]

References

NOVELTIES IN MEDICAL TREATMENT OF GLAUCOMA

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Abstract
The purpose of this study is to review the current medical treatment and the new and better alternatives for patients with glaucoma.
Glaucoma refers to a group of related eye disorders that have in common an optic neuropathy associated with visual function loss. It is one of the leading causes of irreversible blindness worldwide. Glaucoma can damage vision gradually so it may not be noticed until the disease is at an advanced stage.
Early diagnosis and treatment can minimize or prevent optic nerve damage and limit glaucoma-related vision loss. Nowadays, research continues for the improvement of current medical treatment.

Keywords: glaucoma, medical treatment, preservative-free, drug delivery, gene therapy

Introduction
The term glaucoma refers to a group of diseases that have in common an optic neuropathy associated with visual function loss. Although elevated intraocular pressure (IOP) is one of the primary risk factors, it does not have a role in the definition of the disease [1].

Glaucoma is the second most frequent cause of irreversible blindness in developing countries.

The most common form of glaucoma is primary open angle glaucoma. It accounts for over 90% of glaucoma in adults. The incidence of the disorder significantly increases beyond the age of 40, reaching a peak between the ages of 60 and 70 [2].

Quality of life (QoL) is closely linked with visual function; if both eyes have advanced visual function loss, the quality of life is reduced considerably.

In general, patients do not have symptoms of glaucoma until large, irreversible visual field defects have occurred.

The goal of therapy in glaucoma is to achieve a target pressure that will arrest or prevent optic nerve head damage and progression of field defects, to maintain related QoL at a sustainable cost [3,4].

There is no single target IOP level appropriate for every patient; it needs to be estimated for each eye of every patient separately.

There is no ideal treatment of glaucoma. For a drug to be considered close to ideal, it has to have minimal local and systemic side effects,
to generate as few fluctuations as possible in IOP, to have a lasting effect after administration and to generate a high adherence to treatment [5,6].

Medical therapy has a few limitations:
- topical drugs doubles tear production to 2 µl/ min
- only 20% of a drop actually reaches the eye
- the tear film washes the entire active substance in 5 minutes
- pressure on the lacrimal points for 1-2 minutes after administration reduces side-effects and increases absorption.

The overall cost, the difficulty in compliance, and the effects warring off in time make the medical therapy a challenge.

### Indications for initiating the treatment

The decision to initiate therapy in glaucoma is serious. Once started, therapy generally is continued for the rest of the patient’s life. The therapy has untoward side effects, significant costs, and can diminish QoL. In addition, the public health impact of treatment is enormous; therapy is expensive and requires regular medical attention.

Determining when to start treatment is a decision that must be individualized for each patient. Any decision to initiate therapy must weigh the patient’s risk factors for the development or progression of glaucoma against the risk of side effects and inconveniences of treatment [7].

Patients considered glaucoma suspects and patients with risk factors such as a family history of the disorder, middle myopia, glaucoma in the other eye, or differences between the optic cup in the two eyes should be monitored closely. Follow-up examinations should be performed three to four times a year, especially for patients not undergoing treatment [2].

It is recommended to initiate the treatment with monotherapy. If it reduces IOP to the target and is well tolerated, therapy can be left unchanged. If it does not seem effective, first it should be switched with another monotherapy from the same class of drugs or another class entirely.

If monotherapy is well tolerated but it did not succeed in achieving the target IOP, the addition of a second drug should be considered. It is recommended to combine agents with different modes of action to achieve a superior IOP lowering.

However, multiple drugs reduce the adherence to treatment so, when available, a fixed combination should be used [4].

### Classes of topical antiglaucoma drugs

The number of available agents for the medical treatment of glaucoma has expanded greatly. At first, the choice was limited to miotics, epinephrine, or oral carbonic anhydrase inhibitors.

Topical beta-blockers were introduced as a therapy for glaucoma in the 1970s and they represented a significant advance. Topical carbonic anhydrase inhibitors, alpha-adrenergic agonists, and prostaglandin analogs have also become available; they effectively lower intraocular pressure (IOP) and have advantageous side-effect profiles for most patients [7].

There are 5 classes of drugs:
- prostaglandin analogs (latanoprost, tafluprost, travoprost) and prostamides (bimatoprost)
- beta-receptor antagonists: nonselective (timolol, levobunolol, metipranolol, carteolol, befunolol) and beta-1-selective (betaxolol)
- carbonic anhydrase inhibitors: topical (brinzolamide, dorzolamide) and systemic (acetazolamide, methazolamide, dichlorphenamide)
- alpha-2 selective adrenergic agonists: apraclonidine, brimonidine, clonidine
- parasympathomimetics (pilocarpine, carbachol).

For a drug to be considered effective, it has to lower the IOP with at least 20%. A 10% decrease in IOP is considered ineffective. The IOP reduction varies between classes of drugs: 25-35% with prostaglandin analogs, 20-25% with beta-receptor antagonists, 20% with carbonic anhydrase inhibitors, 25-35% with alpha-2 selective adrenergic agonists and 20-25% with parasympathomimetics [4].
Side effects and contraindications of topical antiglaucoma drugs

**Prostaglandin analogs**

Local side effects: burning sensation, conjunctival hyperaemia, foreign body sensation, itching, periorbital fat atrophy, increased pigmentation of periocular skin, eyelash changes, increased iris pigmentation, reactivation of herpes keratitis, uveitis, cystoid macular oedema in eyes with known risk factors for macular oedema.

Systemic side effects: exacerbation of asthma, dyspnea, chest pain, muscle-back pain.

Contraindications: contact lenses, unless reinserted 15 minutes following the administration of the drug [4].

**Beta-receptor antagonists**

Local side effects of nonselective agents: dry eye, conjunctival hyperaemia, corneal anesthesia, allergic blepharoconjunctivitis.

Local side effects of selective agents: burning, stinging.

Systemic side effects of nonselective agents: bradycardia, hypotension, arrhythmia, heart failure, syncope, bronchospasm, depression, sexual dysfunction.

Systemic side effects of selective agents: respiratory and cardiac side effects less pronounced when nonselective agents, depression, sexual dysfunction.

Contraindications: asthma, history of COPD (chronic obstructive pulmonary disease), sinus bradycardia (<60 beats/ min), heart block, cardiac failure [4].

**Carbonic anhydrase inhibitors**

Local side effects: burning, stinging, superficial punctuate keratitis, bitter taste, blurred vision, tearing.

Systemic side effects: headache, urticaria, pruritus, angioedema, asthenia, dizziness, paresthesia, and transient myopia.

Contraindications: patients with low corneal endothelial count, due to increased risk of corneal oedema.

**Alpha-2 selective adrenergic agonists**

Local side effects: lid retraction, limited mydriasis, conjunctival blanching, periocular contact dermatitis, allergy or delayed hypersensitivity, allergic blepharoconjunctivitis.

Systemic side effects: dry mouth and nose, fatigue, sleepiness, bradycardia, hypotension.

Contraindications: oral monoamine oxidase (MAO) inhibitor users, pediatric age, very low body weight [4].

**Parasympathomimetics**

Local side effects: conjunctival hyperaemia, reduced vision due to accommodative myopia, retinal detachment, lens opacities, precipitation of angle closure, iris cysts.

Systemic side effects: intestinal cramps, headache, bronchospasm.

Contraindications: post-operative inflammation, spastic gastrointestinal disturbances, uveitis, neovascular glaucoma, patient at risk for retinal detachment, peptic ulcer, bradycardia, hypotension, recent myocardial infarction, epilepsy, Parkinsonism [4].

**New research in prostaglandin analogs**

**Generalities**

The prostaglandin analogs have become the preferred choice for initial therapy.

Since their development in the 1990s, prostaglandin derivates (latanoprost, travoprost, bimatoprost, and tafluprost) have progressively replaced beta-blocker as first-choice therapy because they are the most effective IOP-lowering agents, they lack relevant systemic side effects, and they require only one daily administration [4].

The research continues for the improvement of these agents.

**Latest studies about prostaglandin analogs**

It is known that cyclodextrins (CDs) can form complexes with hydrophobic drugs, influencing their stability, availability, solubility, and tolerance.

A variety of CDs were screened and the most appropriate CD for the formulation of latanoprost for an ocular topical application was selected. PropylaminoβCD was demonstrated to have the best trade-off between latanoprost stability and availability. It formed a complex
involving the ester group of latanoprost providing protection to its ester bond, while ensuring proper latanoprost solubilization.

In vivo experiments demonstrated that the latanoprost-propylaminoβCD formulation led to lower ocular irritation than the commercial latanoprost formulation used as a reference [8]. Comparing bimatoprost 0.01% with bimatoprost 0.03% showed no differences in lowering IOP between the two agents. Patients who were given bimatoprost 0.01% showed a lower rate of side effects, a reduced rate of conjunctive hyperaemia with 65% and a better adherence to treatment [14].

Preservative free prostaglandin analogs

Recently, a number of generics, preservative-free and BAK (benzalkonium chloride) -free prostaglandin formulation have entered the glaucoma market. Preservatives are substances that prevent contamination of the solution during usage and facilitate the diffusion of drugs through ocular surfaces. The most common preservative used in glaucoma drugs is BAK. However, its use is known to be associated with side effects on the ocular surface.

The preservatives used in antiglaucoma drugs are the following:
- quaternary ammonium salts (BAK, Poliquad)
- mercury derivatives (thimerosal)
- oxidative complexes (sodium perborate, oxychloro complex)
- amidines (chlorhexidine)
- molecular tampon ionic system (SofZia)
- alcohols (chlorobutanol, phenylethanol).

Clinical studies have now demonstrated that preservative-free formulations of antiglaucoma medications have the same efficacy as preserved formulations, achieving equivalent reductions of intraocular pressure, with fewer side effects on ocular surface [9].

Current substances available without preservative are the following: timolol, betaxolol, carteolol, dorzolamide, travoprost, latanoprost, tafluprost. The BAK-free fixed combination on the market is travoprost + timolol (DuoTrav).

The first PGF\textsubscript{2α} analogue with a preservative-free formulation is tafluprost 0.0015%. Tafluprost demonstrated more potent fluoroprostaglandin (FP)-receptor binding than latanoprost and reduced IOP to a greater extent than latanoprost and was well tolerated [10]. Travoprost BAK-free was released. These formulations are preserved with Sofzia™, an oxidizing agent that contains borate, zinc and sorbitol, which provides an antimicrobial effect through a proprietary formulation of several buffering agents or with Polyquad, a detergent-type preservative. Compared with travoprost 0.004% with BAK, travoprost 0.004% BAK-free proved to be equivalent in both safety and efficacy [11].

A study comparing the status of the ocular surface, as documented by TBUT (tear break-up time), corneal staining and OSDI (ocular surface disease index), in patients switching from latanoprost with BAK to travoprost without BAK concluded that BAK, a common preservative for glaucoma drops, may increase OSDI by disrupting the tear film and increasing conjunctival inflammation. A change to a non-BAK-preserved PGA resulted in a measurable improvement of TBUT, corneal staining and OSDI and also a reduction in toxicity [12-15].

New research in beta-receptor antagonist agents

Generalities

Although the discovery of prostaglandin agents was an important step in the treatment of glaucoma, research for improving beta-receptor antagonists, continues.

Preservative free beta-receptor antagonists agents

Preservative-free betaxolol was studied to evaluate ocular surface changes in patients with primary open-angle glaucoma (POAG) as well as the hypotensive effect. The study proved preservative-free betaxolol to be safe and efficient in the treatment of glaucoma [16].

It is known that beta-blockers have the potential to be systemically absorbed, which may cause adverse cardiovascular effects. A study was conducted to determine whether the initiation of ophthalmic timolol was associated with an increased risk of hospitalization for bradycardia. The risk of bradycardia was significantly increased in the 31-180 days after timolol initiation. No increased risk was
observed in the first 30 days or beyond 180 days of continuous exposure.

The study concluded that the use of timolol might lead to bradycardia. The patients should be closely monitored after treatment initiation with topical nonselective beta-blocker eye drops [17].

**Fixed combinations**

**Generalities**

When a patient does not respond to monotherapy, the use of multiple topical treatments may jeopardize adherence to treatment. Therefore, when available, a fixed combination is preferable.

Currently, all fixed combinations available in Europe contain a beta-blocker agent. Knowing the side effects of beta-blockers, patients with serious cardiopulmonary diseases must be excluded before prescribing fixed combinations [4].

Existing fixed combinations:
- prostaglandin analogs (PG) and beta-blockers (BB): travoprost + timolol (DuoTrav), latanoprost + timolol (Xalcom, Xaloptic Combi), bimatoprost + timolol (Ganfort)
- carbonic anhydrase inhibitor and BB: dorzolamide + timolol (Cosopt), brinzolamide + timolol (Azarga)
- parasympathomimetics + BB: pilocarpine + timolol (Fotil)
- alpha -2 selective adrenergic agonists and BB: brimonidine + timolol (Combigan).

Recently, new fixed combinations have been submitted to EMEA (European Medicines Agency): a combination containing a carbonic anhydrate inhibitor (brinzolamide 1.0%) and an alpha 2 adrenergic receptor agonist (brimonidine tartrate 0.2%) (SIMBRINZA®) and a combination of tafluprost 0.0015% and timolol 0.5% (TAPCOM®).

**Latest studies about fixed combinations**

The direct comparison between a fixed combination of bimatoprost-timolol and travoprost-timolol showed no significant difference in lowering IOP. Both fixed combinations had no significant effect on conjunctiva hyperaemia. Patients on travoprost-timolol fixed combination had significantly less superficial punctuate keratopathy. However, bimatoprost-timolol fixed combination produced additional IOP lowering in patients previously treated with non-fixed combination of latanoprost and timolol [20].

Transition to fixed-combination travoprost 0.004%/ timolol 0.5% preserved with polyquaternium-1(polyquad) in patients with insufficient response to bimatoprost 0.03%/ timolol 0.5% preserved with benzalkonium chloride proved to be effective in significantly reducing IOP [21].

**Anti-VEGF agents in the treatment of neovascular glaucoma**

**Generalities**

Neovascular glaucoma (NVG) is a group of secondary angle closure glaucoma which led by a variety of diseases that have anoxia or ischemia to the retina. Some studies have found that the etiology was related to the vascular endothelial growth factor (VEGF) [22].

The role of antivascular endothelial growth factor (anti-VEGF) agents in treating various ophthalmic diseases is currently being investigated. Many advances have been made in order to understand the way anti-VEGF agents work and when to implement them clinically for neovascular glaucoma.

Their use leads to regression of iris and angle neovascularization, intraocular pressure control when the angle remains open and prompts symptomatic improvement. In addition, research of anti-VEGF agents has revealed a dose-dependent inhibition of fibroblast proliferation.

