ORIGINAL ARTICLE

Classification Criteria for Varicella Zoster Virus Anterior Uveitis

THE STANDARDIZATION OF UVEITIS NOMENCLATURE (SUN) WORKING GROUP[1,2,3,*]

• PURPOSE: To determine classification criteria for varicella zoster virus (VZV) anterior uveitis.

• DESIGN: Machine learning of cases with VZV anterior uveitis and 8 other anterior uveitides.

• METHODS: Cases of anterior uveitides were collected in an informatics-designed preliminary database, and a final database was constructed of cases achieving supermajority agreement on the diagnosis, using formal consensus techniques. Cases were split into a training set and a validation set. Machine learning using multinomial logistic regression was used on the training set to determine a parsimonious set of criteria that minimized the misclassification rate among the anterior uveitides. The resulting criteria were evaluated on the validation set.

• RESULTS: One thousand eighty-three cases of anterior uveitides, including 123 cases of VZV anterior uveitis, were evaluated by machine learning. The overall accuracy for anterior uveitides was 97.5% in the training set and 96.7% in the validation set (95% confidence interval 92.4, 98.6). Key criteria for VZV anterior uveitis included unilateral anterior uveitis with either (1) positive aqueous humor polymerase chain reaction assay for VZV; (2) sectoral iris atrophy in a patient ≥60 years of age; or (3) concurrent or recent dermatomal herpes zoster. The misclassification rates for VZV anterior uveitis were 0.9% in the training set and 0% in the validation set, respectively.

• CONCLUSIONS: The criteria for VZV anterior uveitis had a low misclassification rate and seemed to perform sufficiently well for use in clinical and translational research. (Am J Ophthalmol 2021;228: 165–173. © 2021 Elsevier Inc. All rights reserved.)

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Varicella zoster virus (VZV) is a common herpes family DNA virus, causing varicella ("chicken pox") in children, herpes zoster in adults, and, in immunocompromised adults, disseminated herpes zoster. Herpes zoster may erupt along the distribution of the first branch of the trigeminal nerve, resulting in herpes zoster ophthalmicus. Herpes zoster is estimated to affect 20% to 30% of the population at some point during their lifetime, and 10% to 20% of these individuals are estimated to have herpes zoster ophthalmicus.[1] Ocular disease attributable to herpes zoster ophthalmicus is common, affecting an estimated 50% of patients with trigeminal nerve dermatomal herpes zoster, and one of the most common manifestations is anterior uveitis.[1-3] A population-based study from Taiwan estimated the incidence of anterior uveitis at 0.3%/person-year after any herpes zoster with a 13-fold increased risk of uveitis for herpes zoster ophthalmicus.[4] Prospective trials of acyclovir for herpes zoster ophthalmicus estimated the risk of anterior uveitis in patients not treated with antivirals at ~60%, which was substantially reduced by the early use of antiviral agents, such as acyclovir and valacyclovir.[5-7] One study in 2014 from North Africa similarly estimated that ~60% of patients with herpes zoster ophthalmicus would develop anterior uveitis.[8]

VZV anterior uveitis is presumed to be attributable to active viral replication in the eye, as evidenced by the detection of VZV DNA in the anterior chamber using

