Classification of Uveitis – Current Guidelines

a report by

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Today, uveitis includes all types of intraocular inflammation. With an incidence of approximately 50/100,000 people and a prevalence of 100/100,000,[1] uveitis remains one of the leading blinding disorders. All age groups can be affected.

The use of classification criteria, supported by standardisation guidelines, is very important for disorders that have a multitude of associated aetiologies. At least 150 disorders are known to be associated with intraocular inflammation. Some are caused by infectious agents; others may be of autoimmune nature, including some associated with an underlying systemic disease. In 1987, the International Uveitis Study Group (IUSG) developed criteria based on the anatomical localisation of the inflammation.[2] In 2004, the Standardization of Uveitis Nomenclature (SUN) workshop analysed these criteria, found them very useful and added criteria for onset, duration and course of the disease.[3] Despite being of great help in clinical practice, the IUSG criteria do not include criteria for specific uveitis entities.

The American College of Rheumatology (ACR) has developed classification criteria for many rheumatic diseases and systemic lupus erythematosus.[4] These ACR criteria have been developed in a standard process and then validated against large databases, resulting in the highest achievable grade of sensitivity and specificity. Unfortunately, only provisional criteria have been developed for some uveitis-associated disorders, as they have not yet all been validated: these disorders include Vogt-Koyanagi-Harada disease,[5] acute retinal necrosis,[6] progressive outer retinal necrosis,[7] birdshot retinopathy,[8] tubulointerstitial nephritis associated uveitis,[9] Behçet´s Disease[10,11] and, recently, ocular sarcoidosis (submitted for publication).

Classification of Uveitis

Localisation of Uveitis

The most simple but essential criterion is the location of the uveitis. *Table 1* shows the updated anatomical classification of uveitis. Important to note here is that the primary site of inflammation defines the type of uveitis. It has to be emphasised that the primary site of inflammation and the complications of the inflammation need to be differentiated. Thus, the existence of macular oedema (MO), a major complication of any type of uveitis, does not directly lead to the naming of 'posterior uveitis'. This needs an underlying retinal or choroidal inflammation, which may then result in MO. These four anatomical types of uveitis can all be associated with or without other disorders. Illogically, the term 'pars planitis' is used for a subset of intermediate uveitis, characterised by snow bank formation and/or snowballs without any associated disorder.

The term 'retinal vasculitis' also remains unclear; this will need further work regarding classification. For ocular vasculitis it seems that the Chapel-Hill Classification for systemic vasculitis, which uses the various sizes of the inflamed vessels for their classification, is unhelpful.

Table 1: Anatomical Classification of Uveitis

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

**As determined clinically. Adapted from Bloch-Michel et al, 1987.[2]*

Table 2: Definition of Onset, Duration and Course of Uveitis[3]

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

Onset, Duration and Course of Uveitis

The SUN group also defined criteria for the onset, duration and course of the uveitis, which are summarised in *Table 2*. Therefore, the onset should now be defined as either 'sudden' (prototype human leukocyte antigen B27 (HLA-B27)-associated acute anterior uveitis), characterised by pain, redness and photophobia, or 'insidious' (prototype anterior uveitis, associated with juvenile idiopathic arthritis), characterised by a painless, white eye.

Previously, the terms 'acute' and 'chronic' were used for characterising onset, duration or even the course of the disease. Using the SUN criteria, both these terms now should be used exclusively for the course of the uveitis. Using the term 'recurrent uveitis' suggests that between attacks there is a period of inactivity without treatment of at least three months.

Table 3: Grading Scheme for Anterior Chamber Cells[3]

Grade	Cells in Field*
0	<1
0.5+	1–5
1+	6–15
2+	16–25
3+	26–50
4+	>50

**Field size is a 1x1mm slit beam.*

Table 4: Grading Scheme for Anterior Chamber Flare[3]

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

Table 5: Grading Scheme for Vitreous Haze[13]

Score	Description	Clinical findings
0	Nil	None
1	Minimal	Posterior pole clearly visible
2	Mild	Posterior pole details slightly hazy
3	Moderate	Posterior pole details very hazy
4	Marked	Posterior pole details barely visible
5	Severe	Fundal details not visible

Table 6: Activity of Uveitis Terminology[3]

Term	Definition
Inactive	Grade 0 cells
Worsening activity	Two-step increase in level of inflammation (e.g. anterior chamber cells, vitreous haze) or increase from grade 3+ to 4+
Improved activity	Two-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 treatments for eye disease

Persistent inflammation with relapse within three months after discontinuation of the treatment should be termed 'chronic'.

Severity and Activity of Uveitis

Grading the degree of inflammation in uveitis has been achieved only for cells and flare in the anterior chamber (AC) (see *Tables 3* and *4*), but not for vitreous cells. For vitreous cells, a grading for haze has been established (see *Table 5*). In contrast to the previous IUSG grading,[2] the SUN criteria now have a 0.5+ level for AC cells and flare, and also for the vitreous haze (adopted from the National Eye Institute system for grading).[13] While AC cells and flare are homogeneously distributed in the AC, supporting the necessity of such a grading for the definition of activity, this may be not the case for the vitreous. Here, haze and cells, especially in still formed vitreous, may not be evenly localised. While a 2+ haze of the central vitreous may imply a massive drop of visual acuity and a high risk for the development of MO, the same degree of haze located more peripherally may not even require treatment. At the moment, the distribution of vitreous haze is not included in the grading system. Unlike AC activity, vitreous cells *per se* could be fresh or old, and there is much debate as to how these should be differentiated.

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Table 6 summarises the actual criteria for activity of uveitis, differentiating inactive from worsening and improved activity. Remission is defined as inactive disease for at least three months after discontinuing all treatment for uveitis. Accurate clinical tools are required to differentiate and assess disease activity and damage for treatment decisions, and for the performance of clinical trials. Validated clinical assessment tools have been developed for systemic vasculitis,[14,15] but as yet none exist for uveitis.

Conclusion

Today's uveitis nomenclature has been revised regarding the anatomical location and the grade of inflammation, and supplemented by the inclusion of definitions for onset, duration and course. While helpful for clinical practice and clinical trials, further work still needs to be carried out concentrating on definitions of ocular vasculitis in order to provide validated clinical assessment tools for activity and damage and for specific uveitis entities that are associated with other conditions. While some of these conditions have at least provisional criteria, not all are validated. Future work has to define criteria particularly for important often seen disorders, such as juvenile idiopathic arthritis-associated uveitis, HLA-B27-associated disorders and the uveitis seen in association with multiple sclerosis. ■

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