Through future research, the antiangiogenic and anti-fibroblast properties of anti-VEGF agents might prove beneficial in patients treated for various forms of glaucoma [23].

**Latest studies about anti-VEGF agents in neovascular glaucoma**

The efficacy and safety of intravitreal bevacizumab (IVB) in the treatment of neovascular glaucoma (NVG) is a subject of current research.

Studies concluded that the use of bevacizumab might be effective in manipulating
growth factors in the anterior chamber. It could serve as a first line treatment for NVG. Also it seemed to reduce iris neovascularization. Clinical trials are needed to confirm these results before its use is authorized [24,25].

Aflibercept was also considered for the treatment of neovascular glaucoma. Intravitreal aflibercept resulted in rapid regression of neovascularization of the iris and angle (NVI and NVA) and stable or reduced IOP. These results suggested that intravitreal aflibercept might be an effective treatment for stage 1 and 2 NVG, resulting in rapid and sustained regression of NVI and NVA and control of IOP [26].

Generic drugs

Generic drugs have been of interest lately. Per FDA requirements, generic drugs must have the same active ingredients, strength, dosage forms, labeling, indications, and routes of administration as the corresponding branded drugs. Also, the FDA mandated that generic drugs are bioequivalent to branded drugs, meaning that the amount of absorption of a generic drug must be within a certain range relative to the branded drug. Currently, there has been an economic push for generic drugs to be the preferred drug of choice given the financial relief provided by these compared to branded drugs [18].

Based on clinical experience, the doctor is the one who decides if a patient should be treated with generic drugs or the original molecule.

Given that cost can significantly determine adherence, switching patients to generic medications might help improve patients’ drug-regimen adherence (by 28%). Lower co-pay was associated with improved adherence after generic drug's introduction [19].

However, the efficacy and tolerability of generics was not well studied and some clinical studies showed inconsistent results depending on the type of the generic drug.

Neuroprotection

Generalities

Visual field loss in glaucoma is due to death of retinal ganglion cells. Neuroprotection (reducing or slowing down the loss of ganglion cells in glaucoma) appears to be the only way forward.

Experimental data showed that patients are more likely to benefit from neuroprotectants in diseases in which the neurons die slowly, such as in glaucoma, than in a disease in which the death of a set of neurons is rapid.

If a neuroprotectant can be administered in such a way that it reaches the retina in appropriate amounts, with insignificant side effects, it is likely to attenuate ganglion cell death and thus the glaucoma patient will benefit from this.

Latest studies about neuroprotection

A lot of studies focused on Rho kinase inhibitors as promising therapeutics in neuroprotection and neuroregeneration. Rho-associated coiled-coil forming protein kinase (ROCK) inhibitors have the potential to become very prominent drugs for future glaucoma treatment. Their field of action in the eye is not restricted to IOP reduction by targeting the trabecular meshwork or improving filtration surgery outcome. Progress has been made in elucidating their ability to improve ocular blood flow, to prevent retinal ganglion cells (RGC) death, increase RGC survival and to slow down axonal degeneration or induce proper axonal regeneration [27,28].

Irbesartan, an angiotensin II blocker was studied as a possible retinal ganglion cell neuroprotector in an ex vivo retinal explant model. Irbesartan (10 µM) almost doubled ganglion cell survival after four days, contrary to angiotensin II (2 µM) reducing cell survival by 40%. The study concluded that angiotensin II blockers protect retinal ganglion cells in this model and may be worth further investigation as a neuroprotective treatment in models of eye disease [29].

Ghrelin was also studied for possible antioxidant and neuroprotective effects on the retina in an experimental glaucoma model. Immunohistochemistry staining of retinas for glial fibrillary acidic protein (GFAP), S-100 and vimentin expression showed that in the ghrelin group, apoptosis and expression of GFAP, S-100 and vimentin was significantly lower than in the vehicle control group.
This study suggested that ghrelin had antioxidant and neuroprotective effects on the retina in an experimental glaucoma model. Further studies are needed to back these findings [30].

Another drug with potential neuroprotective effects is edaravone. Studies showed that the neuroprotective activity of edaravone was found to be more influential by administration at the start of the glaucoma process [31].

Other agents are still studied: memantine, calcium channel blockers, Gingko biloba derivatives.

New methods for drug delivery in glaucoma patients

Generalities

Ocular drug transport barriers pose a challenge for drug delivery: the ocular surface epithelium, the tear film and internal barriers of the blood-aqueous and blood-retina barriers. Traditional drug administration reduces the clinical efficacy especially for poor water-soluble molecules and for the posterior segment of the eye.

Durasert is a fully bioerodible, long-term, sustained release implant delivering latanoprost. The product is designed to be administered by an eye care professional into the subconjunctival space of the eye in a minimally invasive procedure. The effect lasts from 3 to 6 months. The implant solves the problems of non-compliance and the inability to administer the drops [34].

Nanoparticles (NPs) have been designed to overcome the ocular barriers, increase the drug penetration at the target site and prolong the drug levels by fewer drug administrations in lower doses without any toxicity compared to the conventional eye drops.

Drug delivery systems have the potential to improve patient adherence, reduce side effects, increase efficacy, and preserve sight for glaucoma patients. Mucus-penetrating particle topical administration nanotechnology could improve the effectiveness of approaches for glaucoma [32].

Latest studies about drug delivery methods

Hybrid polyamidoamine (PAMAM) dendrimer hydrogel/ poly (lactic-co-glycolic acid) (PLGA) nanoparticle platform (HDNP) for codelivery of two traditional antiglaucoma drugs brimonidine and timolol maleate showed no cytotoxic effect and prolonged residence time with slowly released period thus enhancing drug bioavailability in glaucoma treatments [32,33].

Formulation of dorzolamide hydrochloride and methazolamide-loaded solid lipid NPs (SLN) in a nanemulsion form offers a more intensive treatment of glaucoma, a decrease in the number of applications per day and a better patient compliance compared to conventional eye drops [32,35,36].

A study about nanoliposome drug delivery system for the longer-term delivery of latanoprost was published to establish the safety and efficacy of a single subconjunctival injection of nanoliposomal latanoprost in subjects with a diagnosis of either ocular hypertension (OHT) or primary open-angle glaucoma (POAG).

A clinically and statistically significant IOP reduction (≥20% IOP reduction) was observed through 3 months after injection. The nanomedicine reported in this study is the first nanocarrier formulation that has an extended duration of action in humans, beyond a couple of weeks. The findings opened up a new treatment modality, which will greatly enhance patient compliance and improve treatment outcomes [37].

Other means of improving drug delivery were also studied.

Recently, a study was published on the effect of the dinucleotide P(1), P(4)-Di (adenosine-5′) tetraphosphate (Ap4A) in improving adrenergic anti-glaucomatous delivery by modifying the tight junction proteins of the corneal epithelium.

The study concluded that, when Ap4A was topically applied two hours before the adrenergic compounds, the concentration of brimonidine or timolol in the aqueous humour increased, producing a more profound effect on IOP. Therefore, Ap4A treatment resulted in a better entrance of adrenergic anti-glaucomatous compounds within the eye and improved
therapeutic efficiency by increasing corneal epithelial barrier permeability [38].

**Melatonin agonist– agomelatine**

Agomelatine is an agonist of melatonin that is used in the treatment of major depressive disorders. A study addressing for the first time agomelatine effects on the IOP of patients affected by POAG was published. An ability to decrease IOP in experiment animals and in normal human subjects was shown.

Given orally, Agomelatine showed a significant hypotonising effect, stably decreasing IOP roughly by 30% of the enrolment value after 15 and 30 days of treatment [39].

**Angiotensin and bradykinin system axes**

Recently discovered, novel IOP-lowering agents that pertain to the renin-angiotensin and kallikrein-kinin axes offer new means of treating and controlling ocular hypertension (OHT).

A study presenting the properties and actions of diminazene aceturate (DIZE; a novel angiotensin-converting enzyme-2 activator) and FR-190997 (a non-peptide bradykinin receptor-2 agonist) was published in relation to their anti-OHT activities in rodent and respectively in cynomolgus monkey eyes. It is anticipated that these compounds will pave the way for future discovery, development, and marketing of novel drugs to treat glaucoma and thus help save sight for millions of people affected by this slow progressive optic neuropathy [40].

**Gene therapy in glaucoma**

**Generalities**

Glaucoma is a chronic progressive disease for which the ideal treatment would provide a localized long-lasting therapy with minimal side effects. A gene therapy approach in which a mutated gene is replaced or inactivated, or in which a new gene is introduced, could provide a novel and more effective way of targeting the disease.

**Latest studies about gene therapy**

Using viral and nonviral vector gene delivery systems to target specific tissues involved in the pathogenesis of glaucoma, possible gene therapy targets were identified: trabecular meshwork, ciliary body, ciliary epithelium, Müller cells, and retinal ganglion cells [41].

Three genes involved in the pathogeny of glaucoma were identified: the myocilin gene (MYOC), optineurin gene (OPTN) and WD repeat domain 36 (WDR36).

Mutations in the myocilin gene cause autosomal dominant juvenile primary open-angle glaucoma and approximately 3% of cases of adult-onset open-angle glaucomas.

A recently described causative gene for normal-tension glaucoma, optineurin (optic neuropathy-inducing protein) is another potential target and additional targets are likely to be identified.

Four basic notions should be met by any genetic therapy targeted to an ocular disease: an efficient and nontoxic gene delivery technique, sufficient knowledge of the genetic basis of the disease to select an appropriate therapeutic approach, proper control of the expression of the therapeutic gene and the availability of an animal model of the disease for preclinical testing. Glaucoma is a disease in which some of these conditions can be met [42].

**Stem cells and ocular tissue regeneration**

Stem cells, including putative resident eye stem cells, mesenchymal stem cells, embryonic stem cells, and induced pluripotent stem cells have been investigated for their potential in various eye-specific pathologies to replace the loss of retinal ganglion cells and photoreceptors in retinal degenerative diseases and toward engineering transplantable patient-specific cornea or lenses.

Studies show that different stem cell types have distinct capacities to produce eye-specific cells or even the entire retina [43].

Stem cells research offers great hope for treating various eye pathologies. However, there are many challenges ahead before the era of stem cell-based therapy in the eye truly arrives.
Conclusions

Glaucoma is an optic neuropathy characterized by retinal ganglion cell death and axonal loss. It remains a major cause of blindness worldwide. All current modalities of treatment are focused on lowering the intraocular pressure. However, it is clear that a significant number of glaucoma patients show disease progression despite the pressure lowering treatments.

As the market developed, generic drugs appeared, providing corresponding efficacy (but not enough studied) as the original molecule at a lower price.

To reduce side effects on the ocular surface, preservative-free drugs entered the market. Studies proved them as effective as their predecessors in lowering the IOP.

To improve adherence to treatment, fixed combinations were developed. Current fixed combinations available contain a beta-receptor antagonist. Given the systemic side-effects of beta blockers, patients with serious cardiopulmonary diseases cannot receive such therapy.

The role of antivascular endothelial growth factor (anti-VEGF) agents in treating various ophthalmic diseases is currently being investigated. Studies concluded that intraocular injections of anti-VEGF agents reduce iris neovascularization and lowers IOP in patients with neovascular glaucoma.

Much attention has been given to the development of neuroprotective treatment strategies and gene therapy, but the identification of such has been difficult by lack of understanding of the etiology of glaucoma.

Methods to improve drug delivery have also been studied. Nanoparticles have the potential to revolutionize drug delivery, thus increasing adherence to treatment, diminishing the possibility of side-effects and prolonging actual effects.

Studies have focused on other potentially new antiglaucoma agents such as agomelatine (an agonist of melatonin), diminazene aceturate (a novel angiotensin-converting enzyme-2 activator), PR-190997 (a nonpeptide bradykinin receptor-2 agonist), and stem cells. It is anticipated that these compounds will pave the way for future discovery, development, and marketing of novel drugs to treat glaucoma and thus help save sight for millions of people afflicted with this slow progressive optic neuropathy.

References

13. Yee RW, Norcom EG, Zhao XC. Comparison of the relative toxicity of travoprost 0.004% without benzalkonium chloride and latanoprost 0.005% in an immortalized human cornea epithelial cell culture system. Adv Ther. 2005; 23:511–519.


21. Schnoor D, Hubatsch DA, Scherzer ML. Efficacy and safety of fixed-combination travoprost 0.004%/timolol 0.5% in patients transitioning from bimatoprost 0.03%/timolol 0.5% combination therapy. Clin Experiment Ophthalmol. 2015 May; 7:825-32.


THE PATHOGENY OF PROLIFERATIVE VITREORETINOPATHY

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Abstract
Proliferative vitreoretinopathy (PVR) is the most important complication of rhegmatogenous retinal detachment (RRD) and the main cause of RRD surgery failure. This is a review of recent literature data, which concerns PVR pathogeny and risk factors. The occurrence of pre- and subretinal membranes is a consequence of retinal pigment epithelial cells activation and migration, with concomitant participation of inflammatory cells. The newly synthesized extracellular matrix interacts with cells promoting membrane contraction. Photoreceptor apoptosis limits functional recovery – but there is ongoing research for neuroprotective mechanisms. A lot of evidence has been accumulated about the role of growth factors (PDGF, VEGF, HGF, EGF, TGF α and β, G-CSF, FGF, IGF-1,CTGF), cytokines (interleukins IL-1, -6, -8, -10 and interferon γ), matrix metalloproteinases and chemokines, by measuring their concentrations in the vitreous or the subretinal fluid of PVR patients. A list of risk factors (common or more controversial) may help the surgeon make the best approach for the management of individual cases. Adjuvant therapies tested for PVR prevention (steroids, heparin, 5 fluorouracil, daunomycin, colchicine and 13-cis retinoic acid) did not enter current practice, but there are numerous research directions currently being developed. Keywords: proliferative vitreoretinopathy, pathogeny

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Proliferative vitreoretinopathy (PVR) is the most important complication of rhegmatogenous retinal detachment (RRD) and the main cause of RRD surgery failure. This is a review of recent literature data, which concerns PVR pathogeny and risk factors. The occurrence of pre- and subretinal membranes is a consequence of retinal pigment epithelial cells activation and migration, with concomitant participation of inflammatory cells. The newly synthesized extracellular matrix interacts with cells promoting membrane contraction. Photoreceptor apoptosis limits functional recovery – but there is ongoing research for neuroprotective mechanisms. A lot of evidence has been accumulated about the role of growth factors (PDGF, VEGF, HGF, EGF, TGF α and β, G-CSF, FGF, IGF-1,CTGF), cytokines (interleukins IL-1, -6, -8, -10 and interferon γ), matrix metalloproteinases and chemokines, by measuring their concentrations in the vitreous or the subretinal fluid of PVR patients. A list of risk factors (common or more controversial) may help the surgeon make the best approach for the management of individual cases. Adjuvant therapies tested for PVR prevention (steroids, heparin, 5 fluorouracil, daunomycin, colchicine and 13-cis retinoic acid) did not enter current practice, but there are numerous research directions currently being developed. Keywords: proliferative vitreoretinopathy, pathogeny

Proliferative vitreoretinopathy (PVR) is a complex reaction that represents a healing path for vitreoretinal pathology, with typical clinical aspect: fibrocellular pre- or subretinal membranes, opposing the retinal reattachment [1]. It may occur after rhegmatogenous retinal detachment (RRD), surgical interventions or trauma.