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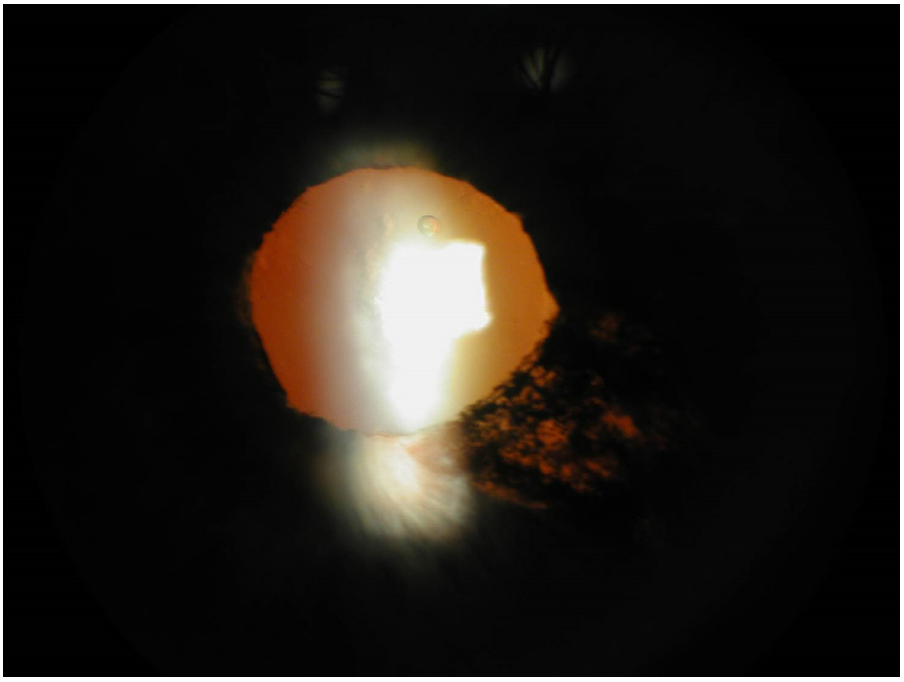

FIGURE 1. Sectoral iris atrophy in a patient with varicella zoster virus anterior uveitis.

polymerase chain reaction (PCR) analysis of aqueous humor obtained by paracentesis[9-13] and the response to antiviral therapy.[5-7] Anterior uveitis due to VZV in the absence of dermatomal herpes zoster occurs, albeit less commonly, and can be diagnosed by PCR analysis of an aqueous humor specimen.[11,12] In 1 case series of patients with VZV anterior uveitis, 6% of cases of VZV anterior uveitis occurred without dermatomal zoster.[12] A syndrome of herpetic anterior uveitis with sectoral iris atrophy is attributable to either herpes simplex virus (HSV) or VZV in more than 95% of cases. In younger patients (<50 years of age) it typically is due to HSV, and in older patients (≥60 years of age) overwhelmingly to VZV.[13]

The Standardization of Uveitis Nomenclature (SUN) Working Group is an international collaboration that has developed classification criteria for 25 of the most common uveitides using a formal approach to development and classification.[14-20] Among the anterior uveitides being studied is VZV anterior uveitis Figure 1.

METHODS

The SUN Developing Classification Criteria for the Uveitides project proceeded in 4 phases, as previously described: (1) informatics, (2) case collection, (3) case selection, and (4) machine learning.[16-18,20]

• **INFORMATICS:** As previously described, the consensus-based informatics phase permitted the development of a standardized vocabulary and the development of a standardized, menu-driven hierarchical case collection instrument.[16]

• **CASE COLLECTION AND CASE SELECTION:** De-identified information was entered into the SUN preliminary database by the 76 contributing investigators for each disease, as previously described.[18,20] Cases in the preliminary database were reviewed by committees of 9 investigators for selection into the final database, using formal consensus techniques described in the accompanying article.[18,20] Because the goal was to develop classification criteria, only cases with a supermajority agreement (>75%) that the case was the disease in question were retained in the final database (ie, were "selected").

• **MACHINE LEARNING:** The final database then was randomly separated into a training set (~85% of cases) and a validation set (~15% of cases) for each disease, as described in the accompanying article.[20] Machine learning was used on the training set to determine criteria that minimized misclassification. The criteria then were tested on the validation set; for both the training set and the validation set, the misclassification rate was calculated for each disease. The misclassification rate was the proportion of cases classified incorrectly by the machine learning algorithm when compared to the consensus diagnosis. For VZV anterior uveitis, the diseases against which it was evaluated were cytomegalovirus (CMV) anterior uveitis, HSV anterior uveitis, juvenile idiopathic arthritis–associated anterior uveitis, spondylitis/HLA-B27-associated anterior uveitis,

tubulointerstitial nephritis with uveitis, Fuchs uveitis syndrome, sarcoidosis-associated anterior uveitis, and syphilitic anterior uveitis.

