- **Uveitis is the fourth leading cause of blindness among the working age population in the Western world. It affects over 300,000 patients in the United States, and a similar number in Europe.**

- **Uveitis is particularly prevalent in younger people. The mean age of uveitis patients is 39 and, if left untreated, uveitis can cause irreversible sight loss in just three years.**

- **Uveitis is an autoimmune disease involving the eye. It is often associated with other autoimmune diseases, such as psoriasis or rheumatoid arthritis, and often precedes these. While in recent years new treatment options for psoriasis or rheumatoid arthritis have changed the prospect of these patients, uveitis has remained poorly noticed and under-recognized.**

- **The loss of vision is correlated with the severity, frequency and duration of inflammatory episodes. Hence, early detection and continued control of the disease are critical.**

- **Current treatment options are limited and the standard of care has not changed since the 1960's: Steroids. While effective in controlling the inflammation, chronic steroid use is burdened by multiple side effects, including such serious complications as bone loss, increase in cardiovascular risks (high blood pressure, serum lipids, diabetes, weight gain) as well as mood and sleep disorders that can add significantly to health care costs. Hence, physicians are faced with difficult choices and try to balance between conflicting goals.**

- **Though awareness of eye diseases such as Age-Related Macular Degeneration (AMD) has increased over the past decades, uveitis remains virtually unknown to most people and is often under-diagnosed by physicians.**

Uveitis – Inflammation of the Eye

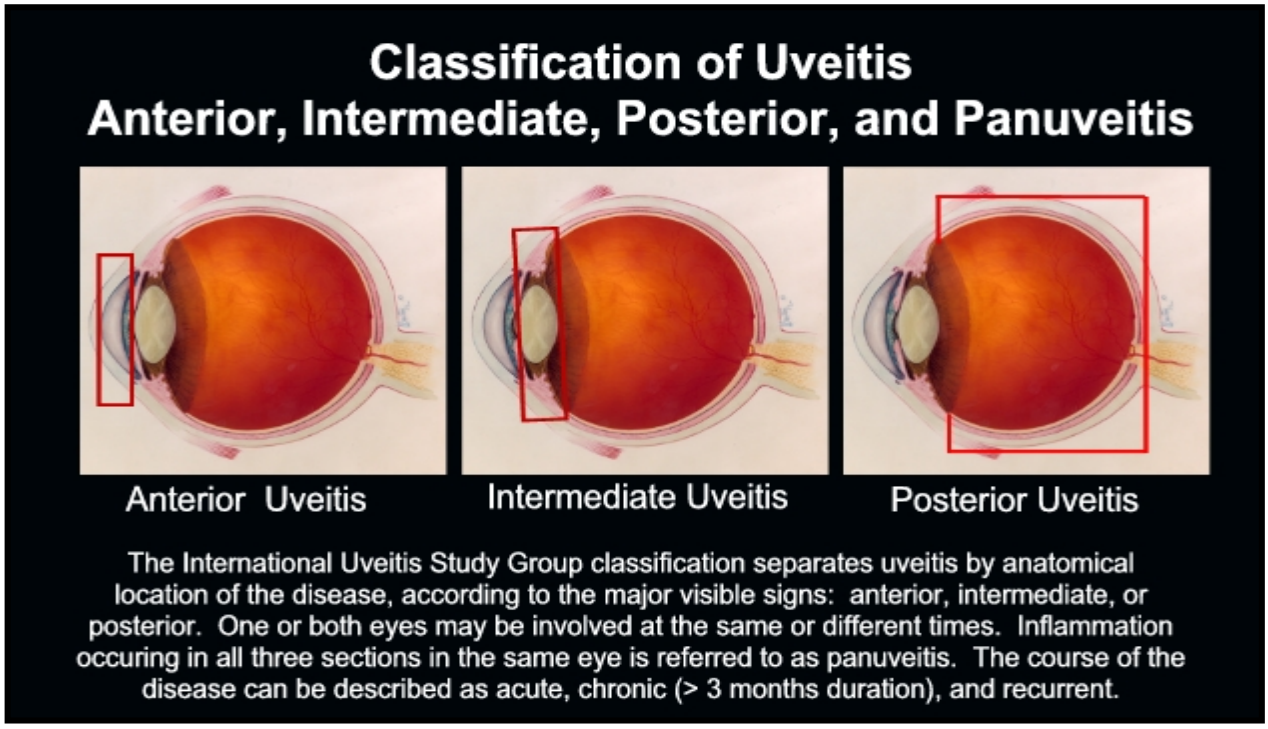
Uveitis is an autoimmune disease that results in chronic inflammation of several parts in the eye. Autoimmune diseases occur when an individual's immune system mistakenly recognizes specific proteins within the body as foreign and mounts an attack against them, causing a chronic inflammatory reaction that can result in progressive and irreversible damage to tissues over time. In arthritis, for example, the body's own defense mechanisms attack the joints, while in multiple sclerosis, the protective sheath on nerves is affected.

Symptoms of uveitis include redness of the eye, light sensitivity, pain, blurred vision and “floaters” that is particles in the eye that cause cloudiness and the sensation of flickering objects. Uveitis affects a younger, usually working age population than many other diseases associated with risk of blindness – the median age group of patients in the United States is 39. Experts estimate that uveitis causes 10% of new cases of blindness in the United States each year. Approximately 300,000 people suffer from uveitis in the United States alone, with European prevalence estimated at about 200,000.