The incidence of PVR in RRD is estimated at 5-11% - but it is much higher in the case of giant retinal breaks (16-41%). After perforating trauma, the incidence is largely variable, between 10 and 45% [2].

PVR is a major cause for the failure of RRD surgery (with 50-75% of failures attributable) [3].

The next pages are trying to provide an update on the current knowledge concerning the etiopathogenesis, physiopathology, and current directions of research with therapeutic purposes in this important complication.
**Pathology**

The evolution of PVR is the result of a balance (or disruption of balance) between destructive and protective mechanisms that are triggered by the occurrence of a retinal break.

The clinical aspect of PVR is correspondent to the histopathological appearance, represented by fibrocellular (and, in evolution, contractile) membranes on the anterior or posterior retinal surface [4].

The primordial element seems to be partial de-differentiation, migration, and proliferation of retinal pigment epithelial (RPE) cells, creating areas of hyperplasia, first at the limit between detached and attached retina and at the margins of retinal breaks. This process may start in the third day of retinal detachment evolution. The next step is the activation of glial cells, with proliferation of astrocytes, Müller cells, microglia, and capillary endothelial cells [2].

De-differentiated RPE cells acquire fibroblast-like (predominant in contractile membranes) or macrophage-like morphology. Since the extracellular matrix of PVR membranes does not have a contractile ability, and de-differentiated cells do not possess actin or myosin, it is believed that contraction is a result of interaction between cells and extracellular matrix.

Neuronal processes found in membranes extracted during surgery were considered an evidence for glial proliferation inside retina. Fragments of internal limiting membrane are also frequently found in PVR membranes, explaining the difficulty of peeling certain membranes (and the capacity of PVR membranes to induce new breaks) [4]. An intraretinal invasion of fibrotic tissue is being discussed.

In contrast, membranes found after successful retinal reattachment contain a small number of immune cells and no glial cells.

The surgical technique (especially the use of silicon oil) seems to favor attraction of macrophages that will subsequently produce cytokines and growth factors, further influencing PVR development.

The proliferation and metamorphosis of the main cells involved (RPE and glial cells) is accompanied to a lesser extent by the presence of polymorphonuclear leucocytes, macrophages, lymphocytes and platelets. A progressive cellular invasion of vitreous (mirrored in the first clinical sign of PVR stage A, the presence of cells and pigment particles in the vitreous, “tobacco dust”) starts from the level of the retinal break. Subsequently, the margins of retinal breaks will present a rolled appearance (PVR stage B). In stages C and D collagen synthesis is obvious by the presence of clearly demarcated membranes that promote tractions on the retina.

**Apoptosis and neuroprotection**

The loss of retinal viability by apoptosis of photoreceptors that have lost contact with subjacent pigment epithelium starts the next day after the occurrence of a RRD. In an animal model, 80% of photoreceptors are definitively lost in a retina that has been detached for 3 months [5]. Lactic acidosis (caused by hypoxia) seems to be an important trigger for both cellular migration and cellular death [6]. Surgical reattachment of retina can be followed by a (slow and incomplete) structural recovery that takes several months [7].

An association between certain cytokines and protection of neural cells from ischemia consequences has been suggested. In an experimental model (obtained by deprivation of glucose and oxygen), leptin and interleukin 1-beta seem to have a protective action for neurons [8]. Neuroprotective mechanisms based on Bax inhibitor-1, a protein situated in the membrane of the endoplasmic reticulum, have been identified in the brain. Consequently, promoting the expression or activation of BI-1 may offer hope for countering the neuronal ischemic injuries in the first fases of a retinal detachment [4].

**The role of growth factors, cytokines, and chemokines**

Is highlighted by an ever-growing body of literature, the sampling of vitreous and subretinal fluid being relatively easy during modern vitreoretinal surgery. The measuring of different factors is also made easier by tests that use minute quantities of biological material.

Under these circumstances, the main growth factors being studied are the following: platelet derived growth factor (PDGF), vascular
endothelial growth factor (VEGF), hepatocytes growth factor (HGF), epithelial growth factor (EGF), transforming growth factor (TGF α and β), granulocyte colony stimulating factor (G-CSF), fibroblast growth factor (FGF), insulin-like growth factor-1 (IGF-1) and connective tissue growth factor (CTGF).

PDGF and its receptor (PDGFR) seem to be synthesized by RPE cells and glial cells when separation between photoreceptors and RPE occurs. In turn, PDGF is a chemotactic and mitogen factor for glial cells [9]. After the retinal reattachment, the concentration of PDGF diminishes.

Variations of growth factor levels might be genetically individualized, since it has been shown that the polymorphism of the tumor necrosis factor (TNF) locus is associated with biological media being modified in a manner that is also present in PVR [10].

The infiltration of polymorphonuclear leucocytes starts in the first hours after a retinal detachment, and they release growth factors like FGF – which in turn continue to stimulate the influx of monocytes and their differentiation to macrophages. In the next (proliferative) phase, the macrophages stimulate the proliferation of fibroblasts [4].

TGF β is responsible for the increased production of extracellular matrix [11].

RPE, glial and inflammatory cells communicate through an array of cytokines, but the relationships are difficult to individualize and understand. The vitreous of PVR eyes contains increased levels of interleukins IL-1, -6, -8, -10 and interferon (IFN) γ. Most studies have used as controls, patients who were subject to pars plana vitrectomy for macular conditions like idiopathic epiretinal membranes or macula holes.

The intravitreal presence of messenger RNA for IL-1, -6, -8 and TNF α is an evidence of local production of these cytokines [12]. In vitro, the growth of RPE cells is promoted by IL-1, IFN γ and TNF α [13].

The role of IL-6 in the expression of matrix metalloproteinases (MMP) is well known. A significant correlation was demonstrated between IL-6 and an increased MMP/TIMP ratio in the subretinal fluid from RRD patients. The tissue inhibitor of metalloproteinase (TIMP) is considered the physiological response to a significant increase of MMP activity. In the pathological circumstance of a retinal detachment, the degradation of extracellular matrix was associated with an increased activity of MMP-1 and -8, and with the presence of latent forms proMMP-2 and proMMP-9. MMP-3 (stromelysin 1) is present in most membranes found in PVR patients [14]. A degradation of extracellular matrix by collagenases activation is an important step in any proliferative reaction.

The chemokines are small proteins that regulate the migration of leucocytes to inflammation sites. A study that investigated the levels of 15 chemokines in subretinal fluid has shown increased values of MIF (macrophage migration inhibitory factor), CCL2, CCL11, CCL17, CCL18, CCL19, CCL22, CXCL8, CXCL9 and CXCL10. CC type chemokines attract monocytes, macrophages, T lymphocytes, eosinophils, and basophiles, while CXC chemokines recruit the neutrophils and activated T lymphocytes [15].

The subretinal fluid of RRD patients has a high procoagulant activity, due to the presence of tissular factor, the major factor that initiates normal haemostasis. The tissular factor may also induce an array of cellular responses, including inflammation and cellular migration. This has been illustrated by the up-regulation of IL-6 and IL-8 in macrophages after formation of tissular factor-VIIa factor complex [16].

A personal research in cases of RRD targets the gradients of vitreal concentrations of cytokines and growth factors – together with possible correlations with the clinical evolution – since the late presentation is a frequent occurrence in our patients.

**Risk factors**

Retinal detachments caused by atrophic holes or retinal dialyses do not develop PVR, thus confirming the role of vitreoretinal interface in the occurrence of this complication [2].

Several preoperative risk factors are known:

- duration of retinal detachment – especially in cases of RD that have been present for over one month, RPE cells migration and glial proliferation are to be expected.
- choroidal detachment.
- aphakia – more frequently associates multiple small size retinal breaks and a disruption of hemato-ocular barrier.
Pseudophakia is not considered a risk factor for PVR [2].

- vitreal haemorrhage is a controversial risk factor – obvious for some authors [17], insignificant for others [2] – our personal experience leaning towards the first category.
- the type, shape and extension of retinal breaks: an extension of breaks over 90° (either a giant break, or as multiple breaks) would increase the risk for PVR. It has been postulated that the risk is in fact due to the tissue trauma represented by these breaks, that stimulate the release of cytokines in the periretinal space, followed by a break of hemato-ocular barrier, resulting in a new influx of cells, cytokines and growth factors.
- although vitreous levels of IL-1, -6, -8, -TNF α, VEGF and IFN γ are increased, there is no clear correlation to the severity of the disease [4].
- vitreous levels of MMP-2 and -9 and intercellular adhesion molecule (ICAM-1) [2].
- genetic profile (the gene of α lymphotoxin situated on the locus that also codes TNF).
- although literature is scarce on this subject, we should add on the list of risk factors the young age (children with RRD are extremely susceptible to PVR formation, but one can argue that the detachment was most probably caused by a trauma or by the presence of a congenital condition).
- the inflammation that pre-existed in patients with uveitis complicated with RD is also a strong promoter of PVR.
  - Intraoperative risk factors:
    - incomplete vitrectomy.
    - cryotherapy – responsible for freeing RPE cells in the vitreous cavity and aggravating the disruption of hemato-ocular barrier. Excessive photoagulation may have the same effect [4].
    - intraoperative complications: hyphema, subretinal hemorrhage, choroidal hematoma, choroidal detachment, posterior retinal breaks [2]. A legitimate question that remains unanswered is if drainage retinotomies placed outside temporal arcades may enhance the risk of posterior PVR – we support the idea of subretinal fluid drainage through the initial causative break whenever possible.
    - an association between the type of tamponade and the subsequent development of PVR is also questionable. It is obvious that long acting tamponade (C3F8) or silicone oil is applied when preoperative PVR had existed or the surgeon has identified obvious risk factors for postoperative PVR. The use of air or SF6 (usual in recent, uncomplicated detachments) would influence the rate of PVR development only in cases with incomplete vitrectomy [18].

Most of the presented factors were discussed in the research published by the European Vitreoretinal Society, a retrospective analysis of 7678 surgical interventions. The presence of choroidal detachment, significant hypotony, preoperative presence of stage C1 PVR (more advanced PVR cases were not included), the presence of 4-quadrant retinal detachment and giant retinal breaks were identified as independent predictors for the failure of primary surgery. The predictive role of aphakia was not confirmed [19].

**Prophylaxis**

The first step in PVR prevention is to identify the patients at risk, using clinical (and perhaps biological) risk factors that were presented.

The main adjuvants tested for the purpose of PVR prevention are the following: corticosteroids, heparin, 5 fluorouracil, daunomycin, colchicine and 13-cis retinoic acid. It is enough to remember that the results of different studies, although sometimes have proven mild efficacy, did not prompt the use of these strategies by the vitreoretinal surgeons.

We can present a list of substances that might be validated in the future as adjuvants for PVR prevention: N-acetylcysteine, mitomycin C, prinomastat, anti PDGF agents (already intensively tested for neovascular AMD), silicone oil as vector for active substances (like retinoic acid or dexamethasone). Liposomes and microspheres might act as vectors for 5 fluorouracil or daunomycin [20]. For instance, an experimental study on a PVR model in rabbits has reported a reduction of PVR incidence from 89% to 11% by the use of an implant that delivered 1 mg of 5 fluorouracil [21].

Since we still lack a pharmaceutical approach with a proven efficacy, prompt surgical treatment of RRD with closure of all breaks and retinal reattachment is undoubtedly the most important action that we may take for preventing future PVR development [20].

Reviewing the literature in order to update our knowledge about proliferative vitreoretinopathy is a challenging enterprise.
because new papers in this area emerge continuously. As a vitreoretinal surgeon, I am fascinated by the interest shown for this subject in the researchers’ world, but much of the literature makes use of notions and methods that are beyond the comprehension of a clinician. This abundance of papers gives us hope that not far into the future our patients will benefit from an effective pharmaceutical adjuvant that will significantly improve the surgical outcomes in this important complication: proliferative vitreoretinopathy.

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References

THE LIABILITY FORMS OF THE MEDICAL PERSONNEL

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Abstract
Current legislation, namely Law no. 95/ 2006 on healthcare reform in the medical malpractice domain stipulates that medical staff can be held accountable in the following forms: disciplinary liability, administrative liability, civil liability and criminal liability. Each form of legal liability presents its features, aspects that are found mainly in the procedural rules. However, the differences between the various legal forms of liability are not met only in the procedural rules but also in their effects and consequences. It is necessary to know what the procedure for disciplinary responsibility, administrative liability, civil liability, or criminal liability is. In addition to the differentiation determined by the consequences that may arise from the different forms of legal liability, it is important to know the competent authorities to investigate a case further and the solutions which various public institutions can take regarding the medical staff. Depending on the type of legal liability, authorities have a specialized authority. If the Disciplinary Committee is encountered at the College of Physicians, it may not intervene in cases before the monitoring and competence for malpractice cases Committee. The latter two committees cannot intervene directly in the legal assessment of civil or criminal cases, as no criminal investigation authorities cannot intervene in strictly civilian cases. Therefore, the importance of knowing the competent institutions is imperative.

Keywords: legal liability of medical staff, the legal liability forms of the medical staff, liability procedures of the medical staff

The current legislation, respectively Law no. 95/ 2006 regarding the healthcare reform, governs in the medical malpractice domain that the medical personnel can be held liable in the following forms:

- Disciplinary - procedure that takes place before the College of Physicians and that involves the analysis of a complaint regarding a medical malpractice by the special committees set up for this by the College;
- Administrative - procedure that is conducted by analyzing a medical malpractice complaint by the Monitoring and Professional Committee for malpractice cases, established in the public health authorities of each county and in Bucharest;
- Civil - a procedure that involves advancing a civil action based on the principles of misdemeanor liability to a court;
- Criminal - a procedure that involves lodging a criminal complaint against the standards governed by the Criminal Code offenses relating to the person concerned or in connection with the service. Every form of liability has its specific effects, as we are going to show below.