• **COMPARISON OF CASES WITH AND WITHOUT DERMATOMAL HERPES ZOSTER AND WITH AND WITHOUT POLYMERASE CHAIN REACTION CONFIRMATION OF VARICELLA ZOSTER VIRUS IN THE ANTERIOR CHAMBER:** Comparison of cases with and without dermatomal herpes zoster and with and without PCR confirmation of VZV in the anterior chamber for categorical variables was performed with the χ^2 test or Fisher exact test if a cell was less than 5. For continuous variables, the Wilcoxon rank sum test was used. *P* values are nominal and 2-sided.

RESULTS

One hundred sixty-three cases of VZV anterior uveitis were collected, and 123 (76%) achieved supermajority agreement on the diagnosis during the "selection" phase and were used in the machine learning phase. These cases of VZV anterior uveitis were compared to 960 cases of other anterior uveitides, including 89 cases of CMV anterior uveitis, 101 cases of HSV anterior uveitis, 146 cases of Fuchs uveitis syndrome, 202 cases of juvenile idiopathic arthritis–associated anterior uveitis, 184 cases of spondylitis/HLA-B27-associated anterior uveitis, 94 cases of tubulointerstitial nephritis with uveitis, 112 cases of sarcoidosis-associated anterior uveitis, and 32 cases of syphilitic anterior uveitis. The characteristics at presentation to a SUN Working Group investigator of cases with VZV anterior uveitis are listed in Table 1. A comparison of cases with and without dermatomal zoster is listed in Table 2, and a comparison of cases with and without PCR testing for VZV is listed in Table 3. Differences between cases with and without dermatomal zoster included the following for those without dermatomal zoster: younger age, more often men, more often nonwhite, less often normal iris, more vitritis, and more likely to have undergone paracentesis for PCR testing. Differences between cases with and without PCR testing included the following for those with PCR testing: more often nonwhite, suggestion of a normal iris less often ($P = .06$), and dermatomal zoster less often. As 98% of cases without PCR testing had dermatomal zoster, it seems that PCR testing was used in those without dermatomal zoster and more atypical cases. Other than the iris appearance, there were no differences in the appearance of the uveitis between those with and without dermatomal zoster and those with and without PCR testing. The criteria developed after machine learning are listed in Table 4. Key features for the diagnosis of VZV anterior uveitis included the following: (1) positive PCR for VZV in the aqueous fluid obtained on paracentesis, or (2) dermatomal herpes zoster, or (3) anterior uveitis with sectoral

TABLE 1. Characteristics of Cases of Varicella Zoster Virus Anterior Uveitis

Characteristic	Result
Number of cases	123
Demographics	
Age, median, years (25th, 75th percentile)	63 (54, 73)
Age category, years (%)	
≤16	2
17-50	15
51-60	23
>60	61
Sex (%)	
Male	40
Female	60
Race/ethnicity (%)	
White, non-Hispanic	72
Black, non-Hispanic	3
Hispanic	3
Asian, Pacific Islander	11
Other	3
Missing/unknown	8
Uveitis history	
Uveitis course (%)	
Acute, monophasic	38
Acute, recurrent	6
Chronic	41
Indeterminate	15
Laterality (%)	
Unilateral	96
Unilateral, alternating	0
Bilateral	4
Ophthalmic examination	
Cornea	
No keratitis	71
Keratitis	29
Keratic precipitates (%)	
None	30
Fine	42
Round	11
Stellate	3
Mutton fat	13
Other	1
Anterior chamber cells, grade (%)	
½+	29
1+	41
2+	23
3+	5
4+	0
Hypopyon (%)	0
Anterior chamber flare, grade (%)	
0	55
1+	34
2+	11
3+	0
4+	0

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TABLE 1. (*continued*)

Characteristic	Result
Iris (%)	
Normal	79
Posterior synechiae	7
Sectoral iris atrophy	11
Patch iris atrophy	3
Diffuse iris atrophy	2
Heterochromia	2
IOP, involved eyes	
Median, mm Hg (25th, 75th percentile)	14 (12, 20)
Proportion patients with IOP > 24 mm Hg either eye (%)	26
Vitreous cells, grade (%)	
0	88
½+	10
1+	2
2+	1
3+	0
4+	0
Dermatomal herpes zoster (%)	86
Immunocompromised host (%)	7
Laboratory	
Aqueous PCR positive for VZV[a] (%)	20

IOP = intraocular pressure; PCR = polymerase chain reaction; VZV = varicella zoster virus.

