**Intravitreal Injection – A Small Procedure for the Eye, a Giant Leap for Ophthalmology**

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Intravitreal injections are the most common therapeutic procedures in ophthalmology. These injections allow intraocular delivery of drugs that are highly effective for the treatment of a variety of retinal diseases. The procedure is short and simple, has an excellent local and systemic safety profile, and enables restoration and preservation of visual acuity in a large number of patients. Intravitreal injections were introduced to the routine clinical practice of ophthalmology only a little over a decade ago, but have created a therapeutic revolution due to their high efficacy, and today are an integral part of the treatment of ocular diseases. This review will cover the development of intravitreal injection treatment, describe the injected drugs, the injection technique and its possible complications, and the commonly used treatment protocols.

**New Lenses in Modern Cataract Surgery**

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During cataract surgery the natural opaque crystalline lens is replaced by an artificial intraocular lens that compensates for the optical loss following lens removal. The conventional intraocular lens is mono-focal and necessarily requires spectacle correction for the clear vision at various foci in the same eye. In recent years a variety of intraocular lenses were developed including multifocal (bifocal and trifocal), “toric” lenses to correct corneal astigmatism, lenses with extended depth of focus and their combinations, and the commonly used treatment protocols.

**Topical Anti-Inflammatory Agents for Dry Eye Disease**

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Dry eye disease [dry eye] is a multifactorial disorder of the ocular surface. Dry eye is one of the most frequent ocular disorders, affecting 5% to 50% of the entire population at all ages. Evidence suggests that inflammation and hyperosmolarity are considered core mechanisms in the development of dry eye. Dry eye is accompanied by changes in tear composition including enhanced hyperosmolarity and secretion of pro-inflammatory mediators such as cytokines, chemokines, matrix metalloproteinases [MMPs] and adhesion molecules. All these factors may act as mediators of tissue damage leading to lysis of cell membranes and tight junctions in epithelial cells. Eventually these processes lead to corneal and conjunctival epithelial cells death as well as conjunctival goblet cell dysfunction and death. Anti-inflammatory agents for dry eye include corticosteroids, immunomodulator agents and essential fatty acids. Recently, an integrin lymphocyte function-associated antigen-1 [LFA-1] antagonist, lifitegrast ophthalmic solution [Xiidra] was approved in the USA for the treatment of dry eye. Lifitegrast blocks the binding of intercellular adhesion molecule-1 [ICAM-1] to LFA-1. The following review attempts to present a current update of the available anti-inflammatory agents for dry eye disease.
This is an article on a six year follow-up of a patient diagnosed with idiopathic retinal vasculitis. Her medical history, symptoms and findings are presented in detail, related to the diagnostic investigations and the resulting diagnosis. Patient follow-up was marked with repeated attempts to utilize steroid sparing strategies including antimetabolites such as Methotrexate and mycophenolate Mofetyl with only limited success. Biologic agent [anti TNF], Adalimumab, was also not successful. We discuss the difficulties experienced by the patient and her response to therapy given her preserved vision on the one hand and her apparent uncontrolled retinal vascular leakage. The patient’s ability to function in daily life reduces her willingness to endure therapy-related adverse events.

**UNUSUAL VITREOUS DETACHMENT**

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A 49 years old patient with a history of brachytherapy for choroidal melanoma was referred to the ocular emergency room for suspected recurrence due to pigment in the vitreous cavity. On examination, pigmented vitreous secondary to posterior vitreous detachment with traction from the atrophic tumor was observed with no evidence of recurrence.

**DEMODEX PARASITES AND CHRONIC BLEPHARITIS**

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In the current issue of ‘Harefuah’, Livny et al present an article on the prevalence of Demodex parasites in patients with chronic blepharitis and healthy controls in Israel. This prospective case controlled study describes the quantitative connection between the number of parasites found on 6-8 sample eyelashes and chronic blepharitis, one of the most prevalent conditions in the general population and especially prevalent in the ophthalmologist office visits. Blepharitis symptoms may vary from being asymptomatic, chronic condition, dry eye, and sometimes even a severe compromise of ocular surface with a morbid impact on patient quality of life.

In recent decades, progress was presented in a number of published articles including one meta-analysis that connects blepharitis with Demodex and the treatment of both with tea tree oil. Also, two different species of Demodex were identified which prefer to inhabit different areas of the eyelid. While the presented data do indicate a quantitative connection between Demodex and blepharitis, questions are raised as to whether there is a causative relationship between them? Can Demodex cause chronic blepharitis as an only factor? Or a symbiotic parasite which proliferate in blepharitis by consuming the debris and byproducts of blepharitis? Is it both? Although many theories exist, the answer is yet to be proven, but the consensus today is to combine anti-Demodex products while treating refractory chronic blepharitis.