1. Relative to disciplinary form, the law stipulates that the doctor is liable for a disciplinary action for non-compliance with laws and regulations of the medical profession, medical deontology Code, the rules of good professional practice and for any acts committed in connection with the profession, that are likely to harm the honor and prestige of the profession (medical malpractice too since the medical malpractice is a professional error committed in the exercise of the medical or medical-pharmaceutical domain that produced damages to a patient) [1].

The complaint against a doctor is forwarded to the college he is part of, and if the doctor is conational of a Member State of the European Union, the European Economic Area State, or the Swiss Confederation, the complaint is filed with the college within the doctor carries out his activity.

A Disciplinary Board is organized and functions within each territorial college, being independent from the college leadership, and is composed of three members who analyze the offenses committed by doctors enrolled in that territorial college. The Superior Commission of Discipline is organized and operates at the point of the College of Physicians in Romania, being independent from the college leadership, composed of five members and analyzes the appeals against the decisions of territorial disciplinary commissions.

After the investigation of the case, the Disciplinary Commission issues a decision that is communicated to the sanctioned doctor, the person who made the complaint, the Ministry of Health, the Executive and the person whom the sanctioned doctor has an employment contract with. Within 15 days from the communication of the decision, the sanctioned person, the person who made the complaint, the Ministry of Health, the president of the territorial college, or the president of the Medical College of Romania may challenge the decision of the disciplinary commission. Within 15 days from notification, the sanctioned doctor may appeal against the decision of the Superior Commission in cassation to the administrative department of the court in whose jurisdiction he operates, against the decision that the doctor was not sanctioned being no form to appeal.

Note that the disciplinary action can be initiated within 6 months from the date of the deed or from the date of knowledge of harmful consequences were suffered, and the disciplinary procedure does not preclude civil, criminal, or administrative procedures.

Regarding the sanctions against the doctor, they may be: a) reprimand; b) warning; c) censure; d) a fine from 100 lei to 1,500 lei; e) prohibition to practice certain medical activities or medicine for a period of one month to one year; f) withdrawal of membership of the College of Physicians in Romania.

Withdrawal of the membership of the College of Physicians in Romania is determined by the final judgment of the courts when judging the prohibition of the profession, and regarding the other sanctions, the sanctioned doctor may be ordered in conducting training courses or medical education, other forms of training.

Also, the sanctions from letters a) -d) shall be radiated within 6 months from the date of their execution, and the one referred to letter e), within one year after the expiration of the ban. In the case of the sanction provided in letter f), the doctor can make a new application to regain membership after the expiration established by the final judgment or after two years from the date of sanction by the disciplinary committees.

It should be noted that these disciplinary commissions could not order about the indemnification, which means that their jurisdiction is limited and specialized.

2. Monitoring and Professional Committee for malpractice cases is a commission in the public health authorities of every county and in Bucharest, and the main activity is the determination of malpractice case in situations that were addressed before it [2].

The committee may be notified by the person or, where appropriate, legal representative, who is considered a victim of an act of malpractice committed in the exercise of an activity of prevention, diagnosis and
treatment, or the successors of the deceased person as a result of an act of malpractice attributable to activities of prevention, diagnosis and treatment.

Subsequent to the person’s application, the Monitoring Commission shall appoint, by drawing lots from the national list of experts, a group of experts or an expert who has at least the same degree of professional and teaching skill as the person claimed, according to the complexity of the case, who will make a report on the case. Within 30 days, the experts drawn will compile a report on the case and submit it to the Commission, and the Committee shall take a decision on the case within three months from the date of the person’s application.

Following the report of the experts appointed by the Commission, a decision regarding whether or not it was an incident of medical malpractice will be emitted. The decision shall be communicated to all concerned, including the insurer, within 5 working days. If the insurer or any party disagrees with the Commission’s decision, they can appeal it to the competent court within 15 days from the notification of the decision.

It should be noted that the entire procedure for the determination of malpractice cases, until the court is seized, is confidential. Therefore, all the data related to the parties, the medical experts called, the examination stage, are covered by the confidentiality principle; hence, the impossibility of communicating the information about the case to third parties appears.

If the Commission determines that it is a situation of malpractice, the court may order the person responsible to pay damages, which means that the Commission cannot rule on the demand side, but only on the existence or otherwise of a malpractice case. Therefore, there is a special limited competence as in the case of disciplinary committees. However, compensation may be determined amicably if there is a clear civil liability of the insured one (medical personnel). But, if the insured one (medical personnel), the insurer and the injured person do not agree on the fault of the insured, the amount and method of payment of the damages caused by the act of malpractice, compensation shall be determined by the court.

3. The civil liability form, whose essentials are based on the principles of misdemeanor liability, requires proof about the next mandatory elements: guilt, fault, injury, and causal link between the fault and the injury [3]. If there is one element missing, then there is no possibility of issuing a decree. On the way to prove the existence of the four elements, the court has to analyze the proofs (documents, witnesses, questioning, and expertise) to issue if there is or there is not a medical malpractice case.

Currently, there is no special procedure regulated for judging the cases regarding medical malpractice. Therefore, the proceedings before the court, which can be the judicature (if the application has a value of up to 200,000 lei), or the High Court (if the application has a value of over 200,000 lei) found in the area of the respondent residence, or the judicature or High Court from where the act was committed or the damage occurred, is the common one.

The misdemeanor liability is based on the rules governed by the Civil Code, providing in art. 1357 that the one who causes injury to another by an unlawful act committed with guilt is obliged to repair the author responding to the slightest injury fault.

Regarding the guilt, it states that in assessing guilt will take account of the circumstances in which the damage was done, and, where appropriate, that the injury was caused by a professional in a business operation the person being responsible only for his deeds committed intentionally or negligently.

Relative to the wrongful act or fault, legal norms consider such a deed the situation that violates public orders, morals or laws, and the damage born when it affects the rights or interests of another.

In these types of civil causes, the court will issue a decree. The court decision ruling may be appealed to the superior court, and the court can order regarding the payment of damages and additional penalties such as withdrawal of membership of the College of Physicians in Romania.

4. Regarding the criminal liability, the conditions laid down by the Penal Code relating to one offense or more have to be regarded [4]. Regarding the physical injury for example, it is
necessary to have an act that caused disability, injuries or damaged the health of a person who needed for curing more than 90 days of medical treatment, aesthetic and permanent injury, abortion or endangering a person’s life. Each offense presents specific elements that must be followed exactly as they are regulated. Just as in the case of civil liability, when an element of the offense is missing, then the presumed guilty cannot be held legally accountable. Although the proofs are in principle similar in civil and criminal proceedings (documents, witnesses, hearings, expertise) there is a difference regarding the steps that must be followed in dealing with proofs.

The procedure for criminal responsibility of the medical staff requires filing a criminal complaint that will be submitted to the agencies usually investigating or prosecuting. Following the criminal complaint filed, the investigation and prosecution stage will begin; a stage that virtually requires gathering evidence to establish the existence or nonexistence of an offense. Therefore, the parties are heard, all the necessary documents are gathered, an expertise is provided, or other evidence necessary or useful for the research. This stage ends with the issuance of an order by the competent prosecutor for the prosecution of the medical personnel in view of committing a criminal offense or for not continuing the prosecution against the medical personnel. Whatever the solution, it can be attacked in front of the prim prosecutor and subsequently to the competent court. If the court maintains the resolution not to continue the prosecution, the court decision will cannot be appealed to a higher court. If the court considers that the medical staff is guilty of a criminal offense, then its decision can be appealed to the superior court following the latter to give a decision that cannot be appealed.

In conclusion, it should be noted that the choice of following a process of administrative, civil or criminal form, each with its specific effects, does not block the possibility to simultaneously start one or more procedures. For example, if an application is initiated for the disciplinary liability in front of the College of Physicians, it does not mean that a civil court action or a criminal complaint cannot be started against the medical personnel considered guilty. Moreover, starting civil or administrative proceedings shall not preclude the pursuit of a criminal liability by lodging a criminal complaint. However, there are exceptions to this rule due to the criminal offense research that can hold back a civil action, in the sense that a civil action would be suspended until the trial regarding a criminal investigation is judged, and if a court has already ruled on some aspect of the malpractice case, another court cannot judge the same issues. For example, we can specify that if a court issues a judgment that establishes certain damages, and then another court cannot ignore the issue already held by the previous court (speaking of res judicata). However, the civil court is not bound by the provisions of criminal law or by the final judgment of acquittal or termination of a criminal proceeding regarding the damage or the guilt of the fault perpetrator.

The damage will be covered by the insurer in the limit of the insured amount, and if the damage exceeds the insured sum, the injured party (or the one who has made the application) can claim damages from the fault perpetrator (medical personnel) and/ or from the civilly liable party (e.g. the hospital that employed the medical personnel found guilty) regarding the difference to their full recovery.

References

1. art. 442 and the following from Law no. 95/ 2006 on healthcare reform.
2. art. 642-681 from Law no. 95/ 2006 on healthcare reform.
3. art. 1349 and the following from the Civil Code.
4. art. 194 and the following from the Penal Code.
REFRACTIVE SURGERY FOR HIGH AMETROPIES,
A FEW CONCLUSIONS

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Abstract
This paper presents a few clinical cases of patients with high ametropies and/or anisometropia, who underwent one or two surgical procedures in our clinic, in order to obtain independence of glasses or contact lenses.

Twenty cases of high ametropies were included in our study, with or without astigmatism, with transparent lenses, who presented in our clinic for surgical treatment to correct their refractive errors.

Postoperatively, we analyzed the results and took decisions for each case in particular; sometimes a second surgical procedure was needed.

Keywords: High ametropies, Anisometropia, Refractive Lens Exchange, ReLex, PRK

Introduction
High ametropies’ surgical treatment is a continuous challenge in refractive surgery.

Classical corneal refractive LASER procedures such as PRK/ LASEK and LASIK or even much modern ones, like FemtoLASIK, failed to correct high refractive errors, but they had a high success rate in correcting small to medium ametropies, associated or not with anisometropia [1].

At present, we benefit from the revolutionary, third generation corneal refractive procedure, the new technique called ReLEX Smile (Refractive Lenticule Extraction). It combines femtosecond technology with high precision lenticule extraction that provides a minimally invasive refractive correction. Together with ReLex Smile a refractive lenticule is created in the intact cornea, which is removed through a 4 mm incision, without ablation or flap creation. It can only correct myopia with or without myopic astigmatism, but up to 10 diopters, only spherical or combined.

Alternative non-corneal surgical techniques that are able to correct high ametropies are Refractive Lens Exchange (RLE) and Phakic Intraocular Lens Implantation (PIOL). We did not perform the second one in our clinic, so our experience is limited [1,2].

We have a vast experience with the RLE technique, and, we have obtained excellent refractive results so far. We implanted monofocal, multifocal (bi or trifocal) and personalized IOLs, multifocal or toric multifocal ones. For personalized IOLs, the calculation is done by the producer, according to the patient’s keratometry, ACD (anterior chamber depth) and AL (axial length). Complications like posterior capsule rupture, retinal detachments (high
myopic patients) and PCO (posterior capsule opacification) may occur very rarely. We can correct any residual refractive errors by using a bioptic procedure.

An important role in correcting high refractive errors is occupied by combined refractive procedures, bioptic procedures, planned or unplanned, performed in order to correct residual errors from previous ocular surgeries [1,2].

Clinical Cases
We have performed our retrospective study on some selected cases that we operated in our clinic from January 2014 until March 2015. Twenty patients (34 eyes) were included, all had transparent lenses, wanted to correct their refractive error (with one or two procedures). Twelve extreme hyperopic eyes or with hyperopic astigmatism (35,29%) and 22 eyes with extreme myopia or myopic astigmatism (64,70%).

We did not include any ReLex patients yet, even though the results we obtained so far for high myopia are very good, as we have been performing this procedure since November 2014 and those cases will be the object of our future studies.

From the hyperopic cases, we have selected the following for presentation:
A 27-year-old male, with BCVA 0,4-0,5 (+14 Dsf), having cycloplegic refraction for the right eye: +18Dsf/ +1Dcyl ax 4 and for the left eye: +17Dsf/ +0,75Dcyl ax 1. Lens power was calculated to +54 D for the right eye and + 50 D for the left eye, with IOL Ф=9,8mm and optical zone Ф=6mm (ACL=3,1mm; AL=14,73mm). The surgeries and postoperative evolution were good. Regarding refraction, we have done the measurements after one day and one week from the surgeries, but did not take them into consideration so much as it was the recovery period.

After six weeks, UCVA was 0,2 for both eyes and the cycloplegic refraction for the right eye was +4 Dsf and for the left eye it was +2,5 Dsf/ +1,5 Dcyl ax 120. The next examination was done after 3 months, when the BCVA was 0,4-0,5. After six months from the implantation, BCVA for the right eye was 0,5 (+4Dsf) and for the left eye was 0,4cc (+2,5Dsf/ +1,5Dcyl ax120) and then we decided to perform PRK in order to correct the residual refractive error. We followed up the refraction after PRK at six weeks, one, three and six months, the UCVA=0,4-0,5, the patient was completely glasses independent with a spherical equivalent of +0,5 D.

From our myopic cases, we have chosen the following one for presentation:
A 39-year-old male with extreme myopia and reduced astigmatism with BCVA for the right eye 0,4cc (-25 Dsf) and for the left eye 0,4 cc (-21Dsf). The cycloplegic refraction for the right eye was -20,25 Dsf/ -1,25 Dcyl 119 and for the left eye was -16,50 Dsf/ -1,75 Dcyl 163. We implanted monofocal IOLs in both eyes: +1,5D for the right eye and +3,5D for the left eye, due to financial reasons. The powers of the implants were calculated by using Holladay formula, with a medium axial length (AL) of 29,51mm for both eyes. Again, like in every other situation, we examined the patient at one, three and six months after surgeries, when BCVA for right eye was 0,8 cc (-2 Dsf/ -0,5 dcyl 110) and for left eye was 0,8 cc (-1,75 Dsf/ -1,5 Dcyl ax 160). At six months, we decided to perform a LASEK procedure for both eyes as the patient’s wish was to be glasses independent for far vision and have reading glasses. After LASEK at one, three and six months, UCVA for both eyes was 0,8 and the cycloplegic refraction for the right eye was +0,25Dsf/ -0,50Dcyl 156 and for the left eye was +0,50Dsf/ -0,75Dcyl 135.

For both cases presented, we have obtained the best results by using a bioptic procedure, both intraocular and corneal refractive surgeries (RLE+PRK/ LASEK).