[a]A total of 25 patients were tested and 25 (100%) were positive.

iris atrophy in a patient ≥60 years of age. The overall accuracy for anterior uveitides was 97.5% in the training set and 96.7% in the validation set (95% confidence interval 92.4, 98.6).[20] The misclassification rate for VZV anterior uveitis in the training set was 0.9% and in the validation set 0%.

DISCUSSION

Varicella zoster anterior uveitis concurrent with or following herpes zoster ophthalmicus is an anterior uveitis ipsilateral to the cutaneous disease.[1-3,5-7] Anterior uveitis in the context of herpes zoster ophthalmicus has been taken as *prima facie* evidence that the uveitis is due to VZV,[1-3,5-7] and studies employing PCR of the aqueous humor support this approach.[9,10,12] Rare cases of bilateral disease have been described, but typically require aqueous humor PCR testing for confirmation of VZV. In this series 96% of cases were unilateral. Herpes zoster can occur at any age but tends to occur in older patients, with ~50% of reported cases involving patients over 60 years of age,[2,8,21,22] as was present in the cases in this series. Morphologically, no single feature of the uveitis reliably diagnosed VZV anterior uveitis alone, and it can have an appearance similar to HSV anterior uveitis and occasionally CMV anterior uveitis.[22-25] Studies using PCR analysis of aqueous humor suggested that a combination of age and sectoral iris atrophy can be used to morphologically diagnose VZV anterior uveitis and to distinguish it from HSV anterior uveitis.[13,22] However, in the 50-to-59-year age bracket there is sufficient overlap that only ages below 50 years (HSV) and 60 years or above (VZV) can be used for diagnosis. Cytomegalovirus anterior uveitis more often has endothelial cell loss than HSV and VZV anterior uveitis and infrequently has sectoral iris atrophy. Nodular "coin-shaped" endothelial lesions are strongly suggestive of CMV anterior uveitis but are present in a minority of these patients[22,24,25]; when present, they should lead to paracentesis for PCR testing of aqueous humor, as currently that is the only way to reliably diagnose CMV anterior uveitis.[26] However, because of the low yield on routine use, paracentesis for PCR analysis of aqueous humor for viruses is not always performed,[27] and diagnoses may be made morphologically. The classification criteria for

TABLE 2. Characteristics of Varicella Zoster Virus Anterior Uveitis Cases With and Without Dermatomal Herpes Zoster

Characteristic	With Dermatomal Herpes Zoster	Without Dermatomal Herpes Zoster	*P* Value
Number of cases	106	17	
Demographics			
Age, median, years (25th 75th percentile)	62 (50, 74)	54 (43, 63)	.05
Age category, years (%)			.08
≤16	2	0	
17-50	12	29	
51-60	21	35	
>60	60	29	
Sex (%)			.03
Male	36	64	
Female	64	36	

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TABLE 2. (*continued*)

Characteristic	With Dermatomal Herpes Zoster	Without Dermatomal Herpes Zoster	*P* Value
Race/ethnicity (%)			.002
White, non-Hispanic	80	41	
Black, non-Hispanic	3	6	
Hispanic	3	0	
Asian, Pacific Islander	10	24	
Other	1	11	
Missing/unknown	3	18	
Uveitis history			
Uveitis course (%)			.64
Acute, monophasic	37	41	
Acute, recurrent	5	12	
Chronic	42	35	
Indeterminate	16	12	
Laterality (%)			.22
Unilateral	96	94	
Bilateral	4	6	
Ophthalmic examination			
Cornea			.58
No keratitis	70	76	
Keratitis	30	24	
Keratic precipitates (%)			.27
None	29	35	
Fine	45	24	
Round	8	24	
Stellate	4	0	
Mutton fat	12	17	
Other	2	0	
Anterior chamber cells, grade (%)			.11
½+	31	12	
1+	40	35	
2+	22	29	
3+	4	12	
Anterior chamber flare, grade (%)			.69
0	57	47	
1+	33	41	
2+	10	12	
Iris (%)			
Normal	83	53	.005
Posterior synechiae	4	24	.01
Sectoral iris atrophy	8	23	.08
Other iris abnormality	7	24	.03
IOP, involved eyes			
Median, mm Hg (25th, 75th percentile)	15 (12, 20)	18 (14, 22)	.80
Percent patients with IOP > 24 mm Hg either eye	22	41	.21
Vitreous cells, grade (%)			.01
0	91	71	
½+	8	18	
≥1+	1	12	
Immunocompromised host (%)	7	12	.42
Laboratory			
Aqueous PCR positive for VZV (%)	9[a]	88[b]	<.0001

IOP = intraocular pressure; PCR = polymerase chain reaction; VZV = varicella zoster virus.