Uveitis can have a variety of causes. Roughly 50% of uveitis patients also suffer another autoimmune disease. For example, uveitis is common in children with Juvenile Rheumatoid Arthritis (JRA). Uveitis can also result from infection or injury to the eye but in up to 50% of patients, the cause of uveitis is unknown. Patients may suffer single acute episodes of uveitis, the inflammation may be chronic, lasting three or more months, or they may suffer recurrent episodes of inflammation.

Based on recent disease guidelines, there are four forms of uveitis, classified by where the inflammation occurs in the eye:

- *Anterior* – affecting the front of the eye, mainly the area around the iris
- *Intermediate* – affecting the area around the front end of the retina, and the vitreous, a clear gel-like substance that fills the inside of the eyeball between the lens and the retina
- *Posterior* – affecting the rear portion of the eye including the retina and optic nerve
- *Pan-uveitis* – uveitis affecting at least two of the disease forms described above



Anterior uveitis affects approximately 2/3 of uveitis patients and this type of uveitis is usually episodic in nature. Generally diseases that affect the front of the eye are easiest to treat, as medications can be given directly to the affected area with an eye drop. As most cases of anterior uveitis are treatable, it is considered a less severe form of the disease.

The remaining 1/3 of uveitis patients are affected by the more severe and chronic intermediate, posterior, and pan-uveitis. Though these forms of uveitis affect fewer patients, they cause over 50% of cases of blindness and vision loss that occur as a result of the disease. Delivering therapeutics to the back of the eye is a challenge in ophthalmology. Therefore, treating intermediate, posterior, and pan-uveitis is more difficult than anterior uveitis -- eye drops cannot reach the back portions of the eye and thus are not useful in this patient population. As a result, patients with these forms of uveitis generally receive medication to control the inflammation orally or through injections into the eye. New delivery technologies are being developed to counter this treatment challenge -- for example, implants for the controlled release of therapeutics.

Uveitis appears to be an under-diagnosed disease. The more severe forms that are no longer responsive to topical corticosteroids and require systemic treatment are particularly “difficult” to treat and patients require referral to specialists. As is generally the case in diseases with limited treatment options, diagnosis and referral are often inadequate or delayed, and consequently the number of patients is underestimated.

Treatment

The goal of any uveitis treatment is to rid the eye of any inflammation, which is believed to be the main contributor of vision loss and blindness in the disease. The only class of medication that is currently approved by the Food and Drug Administration (FDA) in the United States for treatment of uveitis is corticosteroids. Steroids are available to uveitis patients in the form of eye drops, pills, implants, and injection. Treatment depends on several factors, such as location of the inflammation. As mentioned above, if inflammation occurs in the front of the eye (anterior uveitis) eye drops are sufficient to treat the disease in most patients; if inflammation occurs in the back of the eye (posterior uveitis), patients will likely require injections or pills for therapeutic levels of medication to reach the disease location. The therapy is typically individualized and requires regular monitoring.

The main problem in treating the severe forms of uveitis is that the inflammation is generally chronic, and thus patients require medications (steroids) for long periods of time. Side effects of long-term steroid use are well known in the medical community, as steroids have been a treatment option for several diseases associated with inflammation since the 1960s. Even levels of more than 7.5mg/day of steroids (in pill form) can cause severe side effects, such as bone loss, increased cardiovascular risk (high blood pressure, elevated lipids, diabetes, weight gain), mood and sleep disorders, and swelling of the legs, resulting in high costs for the treatment of these complications. Steroids dosed in the range of 2.5-7.5 mg/kg, well below the currently recommended guidelines for treatment in uveitis, lead to a 1.8 to 2.6 fold increased risk of fracture of the hip and spine, respectively[1]. Recently, demographic data of an ongoing clinical program

[1] Summey, Brett T., Prevention of Osteoporosis Associated with Chronic Glucocorticoid Therapy, Archives of Dermatology, March 15, 2006, Vol. 295, No. 11

was presented, revealing that the mean dose of steroids uveitis patients were taking was 16-23 mg/kg[2]. These high levels of therapy cannot be sustained without incurring major side effects.

Long-term use of local steroids (eye drops, implant, and injection) can also cause side effects. Though generally systemic side effects of local steroid therapy are not a significant problem, the eye itself is at risk of serious side effects resulting from prolonged steroid use. Of these, the most severe are glaucoma (increased pressure in the eye, one of the top reasons for blindness in the United States) and cataracts (clouding of the lens in the age, commonly associated with aging). Recently, the U.S. FDA approved a steroid implant for use in treating posterior uveitis. Though the implant is effective in controlling inflammation, virtually 100% of patients treated in this way require eye surgery to remove a cataract after 30 months, and 30% of patients will require eye fluid draining procedures to relieve ocular pressure due to severe glaucoma.

Conclusion

There is a major need for a safe, effective, and approved medication for the treatment of uveitis, especially for the more severe forms of the disease. Though steroids are effective in quickly controlling inflammation, they cannot be used long-term without incurring serious side effects. New treatment alternatives are required that allow corticosteroids to be tapered off to levels not associated with long-term morbidity, or eliminated altogether, while providing effective control of the chronic eye inflammation. While currently several of these agents, called corticosteroid-sparing agents, are used experimentally, none of these is yet approved in uveitis. Lux Biosciences is developing the first corticosteroid-sparing agent specifically for the uveitis indication and believes the medication has the potential of establishing a new standard of care for this debilitating condition.

[2] Barisani-Asenbauer, Talin, Patient Demograpic Data for Phase 2/3 Clinical Trials of a Novel Calcineurin Inhibitor, Luveniq™, for the Treatment of Non-Infectious Uveitis, 7th International Symposium on Uveitis, International Uveitis Study Group (IUSG), Konstanz, Germany, Sept. 2008