Results and conclusions
Intraocular refractive surgery is a suitable option to correct high ametropies [3]. The higher the level of ametropia, the more difficult it is to obtain an accurate measurement of refraction, and after the ametropia is reduced, a more reliable evaluation of refraction can be achieved. In order to treat high ametropies, another refractive procedure, associated with the intraocular one, BIOPTIC CONCEPT (RLE+ PRK/ LASEK), has to be performed to correct any residual refractive errors [3].

The results obtained among patients included in our study were good; visual acuity
has improved in all the cases. Best results were obtained by bioptic concept; still, we never performed LASEK or PRK earlier than six months after RLE. Mean preoperative spherical equivalent for myopia was -18.5D to +/- 5.50D and for hyperopia was +16.5D to +21.50D. After RLE and before LASEK/PRK, the spherical equivalent was -2.5 D to +/- 3 D and for hyperopia form +4 D to +1.5D. After corneal refractive surgery was performed, the cylinder did not exceed 1D, and postoperative spherical equivalent +/- 1 D. Patients were all glasses independent;

In conclusion, we think that a combined procedure appears to be safer and more predictable for the treatment of high ametropia than any other surgical option currently available, that it is an innovative approach, which is growing in popularity [4]. We also have to take into consideration the fact that is already well known that the higher the refractive error, the higher the possibility of a biometrical error. Also, if it is possible, it is advisable to postpone the surgical treatment until the patient is 35 or 40 years old.

**Disclosure**

Financial disclosure: Alcon, Oftafarma, Zeiss.

**References**

COMPARATION OF REFRACTIVE RESULTS WITH BIFOCAL IMPLANTS AT LISA 809 AND TRIFOCAL AT LISA TRI839

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Abstract
The purpose of this paper is to make a comparison between the results obtained with AT LISA 809 bifocal IOL and trifocal AT LISA 839. Interest was represented especially by the evaluation of intermediate vision for the 2 implants. 18 patients (36 eyes) operated in Gauss Clinic in 2014 were included in the study: 9 patients (18 eyes) with bifocal implant AT LISA 809 and 9 patients (18 eyes) with bilateral implantation AT LISA 839 trifocal lens. Results showed that implant trifocal provided better visual results for intermediate vision to bifocal implant, as there were not significant differences between the two, in terms of distance vision and near vision.

Keywords: implant bifocal, implant trifocal, intermediate

Introduction

Since bifocal implants on the market fail to provide a satisfactory intermediate vision, new models of IOL appeared to satisfy this need.

AT LISA 809 is a single piece diffractive bifocal implant of acrylic hydrophilic material with hydrophobic surface, total diameter of 11 mm, 6 mm optical diameter and addition of 3.75. Light is distributed asymmetrically between distance - 65% and near - 35%. Provides independence regarding pupillary size, microstructure diffractive covering 6 mm optical surface. It can be implanted through 1.5 mm incisions [1].

The new implant trifocal AT LISA 839 tries to solve intermediate vision.

AT LISA 839 is a diffractive trifocal implant with 3.33 addition for near and 1.66 addition for intermediate, with 6 mm optic diameter and a total diameter of 11 mm.

The optics is divided into two areas:

• A central area with a diameter of 4.34 mm built in trifocal concept
• A peripheral ring of 4.34 - 6 mm - in bifocal concept.

It can be implanted through incisions of 1.8 mm. Light is distributed 50% for distance, 20% for intermediate vision and 30% for near [1,2].

Purpose

The aim of the paper is to make a visual comparison between the results obtained with bifocal implants AT LISA 809 and trifocal implant AT LISA 839.
We were particularly interested in assessing intermediate vision for the 2 implants.

**Material and methods**

18 patients (36 eyes) operated in Gauss Clinic in 2014 were included in the study. 9 patients had bilateral implantation of bifocal lens AT LISA 809 and 9 patients bilateral implantation AT LISA 839 trifocal lens. Follow-up of patients was done over a period of 6 months. Distance vision, intermediate vision and near vision were evaluated. We also studied the optimal distance for reading. We conducted a comprehensive eye examination (IOP, anterior pole and FO examination, OCT for retinal and optic nerve.)

**Results**

We measured the average of AV (visual acuity) for distance, intermediate and near. We considered both uncorrected vision and corrected vision and proper correction was used both as intermediate and near.

<table>
<thead>
<tr>
<th></th>
<th>AT LISA 839 TRIFOCAL</th>
<th>AT LISA 809 BIFOCAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>BCVA</td>
<td>0.96</td>
<td>0.96</td>
</tr>
<tr>
<td>UCVA</td>
<td>0.84</td>
<td>0.88</td>
</tr>
<tr>
<td>IVA 70 CM</td>
<td>0.88</td>
<td>0.64</td>
</tr>
<tr>
<td>NAV 35 CM</td>
<td>0.76</td>
<td>0.52</td>
</tr>
</tbody>
</table>

For intermediate vision (70 cm) uncorrected visual acuity was 0.76 for trifocal implant and 0.52 for bifocal implant and BCVA was 0.88 for trifocal implant and 0.64 for bifocal. For near vision (35 cm), uncorrected AV was 0.68 for trifocal implant and 0.80 for bifocal, and corrected visual acuity was 0.92 for trifocal implant and 0.96 for bifocal.

**Fig. 1** Uncorrected visual acuity at distance was 0.84 for trifocal implant and 0.88 for bifocal

**Fig. 2** Corrected visual acuity at distance was 0.96 for trifocal implant and 0.96 for bifocal implant

**Fig. 3** Intermediate vision was better for trifocal implants than for bifocal implants [6]
No patient required any addition for the near vision. For the intermediate zone, the implant trifocal AT LISA 839 of the 9 cases was the following: 2 cases did not require any addition, 4 cases required addition of +0.50 dp and 3 cases required addition of 0.75 dp.

For the intermediate zone, bifocal implant AT LISA 809 of the 9 cases: 7 cases needed a +1 dp addition, one case required addition of +0.75 dp and one case needed addition of +1.25 dp.

The preferred reading distance for patients with bifocal implant AT LISA 809 was ≈ 35 cm and for those with trifocal implant AT LISA 839 was ≈ 40 cm [8].

**Discussions**

Although the group of patients was small, they could not get performance for intermediate vision. This demonstrates that further improvements are needed in the future [3].

**Conclusions**

Following the results, we concluded that the implant trifocal provides better outcomes for intermediate vision to bifocal implant, as there are not significant differences between the two in terms of distance vision and near vision [8].

However, patient satisfaction was very good for both implants and most of them did not request any additional correction [4-7].

**References**

6. Fabian E. The AT LISA tri 839MP-Excellent visual acuity at all distances. CRST. Mar 2013.
7. Mojzis P. High Patient Satisfaction With AT LISA tri. CRST. June 2012.
GRAVES OPHTHALMOPATHY – TERAPEUTICAL ALTERNATIVES

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Abstract
Graves disease associates thyroid and non-thyroid symptoms and signs with autoimmune pathogenicity, including the ophthalmopathy. The treatment of Graves ophthalmopathy consists of medical immunosuppressive therapy, retrobulbar injections and general treatment. Recently, Somatostatin injections have proved their efficiency.

Keywords: ophthalmopathy, hyperthyroidism, Somatostatin

Objective
The study indented to compare therapeutic effects of classic treatment with cortisone derivatives in separated or associated both general (Prednisone) and local periocular administration (Diprophos), and effectiveness of neurohormonal treatment, less known, with Somatostatin subcutaneously [1,2].

Materials and methods
The study included 63 patients (50 women - 79.3% and 13 men - 20.7%), with Graves ophthalmopathy rated according to clinical-paraclinical evaluation indices which compose the ophthalmopathy score [3]. Patients had various degrees of ophthalmopathy depending on the severity of the lesions, rated from 0 to 6, according to the American Thyroid Association [4].

The patients were differently treated, with Somatostatin subcutaneously, one vial per day for 14-21 days or cortisone derivatives following one of the next regimens:
• The general route: orally, Prednisone tablets of 5mg, 40-150 mg/day;
• Local injection, parabulbar: Diprophos 2 vials/week, 10-12 seepage;
• Combined both oral and periocular steroids.

Following a period of three months, the severity of Graves ophthalmopathy was again evaluated according to clinical and paraclinical assessment indices, aiming to score the ophthalmopathy evolution in patients treated with steroids and those treated with Somatostatin.
### Table 1. Ophthalmopathy grades in Graves disease

<table>
<thead>
<tr>
<th>THE DEGREE OF DAMAGE</th>
<th>SCORE</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Periocular soft tissues damages:</strong></td>
<td></td>
</tr>
<tr>
<td>Mild</td>
<td>1</td>
</tr>
<tr>
<td>Moderate</td>
<td>2</td>
</tr>
<tr>
<td>Severe</td>
<td>3</td>
</tr>
<tr>
<td><strong>Exophthalmos (mm):</strong></td>
<td></td>
</tr>
<tr>
<td>16</td>
<td>0,2</td>
</tr>
<tr>
<td>17</td>
<td>0,4</td>
</tr>
<tr>
<td>18</td>
<td>0,6</td>
</tr>
<tr>
<td>19</td>
<td>0,8</td>
</tr>
<tr>
<td>20</td>
<td>1</td>
</tr>
<tr>
<td>21</td>
<td>2</td>
</tr>
<tr>
<td>22</td>
<td>3</td>
</tr>
<tr>
<td>≥23</td>
<td>4</td>
</tr>
<tr>
<td><strong>Differential intraocular pressure (mm Hg):</strong></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>0,1</td>
</tr>
<tr>
<td>2</td>
<td>0,2</td>
</tr>
<tr>
<td>3</td>
<td>0,3</td>
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<tr>
<td>4</td>
<td>0,4</td>
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<tr>
<td>5</td>
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</tr>
<tr>
<td>6</td>
<td>0,6</td>
</tr>
<tr>
<td>7</td>
<td>0,7</td>
</tr>
<tr>
<td>8</td>
<td>0,8</td>
</tr>
<tr>
<td>9</td>
<td>0,9</td>
</tr>
<tr>
<td>10</td>
<td>1</td>
</tr>
<tr>
<td><strong>Diplopia:</strong></td>
<td></td>
</tr>
<tr>
<td>Intermittent</td>
<td>1</td>
</tr>
<tr>
<td>Inconstant</td>
<td>2</td>
</tr>
<tr>
<td>Constant</td>
<td>3</td>
</tr>
<tr>
<td><strong>Cornea:</strong></td>
<td></td>
</tr>
<tr>
<td>Initial injury</td>
<td>1</td>
</tr>
<tr>
<td>Ulceration</td>
<td>2</td>
</tr>
<tr>
<td>Opacification/perforation</td>
<td>3</td>
</tr>
<tr>
<td><strong>Optic neuropathy:</strong></td>
<td></td>
</tr>
<tr>
<td>Evoked visual potentials - abnormal</td>
<td>3</td>
</tr>
<tr>
<td>Visual acuity = 0,5 - 0,9</td>
<td>5</td>
</tr>
<tr>
<td>Visual acuity = 0,1 - 0,4</td>
<td>7</td>
</tr>
<tr>
<td>Visual acuity &lt; 0,1</td>
<td>9</td>
</tr>
</tbody>
</table>

### Table 2. Ophthalmopathy grades in Graves disease

<table>
<thead>
<tr>
<th>DEGREE</th>
<th>SIGNS AND SYMPTOMS</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Without signs and symptoms. Without symptoms, just signs. Objective:</td>
</tr>
<tr>
<td>1</td>
<td>Retraction of upper eyelid</td>
</tr>
<tr>
<td></td>
<td>Fixed gaze</td>
</tr>
<tr>
<td></td>
<td>Oculo-palpebral asynergy</td>
</tr>
<tr>
<td></td>
<td>Proptosis until 22mm.</td>
</tr>
<tr>
<td>2</td>
<td>Impairment of soft tissue (conjunctival congestion, chemosis, eyelid edema).</td>
</tr>
</tbody>
</table>

### Table 3. Distribution of patients according to the degree of Graves ophthalmopathy (G.O.)

<table>
<thead>
<tr>
<th>G.O. DEGREE</th>
<th>I</th>
<th>II</th>
<th>III</th>
<th>IV</th>
<th>V</th>
<th>VI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients</td>
<td>9</td>
<td>25</td>
<td>20</td>
<td>9</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>% patients</td>
<td>14%</td>
<td>40%</td>
<td>32%</td>
<td>14%</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Number of men</td>
<td>-</td>
<td>6</td>
<td>4</td>
<td>1</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>% men</td>
<td>-</td>
<td>9%</td>
<td>7%</td>
<td>2%</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Number of women</td>
<td>9</td>
<td>20</td>
<td>15</td>
<td>8</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>% women</td>
<td>14%</td>
<td>32%</td>
<td>24%</td>
<td>12%</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>No. patients treated with PREDNISON</td>
<td>4</td>
<td>6</td>
<td>1</td>
<td>9</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>% patients treated with PREDNISON</td>
<td>7%</td>
<td>10%</td>
<td>2%</td>
<td>5%</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>No. patients treated with DIPROPHOS</td>
<td>-</td>
<td>3</td>
<td>3</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>% patients treated with DIPROPHOS</td>
<td>-</td>
<td>5%</td>
<td>5%</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>No. patients treated with Prednisone + Diprophos</td>
<td>-</td>
<td>3</td>
<td>6</td>
<td>3</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>% patients treated with Prednisone + Diprophos</td>
<td>7%</td>
<td>10%</td>
<td>2%</td>
<td>5%</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

3. Exophthalmos (proptosis) over 22 mm was measured with exophthalmometer: Normal:
   - Caucasian ≤ 20 mm
   - Yellow race ≤ 18 mm
   - Black race ≤ 22 mm
   Pathological:
   - +3 - 4 mm = mild exophthalmos
   - +5 - 7 mm = medium exophthalmos
   - +8 and more = severe exophthalmos
   CT scan can estimate the size of the eyeball and the dynamic of retroocular intraorbital space.