[a] A total of 10 patients were tested and 10 (100%) were positive.

[b] A total of 15 patients were tested and 15 (100%) were positive.

VZV anterior uveitis developed herein performed reasonably well, with a low misclassification rate.

VZV and HSV are causes of acute retinal necrosis syndrome, which, although primarily a retinitis, typically has anterior chamber and vitreous inflammation.[28,29] Furthermore, unlike CMV retinitis, which nearly always occurs in patients with immunocompromise, acute retinal necrosis occurs in both immunologically "normal" and immunocompromised hosts. Therefore, it is important to exclude retinitis with ophthalmoscopy though a dilated pupil before concluding that the diagnosis is VZV anterior uveitis.

The presence of any of the exclusions in Table 4 suggests an alternate diagnosis, and the diagnosis of VZV anterior uveitis should not be made in their presence. In prospective studies many of these tests will be performed routinely and the alternative diagnoses excluded. However, in

TABLE 3. Characteristics of Cases of Varicella Zoster Anterior Uveitis With and Without Aqueous Polymerase Chain Reaction Testing for Varicella Zoster Virus

Characteristic	WithoutPCR Testing[a]	With PCR Testing[a]	*P* Value
Number of cases	98	25	
Demographics			
Age, median, years (25th, 75th percentile)	66 (56, 74)	55 (50, 70)	.07
Age category, years (%)			.13
≤16	2	0	
17-50	12	24	
51-60	25	32	
>60	61	44	
Sex (%)			.16
Male	37	52	
Female	63	48	
Race/ethnicity (%)			.01
White, non-Hispanic	81	52	
Black, non-Hispanic	3	4	
Hispanic	3	0	
Asian, Pacific Islander	10	20	
Other	1	8	
Missing/unknown	2	16	
Uveitis history			
Uveitis course (%)			.62
Acute, monophasic	34	46	
Acute, recurrent	5	8	
Chronic	42	38	
Indeterminate	18	8	
Laterality (%)			.91
Unilateral	96	96	
Bilateral	4	4	
Ophthalmic examination			
Cornea			.74
No keratitis	71	68	
Keratitis	29	32	
Keratic precipitates (%)			.63
None	31	28	
Fine	44	36	
Round	9	16	
Stellate	4	0	
Mutton fat	11	20	
Other	1	0	
Anterior chamber cells, grade (%)			.33
½+	32	8	
1+	37	16	
2+	23	48	
3+	4	20	

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TABLE 3. (*continued*)

Characteristic	WithoutPCR Testing[a]	With PCR Testing[a]	*P* Value
Anterior chamber flare, grade (%)			.76
0	54	60	
1+	36	28	
2+	10	12	
Iris (%)			
Normal	83	64	.06
Posterior synechiae	6	8	.66
Sectoral iris atrophy	9	16	.25
Other iris abnormality	6	24	.001
IOP, involved eyes			
Median, mm Hg (25th, 75th percentile)	15 (12, 20)	16 (14, 30)	.12
Percent patients with IOP > 24 mm Hg either eye	21	36	.29
Vitreous cells, grade (%)			.08
0	89	84	
½+	10	8	
≥1+	1	8	
Immunocompromised host (%)	8	5	.22
Dermatomal herpes zoster (%)	98	40	<.0001

IOP = intraocular pressure; PCR = polymerase chain reaction.
[a]Testing for varicella zoster virus in aqueous humor.

