Introduction

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The term uveitis is broadly defined as inflammation of the uveal tract comprised by the iris, ciliary body, and choroid. In practice, this term has been more broadly applied to any inflammatory state involving the interior of the eye including iritis, intermediate uveitis, pars planitis, vitritis, retinal vasculitis (phlebitis and arteritis), choroiditis, and papillitis. This area of ophthalmology encompasses multiple pathologic processes that can induce aberrant or exuberant inflammation within the eye such as infections of the eye, autoimmune disorders, trauma to the eye, certain medications which can incite ocular inflammation, and rarely malignancies.

The practitioner in this realm must

- perform a careful history with review of systems as this can often lead to a differential diagnosis and direct subsequent investigations. The adage that "if you listen to the patient, they will very likely give you their diagnosis" is more pertinent in this realm than practically any other in ophthalmology.
- examine the patients' eyes CAREFULLY documenting: visual acuity, pupillary responses, extraocular muscle movements, confrontational or automated visual field testing, the areas of the eye with inflammation (anterior, intermediate, posterior), presence of cells and/or flare (quantified and characterized as granulomatous or non-granulomatous), iris pathology (transillumination defects, nodules, peripheral anterior synechiae, posterior synechiae), lens changes, intraocular pressure, clarity of the vitreous, appearance of the optic nerve and retinal vasculature, and choroidal pathology.
- examine other areas of the patient's body for pertinent findings (joint swelling, rashes, heart murmur, etc.).
- evaluate the information obtained by history, review of systems, and physical exam to parsimoniously order supportive laboratory and radiographic studies. Every patient with uveitis does NOT require complete serologic testing and MRI of the brain/orbit.
- prescribe the most effective and least toxic medication to treat the ocular pathology. This may merely require the use of topical steroids for an episode of iritis or could necessitate intravenous Infliximab or cyclophosphamide for Adamantiades-Behçet's associated retinal vasculitis. The decision of which medication to use should be evidenced based. Are there double-blinded, placebo controlled trials demonstrating safety and efficacy for this indication? If not, are there large cohort series or published reports in this realm? Additionally, the physician must be cognizant of the overall health of the patient and especially comorbidities when prescribing systemic medications (e.g., avoiding methotrexate in

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the alcoholic cirrhotic or cyclosporine in the patient with renal dysfunction).

- refer the patient to the appropriate practitioner if the patient's condition requires care outside of one's area of expertise or seek a second opinion. It entails a generous level of humility to admit to the patient that despite years in medical education and training their ocular problem requires a different specialist with greater experience or unique expertise. A second opinion may merely provide a fresh perspective on a problem and direct therapy or diagnosis in an alternative direction.
- remain current. Since approval of etanercept in 1998, the TNF alpha inhibitors have altered the course of inflammatory disease management and proven to be invaluable therapies in those with recalcitrant ocular inflammatory disease. In 2009, the global market for TNF alpha inhibitors was $22 billion [1]. This is but one example of the explosion in targeted immunomodulatory therapy directed toward specific cytokines, interleukins, cell surface markers, etc. This trend will invariably progress as our knowledge of the immune system and disease mechanisms are further elucidated. It will require that the physician dedicate time to continuing medical education to remain on the cutting edge of therapeutic options.

This is a daunting list to say the least, and I am reminded of the sixteenth century ophthalmologist, Dr. George Bartish, who wrote about the qualities of a "good" ophthalmologist. In Dr. Bartish's era, a "good" ophthalmologist was defined as having descended from religious parents; studied Latin; training by a well-respected ophthalmologist; not being motivated by financial rewards; never promising more than one can deliver. After reviewing his own criteria, Dr. Bartish realized that there were indeed very few well trained ophthalmologists meeting those standards [2]. Similarly, those who treat uveitis patients have considerable expectations, and the risk in performing below standard can have sight threatening and at times life threatening ramifications. The reward of this field is the constant intellectual stimulation, diversity of diseases, and the appreciation of patients and colleagues alike for the skills and knowledge necessary to deter the effects of these infirmities.

Epidemiology

Uveitis can affect patients of any age and is one of the leading causes of preventable blindness in the world accounting for approximately 10 % of blindness worldwide [3]. The worldwide prevalence of uveitis is estimated to be 115–204/100,000 people, and the incidence is estimated at 17–52/100,000 people per year [4]. The mean age of patients with uveitis is 40 years old, thus this disease has a significant impact on patients' productivity in the work force and their long-term health care costs [5].

The prevalence of uveitis in the United States is 38 per 100,000 with an incidence of approximately 15 cases per 100,000 population per year [6]. Uveitis is estimated to be responsible for approximately 10–20 % of the blindness in the United States [7].

The male to female ratio is approximately equal when grouping all uveitic diagnoses in aggregate. There is considerable variability depending upon specific diagnosis (e.g., ankylosing spondylitis is 2.5 fold more common in men than women).

Signs and Symptoms

The signs and symptoms produced by active uveitis are dependent upon the anatomic location of the inflammation in the eye, rapidity of onset of the inflammation, and duration and course of disease.