4. Impairment of external eye muscles (with diplopia, limitation of the eyeballs motricity).

5. Corneal damage (ulceration, opacity, necrosis, perforation).

Table 4. Distribution of treatment regimens on studied patients

<table>
<thead>
<tr>
<th>TREATMENT</th>
<th>No. Patients</th>
<th>% patients</th>
<th>No. Men</th>
<th>% Men</th>
<th>No. Women</th>
<th>% Women</th>
</tr>
</thead>
<tbody>
<tr>
<td>Steroid therapy</td>
<td>35</td>
<td>55%</td>
<td>27</td>
<td>43%</td>
<td>8</td>
<td>12%</td>
</tr>
<tr>
<td>Prednisone (P)</td>
<td>16</td>
<td>26%</td>
<td>16</td>
<td>26%</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Diprophos (D)</td>
<td>6</td>
<td>10%</td>
<td>1</td>
<td>2%</td>
<td>5</td>
<td>8%</td>
</tr>
<tr>
<td>Combined (P+D)</td>
<td>12</td>
<td>19%</td>
<td>9</td>
<td>14%</td>
<td>3</td>
<td>5%</td>
</tr>
<tr>
<td>Somatostatin</td>
<td>28</td>
<td>45%</td>
<td>24</td>
<td>38%</td>
<td>4</td>
<td>7%</td>
</tr>
</tbody>
</table>

Table 5. Comparing G.O. score before and after the treatment with steroid therapy

<table>
<thead>
<tr>
<th>G.O. Score</th>
<th>BEFORE STEROIDIC THERAPY</th>
<th>AFTER STEROIDIC THERAPY</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No. patients</td>
<td>% patients</td>
</tr>
<tr>
<td>4 - 5</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>5 - 6</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>6 - 7</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>7 - 8</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>8 - 9</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>9 - 10</td>
<td>3</td>
<td>5%</td>
</tr>
<tr>
<td>10 - 11</td>
<td>5</td>
<td>14%</td>
</tr>
<tr>
<td>11 - 12</td>
<td>4</td>
<td>7%</td>
</tr>
<tr>
<td>12 - 13</td>
<td>3</td>
<td>5%</td>
</tr>
<tr>
<td>13 - 14</td>
<td>3</td>
<td>5%</td>
</tr>
<tr>
<td>14 - 15</td>
<td>5</td>
<td>8%</td>
</tr>
<tr>
<td>15 - 16</td>
<td>3</td>
<td>5%</td>
</tr>
<tr>
<td>16 - 17</td>
<td>1</td>
<td>2%</td>
</tr>
</tbody>
</table>

Table 6. Comparing G.O. score before and after the treatment with SMS

<table>
<thead>
<tr>
<th>G.O. SCORE</th>
<th>BEFORE THERAPY WITH SMS</th>
<th>AFTER THERAPY WITH SMS</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No. patients</td>
<td>% patients</td>
</tr>
<tr>
<td>7 - 8</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>8 - 9</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>9 - 10</td>
<td>6</td>
<td>10%</td>
</tr>
<tr>
<td>10 - 11</td>
<td>5</td>
<td>8%</td>
</tr>
<tr>
<td>11 - 12</td>
<td>5</td>
<td>8%</td>
</tr>
<tr>
<td>12 - 13</td>
<td>5</td>
<td>8%</td>
</tr>
<tr>
<td>13 - 14</td>
<td>6</td>
<td>10%</td>
</tr>
<tr>
<td>14 - 15</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>15 - 16</td>
<td>1</td>
<td>2%</td>
</tr>
<tr>
<td>16 - 17</td>
<td>1</td>
<td>2%</td>
</tr>
</tbody>
</table>

Table 7. Comparing G.O. score before and after both therapies

<table>
<thead>
<tr>
<th>G.O. SCORE</th>
<th>STEROIDIC THERAPY</th>
<th>SMS</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>BEFORE TREATMENT</td>
<td>AFTER TREATMENT</td>
</tr>
<tr>
<td></td>
<td>No. patients</td>
<td>% patients</td>
</tr>
<tr>
<td>0</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>I</td>
<td>4</td>
<td>7%</td>
</tr>
<tr>
<td>II</td>
<td>13</td>
<td>21%</td>
</tr>
<tr>
<td>III</td>
<td>11</td>
<td>17%</td>
</tr>
<tr>
<td>IV</td>
<td>6</td>
<td>10%</td>
</tr>
<tr>
<td>V</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>VI</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>
Results and discussion

1. Steroid treatment has been more effective in improving the signs and symptoms of eyes involvement in G.O., compared to the treatment with Somatostatin.

2. In the studied group, combined cortisone treatment (oral prednisone and periocular Diprophos) was proven to be more effective compared to the group treated only with oral prednisone [5].

3. The work points out that local anti-inflammatory and partly immunosuppressive effect provided by periocular steroid is certainly higher and safer compared to the group treated only with oral prednisone.

4. The variations of therapeutic results obtained with Somatostatin can be explained by the differences in density of periocular distributed Somatostatin receptors, due to a genetic individual program [6].

5. Technical possibilities of identifying the Somatostatin receptors (by indium 111-labeled Ocreotide scintigraphy) would allow a judicious selection of patients, with maximal therapeutic benefit.

Conclusions

1. Graves ophthalmopathy treatment requires a competent therapeutic approach, applied to patients at the right time.

2. General and local steroid therapy is an effective treatment, safe and fast, in controlling infiltrative processes.

3. Although effective, Somatostatin therapy is limited by individual patient response, based on the existing specific hormone retroocular receptors.

References

5. Croxon MS, Hall TD, Nicoloff JT. Combination Drug Therapy for Treatment of Hyperthyroid Grave’s Disease. doi: http://dx.doi.org/10.1210/jcem-45-4-623.
MY EXPERIENCE OF TEACHING PHACOSURGERY ON VISALIS 100 IN SUDAN AND NIGERIA

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Abstract
At the invitation of the director of The National Eye Center, Kaduna, Nigeria and The Makkah Eye Hospital of Khartoum, Sudan I visited both these institutions to teach phacoemulsification surgery to their aspiring surgeons on Visalis 100 (Carl Zeiss Meditec, Germany). This article highlights the experience of teaching phacoemulsification surgery in foreign African countries like Nigeria and Sudan. In Nigeria I had the opportunity to give training in both wet lab and live surgery settings whereas in Sudan only hands-on live surgery. Sudan being an Islamic nation pigs are not slaughtered there and hence no pig eyes. Goat eyes differ significantly from human eyes and hence have almost no value in wet lab teaching.

The training program included theoretical discussions, wet lab, surgery and finally discussions related to the days' surgery. It became clear that quality of learning depends on three main factors.
Thorough understanding of theory and observation of senior surgeons in operation room
Good wet lab and finally doing the surgery oneself in step by step manner.
Dedicated teachers and instructors can make all the difference.

The learning curve also significantly shortens if the trainees are exposed to all types of cataract surgery like ECCE, SICS and phacoemulsification surgery. The main problem faced by those surgeons who have done only ECCE/SICS is that they are not used to handling microscope and instruments in both hands at the same time. Hence I strongly recommend them wet lab where they can sit and practice using both hands and feet and microscope simultaneously and in coordinated fashion.

Keywords: Learning curve, CCC, S.I.C.S., phacoemulsification machines, Ultrasound delivery modes

Accepted: April 9, 2015

Introduction
Learning phacoemulsification surgery for cataract is desired by every ophthalmology resident in the world. Every ophthalmology resident wants to learn this technique and master it by the time he/ she plans to endeavor into private practice.

The history and evolution of this technique has run almost parallel with the technique of
laparoscopic surgery and certain dental procedures like ultrasonic removal of dental calculi [1] and at the same time borrowing a few concepts from them both.

In fact, phacoemulsification procedure owes its existence to dentistry.

Like every new thing, learning phacoemulsification also has three distinct phases.

1) Phases of fear: I AM GOOD FOR NOTHING phase
2) Phase of excitement: HELL I AM ACTUALLY DOING IT phase
3) Phase of adaptability: I AM COOL BUT COULD DO BETTER phase

**What is a learning curve?**

The earliest definition of the learning curve as given by the psychologist Hermann Ebbinghaus in 1885 states that: Progress in learning steps plotted against time is the learning curve [2]. In other words, a graphical representation of the time it takes to learn all steps of a said procedure.

The application of the learning curve was first introduced in the aviation industry [3].

However, it can be applied to any learning procedure.

**On what factors is a learning curve of phacoemulsification surgery dependent on?**

Intrinsic factors like:
1) Tech savvy or not
2) Age (?) debatable
3) Peers pressure
4) Instructors
5) Previous surgical experience
6) Possibility to put this learning into practice.

Extrinsic factors like:
1. If the trainee surgeons has undergone training on all evolutionary stages of cataract surgery like ECCE --→ SICS--→ PHACO
2. In phacoemulsification surgery DIVIDE & CONQUER -→ STOP & CHOP -→ PHACO CHOP
3. Confidence of trainees increases when they are given reliable, safe and a simple machine to get trained on.
4. Confidence is also inversely proportional to the number of complications created during the learning cases. The less the complication during this time, the more is the confidence to travel further.

**What is a reliable machine?**

A reliable phacomachine should fulfill the following criteria:
1. which has good aspiration pump
2. whose phaco hand piece is ergonomic in design and light weighted
3. whose ultrasound delivery is predictable
4. which comes with the wide range of needles and sleeves to choose from
5. which has good surge controlling mechanism (pressure sensors)
6. I/ A parameters safe for removal of viscoelastic material from the eye.

In Nigeria and Sudan I was asked to give training on Visalis100 (Carl Zeiss Meditec GmbH, Germany) phacomachine.

I found Visalis100 best suited to carry out phaco-training for beginners because of the following technical specifications:

I. **Aspiration pump:** Visalis100 uses a peristaltic pump. For beginners this is the safe cushion. It offers vacuum buildup of up to 500mmHg and a flow rate of up to 50 cc/ min.

   II. **Rise time adjustment:** The pump ramp can be controlled from as fast as 0.5 sec to as slow as 12 sec, depending upon the preference of the user and the use case. It makes sense for beginners to set a rise time on slower side. At very fast settings, you will get venturi effect of the peristaltic pump.

III. **Ultrasound delivery system:** In this machine, it is expressed in terms of micrometers of the stroke length of the needle. It is calibrated to work between 0-100µ. The modulation of the ultrasound can be programmed in continuous, pulsed, multi burst and continuous burst modes. The pulsed mode can be further modulated to High (50% duty cycle), Medium (16ms ON time) and Low (8ms ON time) modulations for any selected pulse frequency.

   IV. **Adaptive Power Control** is a feature, which optimizes ultrasound use irrespective of hardness of the nucleus.

   V. **Foot Control Panel** can effectively control the choice of single linear or dual linear operation. The foot pedal design is ergonomic and user friendly.

   VI. **Warning sounds and enhanced safety alarm system** prevents unintended changes
from being applied. For example if the vacuum is increased by more than 30% of preset even when the foot control panel is active, then the machine sends out warning sounds and message and only after clicking the OK button does the change actually apply.

VII. Surge effect is minimized due to S3 (i.e. surge security system). The S3 delays the restart of the pump exponentially after the occlusion break occurs.

VIII. Phaco tips are titanium and available in straight, angled, flared and biconical shapes. Gauge 19G, 20G and 21G.

IX. Anterior Vitrectomy can be done by using pneumatic cutters with a maximum cut rate of 700/ min. in single cut or multiple cut option also delivered in linear and dual linear foot control pedal. An inbuilt compressor provides the necessary compressed air. However, it is not useful for doing posterior vitrectomy.

In 2013, I was invited by the Director of The National Eye Center, Kaduna Nigeria and in 2014 by the Director of The Makkah Eye Complex, Khartoum Sudan to train their ophthalmologists.

I was given a group of 4 surgeons from Nigeria and 4 from Sudan.

The machine given was Carl Zeiss Meditec's Visalis 100, Operating Microscope Carl Zeiss Visu- 160 in Sudan and Nigeria (Also two microscopes Leica F8 and Lumera T from Carl Zeiss).

The Nigerian surgeons were first introduced to the wet lab by using the same machine. The Sudanese surgeons did not have such an opportunity due to religious reasons.

The teaching was classified in three parts.

1. Theoretical discussions.
2. Wet lab to perform the machine independent steps like making tunnel, CCC, hydro-dissection, chopping and IOL implantation. The IOLs implanted during wet lab were mainly foldable IOLs of Indian making.
3. Wet lab to perform the machine dependent steps like trenching, aspiration of the nucleus (in pig eyes no cataract was present) and removal of visco-elastic material from the eye and practicing bimanual Irrigation/ Aspiration.
4. Practical training in operation theatre was carried out every day. On an average, each trainee surgeon operated 20 cases (80 cases in each institute).

5. Both in Sudan and in Nigeria the patients were mature cataracts. Very few were immature cataracts.

6. Chopping presented a challenge for beginners due to this fact.

7. The main complication that occurred in both countries equally, was nucleus “drop”.

8. The availability of the vitreo-retinal surgeon in both institutes made it easy to address this complication.

9. Corneal burn occurred only in one case in Sudan.

Table 1. Comparison of training parameters in NEC and MEC

<table>
<thead>
<tr>
<th>PARAMETERS</th>
<th>NIGERIA NEC</th>
<th>SUDAN MEC</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Number of trainees</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>2. Median age of the trainees</td>
<td>32</td>
<td>35</td>
</tr>
<tr>
<td>3. Gender wise distribution</td>
<td>3 Men 1 Woman</td>
<td>3 Women 1 Man</td>
</tr>
<tr>
<td>4. Previous surgical experience</td>
<td>ECCE (3)SICS(1)</td>
<td>ECCE (3)SICS(1)</td>
</tr>
<tr>
<td>5. Previous experience of doing CCC Using cystitome/rhexis forceps</td>
<td>1 surgeon well conversant</td>
<td>All 4 surgeons well conversant</td>
</tr>
<tr>
<td>6. Basic understanding of the machine</td>
<td>Theoretical</td>
<td>Theoretical</td>
</tr>
<tr>
<td>7. Time taken for CCC on average</td>
<td>60-90 sec</td>
<td>45-60 sec</td>
</tr>
<tr>
<td>8. Making tunnel were graded</td>
<td>1. Good 2. Moderately good 3. Very good 4. Poor</td>
<td>2 3 1 1</td>
</tr>
<tr>
<td>Depending on leakage presence, shape of the tunnel and length of the tunnel into the corneal tissue.</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>


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9. Hydrodissection was graded
   1. Good  2  1
   2. Very Good  1  2
   3. Fair  1  1
   Depending upon the number of attempts taken by the surgeon.

10. Trenching gradation was dependent on the nuclear sclerosis grading.

<table>
<thead>
<tr>
<th>COMPLICATIONS</th>
<th>NEC (KADUNA) NIGERIA</th>
<th>MAKKAH EYE COMPLEX KHARTOUM</th>
</tr>
</thead>
<tbody>
<tr>
<td>NUCLEUS DROP</td>
<td>03</td>
<td>04</td>
</tr>
<tr>
<td>CORNEAL BURN</td>
<td>00</td>
<td>01</td>
</tr>
<tr>
<td>P.C. RENT</td>
<td>09</td>
<td>11</td>
</tr>
<tr>
<td>EXTENDED CCC</td>
<td>10</td>
<td>12</td>
</tr>
<tr>
<td>LEAKING TUNNEL</td>
<td>02</td>
<td>04</td>
</tr>
<tr>
<td>NEED FOR SUTURING</td>
<td>10</td>
<td>11</td>
</tr>
<tr>
<td>CONVERT TO SICS</td>
<td>10</td>
<td>11</td>
</tr>
</tbody>
</table>

**What is the rational behavior?**

**Definition**

A decision making process that is based on making choices that result in the most optimal level of benefit for the individual [5]. That means making decisions that turn out to the benefit of the patient in the end. This Right decision is based on a previous experience like reading, seeing others and making mental record for future reference, remembering similar situations while doing surgery by oneself, etc.