TABLE 4. Classification Criteria for Varicella Zoster Virus Anterior Uveitis

Criteria
1. Evidence of anterior uveitis
a. anterior chamber cells
b. if anterior vitreous cells are present, severity is less than anterior chamber inflammation
c. no evidence of retinitis
AND
2. Unilateral uveitis (unless there is a positive aqueous PCR for varicella zoster virus)
AND
3. Evidence of varicella zoster virus infection in the eye
a. aqueous humor PCR positive for varicella zoster virus OR
b. sectoral iris atrophy in a patient ≥60 years of age OR
c. concurrent or recent dermatomal herpes zoster
Exclusions
1. Positive serology for syphilis using a treponemal test
2. Evidence of sarcoidosis (either bilateral hilar adenopathy on chest imaging or tissue biopsy demonstrating noncaseating granulomata)
3. Aqueous specimen PCR positive for cytomegalovirus or herpes simplex virus

PCR = polymerase chain reaction.

retrospective studies based on clinical care, not all of these tests may have been performed. Hence the presence of an exclusionary criterion excludes VZV anterior uveitis, but the absence of such testing does not exclude the diagnosis of VZV anterior uveitis if the criteria for the diagnosis are met.

Classification criteria are employed to diagnose individual diseases for research purposes.[19] Classification criteria differ from clinical diagnostic criteria in that, although both seek to minimize misclassification, when a trade-off is needed, diagnostic criteria typically emphasize sensitivity, whereas classification criteria emphasize specificity,[19] in order to define a homogeneous group of patients for inclusion in research studies and limit the inclusion of patients without the disease in question that might confound the data. The machine learning process employed did not explicitly use sensitivity and specificity; instead, it minimized the misclassification rate. Because we were developing classification criteria and because the typical agreement between 2 uveitis experts on diagnosis is moderate at best,[18] the selection of cases for the final database ("case selection") included only cases that achieved supermajority agreement on the diagnosis. Because of this, some patients diagnosed by clinicians as having VZV anterior uveitis may not satisfy these criteria.

In sum, the criteria for VZV anterior uveitis outlined in Table 4 seem to perform adequately well for use as classification criteria.

TOC

Using a formalized approach to developing classification criteria, including informatics-based case collection,

consensus technique–based case selection, and machine learning, classification criteria for varicella zoster virus (VZV) anterior uveitis were developed. Key criteria included unilateral anterior uveitis with either (1) positive aqueous humor polymerase chain reaction assay for VZV; (2) sectoral iris atrophy in a patient ≥60 years of age; or (3) concurrent or recent dermatomal herpes zoster. The resulting criteria had an acceptable misclassification rate.