**CHILDHOOD GLAUCOMA**

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“Childhood glaucoma” is a heterogenic group of diseases, characterized by elevated intraocular pressure (IOP) associated with optic-disc damage and other ocular comorbidities. Diagnosis requires two or more of the following: elevated IOP, optic nerve damage, enlarged cornea or Descemet’s membrane ruptures, enlarged eye, high myopia and visual field defects. Childhood glaucoma is classified as primary if it occurs as an isolated ocular disease, and secondary, when the disease occurs along with other ocular anomalies or systemic diseases such as Neurofibromatosis and Sturge-Weber, or with acquired conditions such as uveitis complications, ocular trauma, cataract surgery, as well as from systemic and ocular steroid use.

The clinical manifestations of childhood glaucoma depend on the age of presentation. In newborns, an enlarged eye with an enlarged cloudy cornea can be found, while infants present with an enlarged eye and signs of tearing, blinking and glare. Older children are usually asymptomatic and the disease is discovered incidentally on eye examination for other ocular problems.

Treatment of childhood glaucoma is complicated and demanding. Most types of pediatric glaucoma require surgery in order control IOP, while medical treatment has a supportive role. Different types of glaucoma surgery are indicated for different types of pediatric glaucoma. Regular lifelong monitoring, including IOP control and treatment for the prevention of amblyopia is necessary to obtain and maintain good vision.
Fulminant intracranial hypertension is a rare, acute presentation of idiopathic intracranial hypertension with rapid and devastating visual loss that can lead to blindness. As vision deteriorates quickly and often irreversibly, prevention of further visual loss requires emergent treatment to decrease intracranial pressure. The case presented is that of an 18 years old male with new symptoms of headaches and visual obscurations that had rapid progressive visual loss with findings of severe bilateral swollen discs. Brain MRI and MRV ruled out intracranial mass and cerebral venous thrombosis. A lumbar puncture confirmed highly increased ICP. Due to the fulminant clinical presentation, he underwent an urgent fenestration of both optic nerves with improvement of vision in both eyes. The patient’s clinical scenario accentuates the importance of prompt recognition of this rare disorder and the need for immediate surgical intervention to prevent further visual loss and blindness.

**OPHTHALMIC MANIFESTATIONS OF SILENT SINUS SYNDROME**

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**Purpose:** To describe 7 case reports of “silent sinus syndrome” (SSS) cases and review the literature on this topic.

**Methods:** A retrospective review of 7 consecutive cases of SSS seen by the authors from 2005 to 2017. Data collected included patient demographics, clinical presentation, imaging findings, surgery performed, outcome and follow up.

**Results:** Seven patients were identified presenting with SSS, two of them following trauma, and the rest with no relevant history. All cases developed progressive enophthalmos and hypoglobus, but only 3 developed vertical diplopia symptoms. Three patients underwent functional endoscopic sinus surgery, hypoglobus, but only 3 developed vertical diplopia symptoms. One patient also underwent orbital floor support surgery.

**Conclusions:** Silent sinus syndrome is a slow, progressive, unilateral disorder, with changes occurring over the years. Most patients present with enophthalmos and hypoglobus due to subclinical disease of the maxillary sinus and no obvious preceding sinus symptoms. The mechanism is presumed to be the obstruction of the natural ostium of the maxillary sinus, accumulation of secretions and the development of negative pressure within the sinus leading to its collapse.

**IDIOPATHIC RETINAL VASCULITIS – THE INTERPLAY BETWEEN A CHRONIC IDIOPATHIC OCULAR DISEASE, ITS THERAPY AND THE PATIENT**

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**Purpose:** The sense of vision is highly important for humans and its loss markedly affects function and quality of life. Many inherited retinal diseases (IRDs) cause visual loss due to dysfunction or progressive degeneration of photoreceptor cells. These diseases show clinical and genetic heterogeneity.

**Aims:** The Israeli IRD consortium (IIRDC) was established with the goal of performing clinical and genetic mapping of IRDs in the Israeli population.

**Methods:** Clinical evaluation is carried out at electroretinography (ERG) centers and ophthalmology departments, where the patients undergo a comprehensive eye exam, including testing of visual acuity, refractive error, imaging techniques and ERG tests. Genetic analysis is performed using Sanger sequencing, analysis of founder mutations, and whole exome sequencing.

**Results:** We recruited over 2,000 families including more than 3,000 individuals with IRDs. The most common inheritance pattern is autosomal recessive (65% of families). The most common retinal phenotype is retinitis pigmentosa (RP - 45% of families), followed by cone/cone-rod dystrophy, Stargardt Disease and Usher syndrome.