The signs of ocular inflammation involving the anterior segment of the eye include the following:

- Cells
- Flare
- Fibrin
- Hypopyon
- Synechiae (both anterior and posterior)
- Iris nodules
- Iris atrophy
- Keratic precipitates
- Band keratopathy

The signs of ocular inflammation involving the intermediate segment of the eye include the following:

- vitreal cells
- "snowball" opacities in the vitreous
- exudates over the pars plana (snowbanking)
- neovascularization of the pars plana

The signs of ocular inflammation involving the posterior segment of the eye include the following:

- Vascular sheathing (arteries, veins, or both)
- Retinal pigment epithelial hypertrophy or atrophy
- Cystoid macular edema
- Atrophy or swelling of the retina, choroid, or optic nerve head
- Exudative, tractional, or rhegmatogenous retinal detachment
- Retinal or choroidal neovascularization

The symptoms of uveitis are similarly dependent upon the location of involvement in the eye and include the following:

- Anterior segment (ocular injection, light sensitivity, pain, blurry vision, epiphora)
- Intermediate and posterior segment (floaters, flashing lights, blurry vision)

When counseling patients regarding the symptoms of ocular inflammation, the abbreviation "RSVP" commonly used by primary care physicians in deciding when to refer a patient to an ophthalmologist is simple to remember (**R**edness, Light **S**ensitivity, Change in **V**ision, and **P**ain). Although nonspecific, any of these symptoms should prompt the patient to seek medical attention.

Classification of Uveitis

The classification of uveitis is important for multiple reasons that are as follows:

- The location of ocular inflammation may assist in diagnosis or at least narrow the potential etiologies (e.g., Fuch's heterochromic iridocyclitis involves the anterior chamber; ocular toxoplasmosis primarily effects the retina with significant inflammatory spillover into the choroid and vitreous)
- Uveitis may be a manifestation of an underlying serious or potentially lethal systemic disease. The correct diagnosis can be sight- and on occasion life-preserving.
- Uveitis may be caused by a vast number of conditions including infections, autoimmune disorders, medication induced, traumatic, and neoplastic. The correct characterization of the ocular manifestations may assist in identifying an underlying etiology.

There are several classification models in existence (International Uveitis Study Group, Standardization of Uveitis Nomenclature Working Group). Historically, the variability between the various classification schemes lead to some degree of confusion, and there was a need for an accepted system to improve the comprehension of the disease course, prognosis, and scientifically scrutinize the efficacy of various treatments. The Standardization of Uveitis Nomenclature (SUN) Working Group in 2005 developed an anatomical classification system, standard grading systems, and accepted terminology to use for evaluating patients with uveitis (Tables 1.1, 1.2 and 1.3).

The grading of anterior chamber inflammation is determined via a 1 mm × 1 mm slit beam and the rheostat adjusted to the brightest setting (Table 1.4).

Table 1.1 SUN working group anatomical classification of uveitis

Type of uveitis	Primary site of inflammation	Includes
Anterior uveitis	Anterior chamber	Iritis Iridocyclitis
Intermediate uveitis	Vitreous	Pars planitis Posterior cyclitis Hyalitis
Posterior uveitis	Retina or choroid	Focal, multifocal, or diffuse choroiditis Chorioretinitis Retinochoroiditis Retinitis Neuroretinitis
Panuveitis	Anterior chamber, vitreous, and retina or choroid	

Jabs DA, et al. [10: Table 1]

Table 1.2 The SUN working group descriptors in uveitis

Category	Descriptor	Comment
Onset	Sudden Insidious	
Duration	Limited Persistent	≤3 months duration >3 months duration
Course	Acute Recurrent Chronic	Episode characterized by sudden onset and limited duration Repeated episodes separated by periods of inactivity without treatment ≥3 months duration Persistent uveitis with relapse in <3 months after discontinuing treatment

Jabs DA, et al. [10: Table 2]

Table 1.3 The SUN working group activity of uveitis terminology

Term	Definition
Inactive	Grade 0 cells (anterior chamber)
Worsening activity	2 Step increase in level of inflammation (e.g., anterior chamber cells, vitreal haze) or increase from grade 3+ to 4+
Improved activity	2 Step decrease in level of inflammation (e.g., Anterior chamber cells, vitreous haze) or decrease to grade 0
Remission	Inactive disease for ≥3 months after discontinuing all treatment for eye disease

Jabs DA, et al. [10, Table 5]

Anterior chamber flare is more difficult to objectively quantify at the slit lamp without the use of a laser flare photometer. This instrument can measure the back-scattered light from small molecules such as proteins in the anterior chamber. There is a highly significant linear relationship between laser flare intensity and protein concentration which has been shown both in vitro and in vivo [8, 9]. Without the use of a laser flare photometer, the SUN Working group chose the grading system shown in Table 1.5 which employs a more qualitative metric.

The chapters that follow will provide a basis for evaluating, diagnosing, and treating patients with uveitis. This is not an "all inclusive" reference guide but a reasonable synopsis by experts

Table 1.4 Grading of anterior chamber cell

Grade	Number of cells
0	<1 cell
0.5+	1–5 cells
1+	6–15 cells
2+	16–25 cells
3+	26–50 cells
4+	>50 cells

Jabs DA, et al. [10]

Table 1.5 Grading of anterior chamber flare

Grade	Description
0	None
1+	Faint
2+	Moderate (iris and lens details clear)
3+	Marked (iris and lens details hazy)
4+	Intense (fibrin or plasmoid aqueous)

Jabs DA, et al. [10, Table 4]

in the field to provide adequate depth of information to the practitioner faced with these challenging patients. As with all textbooks, the information contained herein constantly evolves and may not completely represent the latest advances in this realm.

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