**Conclusion**

In conclusion, let me highlight the following points:

1. Use machine for training that is less intimidating like the Visalis100 or its analogues.
2. Undergo wet lab training before starting surgery on patients.
3. See as many videos (especially with commentary) of other surgeons.
4. Watch senior surgeons or colleagues perform.
5. It makes sense to see videos of ECCE, SICS and all methods of phacoemulsification surgery.
6. Be vigilant in observing the complications and the way others came out of that situation.
7. Learning curve is independent of gender and age of the trainee surgeon.
8. Learning curve is shorter in persons who are tech savvy or open minded to technology.
9. Learning curve is definitely short for those trainees who have dedicated instructors by their sides during learning.
10. Stress on the trainees is markedly less when there is a vitreo retinal surgeon available in the institution.
11. Patient selection for training cases is important. Try to choose cataracts with a sufficiently hard nucleus but prefer not to choose very hard nucleus.
12. Use Step-By-Step method. That is doing the same step in as many patients as possible before proceeding to the next step. That way you can master each step thoroughly.
13. Do not be afraid of complications. They are going to happen no matter how advanced your career is. Even the most experienced surgeons encounter them.
14. Record your surgery and play videos at home repeatedly to see where you lack.

**Conflict of interest**

**Declaration**

The author has no financial or commercial gains from the company Carl Zeiss Meditec from Germany.
References

IMPORTANCE OF DEMOGRAPHIC RISK FACTORS FOR PRIMARY ANGLE CLOSURE

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Abstract

According to the Guidelines of the European Glaucoma Society (fourth edition), the family history in the closing angle is an important factor that makes the family screening vital in these families.

It is present in the clinical case in which two twin patients in different circumstances show the same symptoms of angle closure.

Keywords: family history, angle closure glaucoma

Open-angle glaucoma (OAG) and angle-closure glaucoma (ACG) are the second leading cause of blindness worldwide. ACG affects 16 million people, and almost 4 million are bilaterally blind. Although three times more people have OAG than ACG worldwide, the greater morbidity of ACG means that the absolute number blind is similar to that of OAG.

Angle-closure and angle-closure glaucoma result from disturbed physiological mechanisms and anatomical measures with a genetic influence but the future testing can exploit knowledge of these factors [8,9].

At this moment, we recognize the following as Demographic risks factors for Primary Angle Closure (PAC):
- Older Age
- Female
- Asian and Eskimoan Race
- Family History – vital/ first degree relatives may have a 1 in 4 risk of PAC disease but a robust evidence for significant increased risk does not exist yet [2].

Family History of Angle Closure Disease risk was especially high in mothers and siblings. In patients with FHG, knowledge of genetic disposition of the glaucomas, may have led to an earlier diagnosis [5].

The prevalence of narrow angles was 2.2% and twice as high in women. In two subjects (0.03%), an attack of AACG developed in one eye after diagnostic mydriasis [4,5].

Angle-closure and ACG are more common in eyes with shorter axial length (AL), shallower anterior chamber (AC), and a relatively larger lens. Eye size is in part genetically determined-twin studies support a genetic influence of the disease. Many genes were found to be associated with ACG, but no specific gene has yet been identified [9].

Anatomic risk factors for ACG do not adequately explain why many people with small eyes and narrow angles never develop the disease.

Static measurements ignore the internal structures of the eye change from moment to
moment but physiological risk factors are at least as important as the anatomic ones [8,9]. Dynamic Features of the Eye in combination with anatomical structures (small eyes – genetic factors), which contribute to Angle Closure are the following: high resistance in the iris-lens channel, iris volume retention on pupil dilation, high choroidal expansion - small eyes with thick sclera, plateau configuration of the iris, dilatator insertion (anterior positioned process ciliary) [8,9].

Case report

A 34-year-old woman presented in the Ophthalmology Emergency Room for: decreased vision Both Eyes (BE), blurred vision BE, redness BE, pain BE, headache, nausea/vomiting. The history of the present illness begun the last day the patient was examined from an ophthalmological point of view and she was dilated with Tropicamide 1% for fundus examination. The patient did not have a medical history and, in the ocular history, we did not find any ocular disease. However, the patient underwent many ophthalmological consultations and every time she was dilated, she presented severe headaches. Also, in dark, she had ocular pains. Regarding the personal history, the patient had Hyperopia Right Eye (RE) + 1,75/ Left Eye (LE) + 3,75.

Clinical examination
Visual Acuity (VA) Intraocular Pressure (IOP)
RE 10/100 50 mm Hg
LE 10/100 68 mm Hg

Biomicroscopy
RE/LE conjunctival hyperemia with ciliary injection, epithelial corneal oedema, pupil oval, asymmetric, poorly reactive, mild-dilated (LE >RE), central anterior chamber depth – relatively normal, peripheral AC depth grade 0 Van Herick.

Gonioscopy
RE I evaluation
- iridotrabecular contact for 360°
- no visible angle structures
- the iris contour is flat – mild convex
After indentation the iris contour slightly changes.

LE I evaluation was not possible - high corneal oedema
II day in the morning - the iris contour is flat – mild convex
A thicker iris with anterior insertion - ciliary band not seen
After indentation the iris contour slightly changes.

Fundoscopic Examination
BE – normal color and shape of papilla, vertical report, normal neuroretinal rim, without alpha and beta para papillary atrophy, macula with red reflex, normal arteries and veins.
In this case, Diagnosis is RE/ LE Acute Angle Closure (AAC) with plateau iris configuration, Hyperopia.

Differential Diagnosis
1. AAC mechanism of angle closure
- Pupillary block (the iris is very convex, forward–ballooned iris (iris bombe), in contact with the anterior wall of angle; after indentation, the angle becomes wider; the mild iris is convex UBM [1,2].
- Anomaly on the level of the lens and posterior of the lens.

2. Secondary angle closure
Neovascular glaucoma, Inflammation resulting in both PAS and posterior synechiae, which can result in a secluded pupil with iris bombe, Iridocorneal endothelial syndrome, Uveal effusion associated with systemic medications (e.g. topiramate, sulfonamides, phenothiazines, anticholinergics), Suprachoroidal effusions, Malignant glaucoma, Iris or ciliary body mass lesions or cysts, Other secondary causes of pupil block (e.g. aphakia without an iridectomy, phakic intraocular lens [IOL], anterior chamber IOL, silicone oil), History of blunt or penetrating trauma, Axenfeld-Rieger syndrome, Epithelial downgrowth [1,2].

PLAN for Treatment
1. Medical treatment:
   - IOP lowering drops,
   - systemic hyperosmotics medications
2. Surgical treatment RE/ LE
   Laser Iridotomy
3. Clinical assessment
   Argon Laser Peripheral Iridoplasty
   Surgical Iridectomy
On the first day, the patient received the following:

1. Medical treatment
   - *IOP lowering drops systemic*
     *Pilocarpine 2% 1 drop for three times in first hour, afterwards 1 drop/hour*
     *Brimonidine 0,2% 1 drop twice per day*
     *Mannitol 20% 250 ml x2/day*
     *Acetazolamide 250 mg x2/day*
     *Pranoprofen 0,1% 1 drop x4/day*

On the second day, a surgical treatment was performed. Neodymium YAG Laser Iridotomy was performed. The pretreatment measures were the following:

* pilocarpine 2%, brimonidine 0,2%, topical anesthesia oxibuprocaine 4%

The Laser Settings were the following:

- Pulses per burst: 1-3
- Power: 2 mJ
- Spot Size: 50 µm spot size
- superior quadrant

The next day the patient had the following results: VA RE 100/ 100, IOP 12 mm Hg, LE 100/ 100(ps), mild mydriasis, iris atrophy temporal quadrant, IOP 14 mm Hg.

2 days later, RE was IOP 14 mm Hg and LE IOP 15 mm Hg.

At the next evaluation, IOP was normal RE and LE.

But, what was very interesting in this case was that the patient had a twin sister who had the same problems: pain and headache in dark. The twin sister came to consultation and the clinical examination was the following:

VA RE 100/ 100, IOP 12 mm Hg, CCT 546 µm
LE 100/ 100, IOP 13 mm Hg, CCT 551 µm

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</table>

The diagnosis for the Twin Sister was the following:

BE Primary Angle–Closure Suspect (Occludable Angle)

In this case, the Therapeutic Plan was the following:

1. Laser YAG peripheral Iridotomy BE.

After the laser treatment, the patient’s evolution was good.

**Conclusion**

The clinicians previously thought that ACG only had the pupillary block mechanism and that other entities had their own unique mechanisms (plateau iris, malignant glaucoma, and nanophthalmos).

What remained important was the clinical examination: AC depth to biomicroscopy and gonioscopy. Moreover, it was needless to ask about the Family Medical History.

These other mechanisms were dominant in some entities, but they contributed, such as
physiological risk factors for primary ACG. Research in the multiple dynamic features of ACG might explain its risk factors and lead to a better diagnosis [1-3].

The mechanisms behind ACG remain mysterious, but research has begun to reveal some clues. Women might be more prone to choroidal expansion, or Asians might have different iris fluid exchange [3-5]. These hypotheses should be tested in longitudinal studies of individuals at risk for ACG [6,7].

References

Abstract
We report the case of a 9-year-old child operated for intermittent exotropia and V-pattern with a good result 2 months after bilateral Lateral Rectus Muscle Recession. The binocular vision was restored in primary position and down-gaze with excellent stereopsis at near and distance and a deviation of +4 PD in primary position. Three months later, the patient developed a consecutive esotropia of +18 PD in primary position with diplopia in all gazes triggered by Amitriptyline treatment prescribed one month earlier for nocturnal enuresis. Diplopia was solved in time after anticholinergic medication cessation. During the recovery period, Fresnell prisms have been used in order to eliminate diplopia. Three months after diplopia onset, the binocular vision was restored showing a transitory and reversible effect of the Amitriptyline treatment. Fusion vulnerability can be a possible risk factor in developing diplopia and esotropia in patients treated with anticholinergic drugs.

Keywords: anticholinergic drugs, esotropia, diplopia, nocturnal enuresis, reversibility

Introduction
Various anticholinergic drugs can induce pupillary dilation. In children, topical anticholinergic drugs transitory increase the accommodative convergence to accommodation ratio and exacerbate underlying esotropia [1]. Different anticholinergic drugs have been reported as inducing diplopia and/or esotropia as: haloperidol and benztropine mesylate, oxybutynin [2,3].

Tricyclic antidepressants (TCAs) decrease the amount of time spent in REM sleep, stimulate vasopressin secretion, and relax the detrusor muscle. Given the efficacy and safety of enuresis alarms and desmopressin, tricyclic antidepressants which are anticholinergic substances (e.g., imipramine, amitriptyline and desipramine) are a third-line treatment for monosymptomatic enuresis (e.g., children who have failed alarm therapy and/or desmopressin) [4]. In several countries, they are also used as a first line treatment.

Methods
We report the case of 9-year-old child who was referred to us for intermittent exotropia of the right eye. The XT onset according to the parents was the age of 6 months. He was treated with prism glasses. No other treatments such as occlusion or orthoptic exercises have been used.
in order to improve the fusion capacity or vergence amplitude.

Surgery was proposed but initially parents refused it.

The first examination was done in our clinic in June 2012 and revealed:

VA OD=0, 9 with -1, 50 cyl ax 180; VAOS=0, 8 with +1, 50 cyl ax 90; 5 PD base-in were included in each lens of his glasses.

Fusion at distance was intermittently present with better control at near. With the glasses on he had short periods of fusion, diplopia or alternation at the Worth four dots test.

The deviation was measured by prism cover test. The patient had -35 PD exotropia at distance in primary position and -40 PD at near. The deviation was larger in up-gaze (-45 PD) and smaller in down-gaze -35 PD, the patient presenting a discrete V-pattern.

The prism adaptation test with Fresnel trial set showed unstable fusion free of diplopia at -35 PD at distance and near.

Re-evaluation was done 3 months later after prisms-in removal and new correction prescription according to cycloplegic (cyclopentolate 1%) measurements.

New refraction correction according to measurements under cycloplegia: OD -1, 50/ 90; OS -1, 5/ 90. No changes regarding fusion status. New measurements made by prism cover test in September 2012: Maximum deviation at distance and near: -35 PD in primary position, -40 PD in up-gaze, -30 PD in down-gaze. Good adduction and acceptable convergence amplitude on both eyes were present.

The surgery was proposed to the parents and was scheduled for the summer vacation of 2013.

The clinical re-examination was repeated at 6 months (March 2013) and respectively 8 months later (May 2013, preop. examination) showing no changes.

The surgical treatment was provided in June 2013: OD Right Lateral Rectus Muscle Recession 8 mm and OS Left Lateral Muscle Recession 7,5 mm.

We obtained a good result. At two months postop., in August 2013, the patient had a +4 PD esophoria in primary position with stable fusion present at near and at distance, and 40” Stereopsis at near and stereopsis present at distance. A discrete V pattern was still present, the patient having a small XT in up-gaze.

In November 2013, we received a request for an urgent appointment: the patient was accusing subjective diplopia.

The child was examined and the clinical examination found permanent diplopia accompanying an esotropia of +18 PD at distance and near, larger in down-gaze, +22 PD, and smaller in up-gaze: +12 PD. The patient had torticollis by using a down-chin position in order to avoid diplopia. The fusion was possible with 20PD base-out to the PAT. The patient also presented dilated pupils, difficulties in reading caused by reduced accommodation amplitude and also problems in concentration at school.
Anamnestic data completed the examination and brought new and important issues. The diplopia onset was in September 2013 as intermittent diplopia and became permanent in the last months. During the last two months the patient had two episodes of high fever connected with respiratory tract infections and in September started a treatment with Amitriptyline (anticholinergic drug) for nocturnal enuresis.

We presumed that the possible diagnosis was consecutive esotropia as a side effect of the Amitriptyline.

For the moment Fresnel foils +20 PD base-out on glasses were recommended and a detailed letter was send to the Neurologist in order to inform him about the possible side effects of the treatment.