We identified the cause of disease in 51% of families, mainly due to mutations in ABCA4, USH2A, FAM161A, CNGA3, and EYS. IIRDC researchers were involved in the identification of 16 novel IRD genes. In parallel, IIRDC members are involved in the development of therapeutic modalities for these currently incurable diseases.

**Conclusions:** IIRDC works in close collaborative efforts aiming to continue and recruit for the genotype - phenotype study from the vast majority of Israeli IRD families, to identify all disease-causing mutations, and to tailor therapeutic interventions to each IRD patient.
**OPHTHALMOLOGY – FACING THE FUTURE**

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This special issue of HaRefuah is dedicated to Ophthalmology facing the future. This dynamic and forever innovative field of medicine is in a constant state of development in all its sub-specialties. In ophthalmology we often witness immediate rewarding results of treatment and surgery, having a huge impact on one of the most important senses, namely improving sight, stopping deterioration and preventing blindness. We are inviting the readers for an overview of some of the research and special cases, as well as some reviews of the hottest topics in ophthalmology.

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**PREVALENCE OF ASTIGMATISM BEFORE ROUTINE CATARACT SURGERY: COMPARISON BETWEEN BEDOUIN AND JEWISH POPULATION IN SOUTHERN ISRAEL**

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Both authors have contributed equally to this study.

Objective: To assess the prevalence of corneal astigmatism among patients before routine cataract surgery and overall ocular difference between Jewish and Bedouin population in the south of Israel.

Methods: Retrospective research collecting biometric information from IOLMaster (Carl Zeiss Meditec AG, Germany) in patients attending cataract surgery at Soroka University Medical Center, Beer-Sheva, Israel between the years 2015 -2016.

Results: Mean corneal astigmatism among all cohorts was 1.20D ± 0.83, with 1.26D ± 0.83 in Jews patients (p=0.08). Corneal astigmatism among patients before routine cataract surgery was 1.20D ± 0.83 in Jews patients vs 1.17D ± 0.82 in Bedouins patients (p-value=0.08). Corneal astigmatism was higher than 2.5D in 12% of the population, 20% of the population, 28% of the population had corneal astigmatism above 1.5D and lower than 0.5D was seen in 20% of the population. The authors recommend epilating 6-8 lashes of patients withDemodex infestation of the eyelashes to chronic blepharitis. Six to eight eyelashes were epilated from each participant and studied microscopically for the presence of Demodex by a blinded examiner. Fluorescein stain was added to the “clean” samples in order to reduce the false negative results.

Results: Demodex were identified on the eyelashes of 44 patients with blepharitis (73.3%) and 20 controls (40%) (p<0.001). After adjusting for age, blepharitis was still a significant risk factor for the presence of Demodex (OR=2.96, CI 95% 1.2-7.3).

Conclusion and summary: This study supports previous studies demonstrating pathogenic relationship between Demodex infestation of the eyelashes to chronic blepharitis. The authors recommend epilating 6-8 lashes of patients with blepharitis for microscopic identification of these parasites. Fluorescein stain may have a limited role in the recognition of Demodex in parasite free samples.

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**THE ISRAELI INHERITED RETINAL DISEASES CONSORTIUM (IIRDC) - CLINICAL-GENETIC MAPPING AND FUTURE PERSPECTIVES**

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Introduction: Previous studies demonstrated the potential pathogenic relationship between infestation of the eyelashes by the parasite Demodex and chronic blepharitis, whereas other studies did not demonstrate such relations and concluded that Demodex is a normal eyelid flora.

Purpose: This study examines the prevalence of Demodex in patients with blepharitis compared to a healthy control group in Israel, in order to further explore and establish its pathogenic role in cases of chronic blepharitis.

Methods: A case-control study was conducted including 110 participants: 60 patients with chronic blepharitis attending a tertiary medical center and 50 subjects with no signs of blepharitis. Six to eight eyelashes were epilated from each participant and studied microscopically for the presence of Demodex by a blinded examiner. Fluorescein stain was added to the “clean” samples in order to reduce the false negative results.

Results: Demodex were identified on the eyelashes of 44 patients with blepharitis (73.3%) and 20 controls (40%) (p<0.001). After adjusting for age, blepharitis was still a significant risk factor for the presence of Demodex (OR=2.96, CI 95% 1.2-7.3).

Conclusion and summary: This study supports previous studies demonstrating pathogenic relationship between Demodex infestation of the eyelashes to chronic blepharitis. The authors recommend epilating 6-8 lashes of patients with blepharitis for microscopic identification of these parasites. Fluorescein stain may have a limited role in the recognition of Demodex in parasite free samples.