The anticholinergic medication was stopped by the Neurologist in December 2013. The esotropic angle decreased in time after medication cessation. New Fresnel prism foil was adapted at every month in order to compensate for diplopia and the decreasing angle of ET.

In May 2014, the clinical examination showed small ET at distance and near 8 PD (+2 PD in up-gaze, +10 PD in down-gaze) with discrete diplopia at distance without prisms and fusion with 6 PD BO included in glasses.

Discussions

The reversibility of the anticholinergic medication side effect was not complete unfortunately at 6 months after treatment cessation, the remaining ET, larger than the previous one, suggesting possible long-term effects in certain patients.

Conclusions

Patients with anticholinergic medication should be carefully followed especially when they have strabismus history. Some patients are probably more susceptible than others in developing esotropia and diplopia, this explaining why only some patients develop diplopia.

The susceptibility is probably connected with individual factors but fusion vulnerability can be a possible risk factor confirming literature data [5,6].

References

ICE SYNDROME – CASE REPORT

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Abstract
Iridocorneal endothelial (ICE) syndrome encompasses a group of rare ocular pathologies with unilateral involvement, frequently affecting young women. The disease complex includes essential iris atrophy, Chandler’s syndrome, and Cogan-Reese syndrome. In the following article, we present a case of Iridocorneal endothelial syndrome in which a late diagnosis was made and who underwent surgery for advanced glaucoma.

Keywords: Essential iris atrophy, glaucoma, trabeculectomy

Iridocorneal Endothelial Syndrome (ICE) syndrome is a unique ophthalmic disorder that involves an abnormal corneal endothelium that leads to varying degrees of corneal edema, iris atrophy, and secondary angle-closure glaucoma [1]. This syndrome, which typically affects young women unilaterally with no family history [2], encompasses three clinical variants: Chandler Syndrome, Essential (Progressive) Iris Atrophy, Cogan-Reese Syndrome (Iris Nevus Syndrome).

The true etiology of ICE syndrome is unclear. Alvarado et al. have proposed a viral cause for the disease, based on a history of inflammation in certain cases and on the presence of inflammatory cells on histological analysis [3]. Further exploring this hypothesis, the same author revealed Herpes Simplex DNA in the pathological corneas by using the PCR (Polymerase Chain Reaction) technique [4]. The pathological elements observed in the endothelium are the most important clinical findings seen in ICE syndrome, namely “the ICE cell” which is pathognomonic. These cells are abnormally large and show increased pleomorphism [5]. Desmosomes, tonofilaments and numerous microvilli (100 versus 10 in a normal endothelial cell) [3], have all been identified by means of electronic microscopy, proving that the ICE cell shows epithelial-like characteristics [6]. The abnormal endothelial cells may migrate posteriorly, forming a membrane that covers the adjacent structures, iris and trabecular meshwork [7]. The contraction of this membrane leads to characteristic iris changes, iridotrabeocular synechiae, corectopia with the pupil being drawn towards the area where the synechiae are most prevalent and to secondary angle-closure glaucoma [5]. Glaucoma may appear in the absence of synechiae, because of the membrane migration phenomenon that can functionally close the angle, but still allow for an open angle on gonioscopy [2]. Hence, the degree of angle closure is not associated with the IOP level [8].

History

A 43-year-old female, with no relevant familial history, was admitted to our clinic for blurred vision in her left eye, reevaluation and treatment. The patient had been admitted to a
clinic in Vienna six weeks prior for blurred vision in her left eye, nausea drowsiness and vomiting.

Upon examination in Vienna, the patient had BCVA 0.2 OS, IOP OS 80mmHg. After managing the acute phase, clinical examination showed temporal pupil traction, pigment dispersion on the endothelium and cup-disk ratio 0.9. The patient was investigated (Fig. 1 Humphrey Visual Field) and released with the diagnosis of OS Rieger Anomaly. Secondary Glaucoma and maximal glaucoma topical medication (β-blocker, CAI, prostaglandin analogue, α2-agonist).

After 2 weeks, the patient was admitted to a county hospital in Romania with a BCVA 0.3 OS and IOP OS 43mmHg with treatment. Gonioscopy revealed a partially closed angle, CCT was 604µm and cup-disk ratio 0.8.

The patient received i.v. Mannitol 20% (after which IOP OS dropped to 18mmHg), underwent a second visual field analysis (Fig. 2) and was referred to our clinic with the presumed diagnoses OS Posttraumatic glaucoma? Iridodialysis? Acute angle-closure glaucoma 2 weeks prior?

Fig. 1 Humphrey Visual Field OS upon discharge from Vienna. MD=-5.02dB

Clinical examination

Upon admission to our clinic, the patient was in good health and her BCVA was of 0.6 OS and IOP OS 20mmHg.

Slit-lamp examination: pigment dispersion on the endothelium and anterior lens capsule, ectropion uvea, semi-kydriatic pupil with superior traction, corectopia and dyscoria, iris heterochromia, total temporal iris defect with pseudopolycoria, diffuse iris stromal atrophy, and PAS (peripheral anterior synechiae) at 11 and 1 o’clock (Fig. 3).

Fig. 2 Humphrey Visual Field upon discharge from the county hospital. MD=-15.01dB

Fig. 3 Anterior segment OS
On gonioscopy, the angle was completely closed and the cup-disk ratio was 0.9 with nasal shifting of central vessels and peri-papillary atrophy (Fig. 4).

A clinical diagnosis of OS ICE syndrome with secondary glaucoma was made.

Ancillary testing

Visual field analysis, optic nerve head OCT (Fig. 5) and specular microscopy (Fig. 6) were performed.

A final diagnosis was made based on the epidemiological data (unilateral symptoms in a young female with no family history), patient history (sudden onset), clinical examination (ocular symptoms with no systemic manifestations), and ancillary tests (specular microscopy being useful).

The final diagnosis was OS Essential Iris Atrophy (ICE Syndrome) with secondary glaucoma.

Follow-up and management

Surgery was recommended because of uncontrolled IOP in spite of maximal local treatment. A combined trabeculotomy-trabeculectomy with peripheral iridectomy was performed.

Surgery was uneventful and the following morning IOP OS was of 19mmHg with a medium anterior chamber depth. Glaucoma medication was stopped.

At the one month follow-up, BCVA OS was 0.6, IOP OS was 18mmHg without treatment, the ACD (anterior chamber depth) was medium and the filtering bleb was functional (Fig. 7).
At the 4 months follow-up, BCVA OS was 0.6, IOP OS was 20mmHg without treatment, the ACD was medium and the filtering bleb was functional. A visual field was performed, which showed MD=-19.21dB and the patient was given topical medication (fixed combination dorzolamide-timolol).

**Discussion**

Trabeculectomy is the surgery of choice for ICE syndrome. Shields et al. have reported a 69% success rate in a study conducted in 1978 on 33 eyes [10], while Yanoff reported a 64% success rate 1 year postoperatively and a 36% at 3 years [8]. When the trabeculectomy proves to be ineffective, the reason is usually excessive subconjunctival scarring [11] (a frequent occurrence in patients with ICE syndrome, given their young age). ICE-specific phenomena that lead to failure are bleb and/ or filtering ostium endothelialization [12] and PAS formation that obstruct the drainage pathway.

**Case particularity**

This case stands out due to its complexity and the controversies associated with it (3 different diagnoses from 3 different clinics). A long-term follow-up is necessary because the disease itself is progressive in nature. Studies suggest follow-up at 2-3 months intervals when glaucoma is associated and depending on its severity. Serologic testing is also recommended (Epstein-Barr and Herpes Simplex viruses) [13].

**References**

Abstract

Case report: A young healthy patient, health-care worker in a state hospital, presented in the eye department complaining of pain and blurred vision in the left eye for approx. 2 weeks. Examination revealed a VA of 12/20 in the left eye, an interstitial keratitis, some signs of vitreal inflammation and two chorioretinal mass lesions (at echography appearing cystic) in the affected eye. She also mentioned a chronic pain in the right wrist. No systemic association was found. Based on the orthopaedic examination, biopsy, and surgical intervention, a strong suspicion of ocular tuberculosis was made and the patient was advised to start tuberculostatic treatment for 12 months and ocular steroidian treatment for 4 months. The ocular manifestations regressed totally after 3 months of treatment, the VA of the left eye improving at 20/20.

Conclusion: Tuberculosis can present many manifestations, with multi systemic involvement. Ocular tuberculosis is a difficult diagnosis and thus requires thorough multi-disciplinary investigations.

Keywords: choroidal tuberculoma, interstitial keratitis, ocular tuberculosis, osteoarticular tuberculosis, wrist pain

Case report

D.H., a 34-year-old female patient, referred to us complaining of redness, pain and blurred vision in her left eye for the past two weeks, and with noticeable vision loss in the same eye for about three days. She mentioned working in healthcare in an ENT department of a state hospital. She had never been to an ophthalmology consultation before. On detailed questioning, she did not mention any systemic disorders or pathologies or any heredo-collateral antecedents.

Her best-corrected vision at the time of presentation was 20/20 without correction in the right eye and 12/20 without correction in the left eye.

The examination findings were normal for the right eye (anterior pole and fundus).

A detailed examination of her left eye revealed an anterior pole with conjunctival hyperemia, a cornea with an aspect of interstitial
keratitis, without any other signs of inflammation in the anterior chamber, photomotor reflex present and clear lens.

Fundus examination revealed the presence of vitreous cells, flare and two elevated masses in the inferonasal quadrant (about 1.5 and 2 disc diameters size) with sub-retinal exudates and attached retina. The surrounding inferonasal quadrant vitreous showed a marked haze, not allowing a good visualization.

In B-Scan, the lesions were described as cystic, suggestive of abscess (?). There was no evidence of choroidal excavation or any calcifications.

FFA showed a marked hyperfluorescence around the lesion in the early phase. The lesion also showed an early hypofluorescence, the appearance of dye within the lesion was only in the late-phase, this intra-lesional hyperfluorescence increasing over the later phases until the appearance of a homogenous hyperfluorescence.

Right eye FFA and echography were normal.

Her ocular examination and the FFA findings were collaborative for an inflammatory lesion, though a rare possibility of a neoplasm was also suspected.

We explained our suspicions to the patient when she started mentioning a chronic pain in the right wrist joint, which appeared some time before (could not say how much) and for which she did not do any treatment. We recommended a list of investigations: full complete blood count, ESR, CRP, coagulation probes, proteins, uric acid, urea, creatinine, bilirubin, glucose, lipid metabolism probes, hepatic enzymes, Ag Hbs, Ac HCV, HIV, VDRL, TPHA, IgM and IgG Ac antitoxoplasmosis, urine examination, pulmonary X-ray, abdominal and pelvic ultrasound and an orthopedic examination. She received local steroidian anti-inflammatory treatment in that period of results expectation.

After 14 days, she came back with a normal blood profile and biochemistry, except for a mildly raised ESR. Chest X-Ray, abdominal and pelvic ultrasound was normal.

Orthopaedic exam: at the moment of the first visit in our clinic, the patient accused intense pain in the right wrist joint with a slow evolution over time. After the clinical and X-ray exams, the presumed diagnosis was osteoarthritis of the right wrist joint. Clinically, there was no high local temperature of rash, classic signs of bacillary osteoarthritis.

After the primary clinical and paraclinical exams, the orthopaedic surgeon suspected osteoarticular tuberculosis of the wrist and secondary osteoarthritis. In those cases, the protocol recommended a biopsy and surgical treatment. The bioptic examination established the diagnosis of tuberculosis of the wrist. The orthopaedic treatment was wrist arthrodesis with plate and screws with an excellent evolution and a favorable result.
During this time, the patient maintained the VA of 12/20 in the left eye. Also, the anterior and posterior pole aspects were unchanged from the last control. She was advised a depot steroid (triamcinolone) injection in the affected eye, but refused.

The results became evident for the diagnosis of ocular tuberculosis and the patient received tuberculostatic treatment for 12 months.

After three months of treatment, the VA in the left eye was 20/20 without correction, the anterior pole was normal, without any signs of inflammation, and the fundus lesions regressed leaving some infero-nasally pigmentary scars. The local steroidian treatment was continued for one more month and then stopped.

**Discussion**

Ocular tuberculosis usually occurs in apparently healthy individuals and can lead to irreparable, vision threatening damage to the eye. (1,2) On the other hand, an innocuous ocular involvement may be associated with significant systemic tuberculosis. (3)

As in our case, the ocular finding can help the physician make a diagnosis of systemic tuberculosis.

There are only a few reported cases of choroidal tuberculomas, and it may present with or without active extrapulmonary tuberculosis.

A lesion like this needs a differential diagnosis with a choroidal melanoma. (4)

The diagnosis of ocular tuberculosis is usually presumptive and depends upon indirect evidence, a definitive diagnosis requiring an inter-specialty interaction and a high clinical suspicion. (5)

Extrapulmonary tuberculosis is more difficult to diagnose than pulmonary disease, often requiring invasive procedures. (6)

Definitive diagnosis in such cases is difficult but not impossible.

Treatment is another challenge for the treating ophthalmologist.

**Acknowledgement:**

This work received financial support through the project entitled “CERO – Career profile: Romanian Researcher”, grant number POSDRU/159/1.5/S/135760, cofinanced by the European Social Fund for Sectoral Operational Programme Human Resources Development 2007–2013.

**References**

INFORMATION FOR READERS

FIRST ANNOUNCEMENT

ROMANIAN SOCIETY OF OPHTHALMOLOGY (RSO)

www.ofthalmologiaromana.ro

The Romanian Society of Ophthalmology (RSO) is pleased to invite you to its "XIVth NATIONAL CONGRESS with INTERNATIONAL ATTENDENCE", to be held in SINAIA, ROMANIA, between 7 - 10 October 2015.

CONGRESS VENUE:

“Casino” International Conference Center Hall and Congress Center Hall "New Montana Hotel", SINAIA
The meeting will include:
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RESIDENTS SESSION
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EXHIBITION

ABSTRACT SUBMISSION DEADLINE (in Romanian and English): 1st July 2015

Social program:
A wide range of events for both delegates and accompanying partners will provide ample opportunity to enjoy the entertainment and cultural activities in Bucharest.

Language:
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Further information is available from:

XXIV NATIONAL CONGRESS OF OPHTHALMOLOGY ROMANIAN SOCIETY OF OPHTHALMOLOGY
19-21 Virgiliu street, sector 1, Bucharest, ROMANIA
T/F: +40 21 411 80 15
E-mail: mke@otlog.ro

Online to register:
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1st August 2015 - Final Program
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### Registration fees

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**Hotel NEW MONTANA****

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**Hotel SINAIA****

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The process of sending the articles

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