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REFERENCES

1. Liesegang TJ. Herpes zoster ophthalmicus natural history, risk factors, clinical presentation, and morbidity. *Ophthalmology*. 2008;115(Suppl):S3–S12.
2. Thean JH, Hall AJ, Stawell RJ. Uveitis in Herpes zoster ophthalmicus. *Clin Exp Ophthalmol*. 2001;29:406–410.
3. Tugal-Tutkun I, Cimino L, Akova YA. Review for disease of the year: varicella zoster virus-induced anterior uveitis. *Ocul Immunol Inflamm*. 2018;26:171–177.
4. Wang TJ, Hu CC, Lin HC. Increased risk of anterior uveitis following herpes zoster: a nationwide population-based study. *Arch Ophthalmol*. 2012;130:451–455.
5. Cobo LM, Foulks GN, Lass J, et al. Oral acyclovir in the therapy of acute herpes zoster ophthalmicus. An interim report. *Ophthalmology*. 1985;92:1574–1583.
6. Cobo LM, Foulks GN, Liesegang T, et al. Oral acyclovir in the treatment of acute herpes zoster ophthalmicus. *Ophthalmology*. 1986;93:763–770.
7. Colin J, Prisant O, Cochener B, Lescale O, Rolland B, Hoang-Xuan T. Comparison of the efficacy and safety of valaciclovir and acyclovir for the treatment of herpes zoster ophthalmicus. *Ophthalmology*. 2000;107:1507–1511.
8. Kahloun R, Attia S, Jelliti B, et al. Ocular involvement and visual outcome of herpes zoster ophthalmicus: review of 45 patients from Tunisia, North Africa. *J Ophthalmic Inflamm Infect*. 2014;4:25.
9. Yamamoto S, Tada R, Shimomura Y, et al. Detecting varicella-zoster virus DNA in iridocyclitis using polymerase chain reaction. *Arch Ophthalmol*. 1995;113:1358–1359.
10. Sugita S, Shimizu N, Watanabe K, et al. Use of multiplex PCR and real-time PCR to detect human herpes virus genome in ocular fluids of patients with uveitis. *Br J Ophthalmol*. 2008;92:928–932.
11. Kido S, Sugita S, Horie S, et al. Association of varicella zoster virus load in the aqueous humor with clinical manifestations of anterior uveitis in herpes zoster ophthalmicus and zoster sine herpete. *Br J Ophthalmol*. 2008;92:505–508.
12. Neumann R, Barquet D, Rosenblatt A, et al. Herpetci anterior uveitis – analysis of presumed and PCR proven cases. *Ocul Immunol Inflamm*. 2019;27:211–218.
13. Van der Lelij A, Ooijman FM, Kilstra A, Rogthova A. Anterior uveitis with sectoral iris atrophy in the absence of keratitis. A distinct clinical entity among herpetic eye diseases. *Ophthalmology*. 2000;107:1164–1170.
14. Jabs DA, Rosenbaum JT. Nussenblatt RB, the Standardization of Uveitis Nomenclature (SUN) Working Group. Standardization of uveitis nomenclature for reporting clinical data. Report of the first international workshop. *Am J Ophthalmol*. 2005;140:509–516.
15. Jabs DA, Busingye J. Approach to the diagnosis of the uveitides. *Am J Ophthalmol*. 2013;156:228–236.
16. Trusko B, Thorne J, Jabs D, et al. Standardization of Uveitis Nomenclature Working Group. The SUN Project. Development of a clinical evidence base utilizing informatics tools and techniques. *Methods Inf Med*. 2013;52:259–265.
17. Okada AA, Jabs DA. The SUN Project. The future is here. *Arch Ophthalmol*. 2013;131:787–789.
18. Jabs DA, Dick A, Doucette JT, et al. for the Standardization of Uveitis Nomenclature Working Group. Interobserver agreement among uveitis experts on uveitic diagnoses: the Standard of Uveitis Nomenclature experience. *Am J Ophthalmol*. 2018;186:19–24.
19. Aggarwal R, Ringold S, Khanna D, et al. Distinctions between diagnostic and classification criteria. *Arthritis Care Res*. 2015;67:891–897.
20. The Standardization of Uveitis Nomenclature (SUN) Working Group. Development of classification criteria for the uveitides. *Am J Ophthalmol*. doi: 10.1016/j.ajo.2021.03.061. 2021.04.09.
21. Ghaznawi N, Virdi A, Dayan A, et al. Herpes zoster ophthalmicus: comparison of disease in patients 60 years and older versus younger than 60 years. *Ophthalmology*. 2011;118:2242–2250.
22. Takase H, Kubono R, Terada Y, et al. Comparison of ocular characteristics of anterior uveitis caused by herpes simplex, varicella zoster, and cytomegalovirus. *Jpn J Ophthalmol*. 2014;58:473–482.
23. Miserocchi E, Waheed NK, Dios E, et al. Visual outcome in herpes simplex virus and varicella zoster virus uveitis: a clinical evaluation and comparison. *Ophthalmology*. 2002;109:1532–1537.
24. Wensig B, Relvas LM, Caspers LE, et al. Comparison or rubella virus- and herpes virus-associated anterior uveitis: clinical manifestations and visual prognosis. *Ophthalmology*. 2011;118:1905–1910.

25. Relvas LJ, Caspers L, Chee SP, Zierhut M, Willermain F. Differential diagnosis of viral-induced anterior uveitis. *Ocul Immunol Inflamm*. 2018;26:726–731.
26. The Standardization of Uveitis Nomenclature (SUN) Working Group. Classification criteria for cytomegalovirus anterior uveitis. *Am J Ophthalmol*. doi: 10.1016/j.ajo.2021.03.060. 2021.04.09.
27. Anwar Z, Galor A, Albini TA, Miller D, Perez V, Davis JL. The diagnostic utility of anterior chamber paradentesis with polymerase chain reaction in anterior uveitis. *Am J Ophthalmol*. 2013;155:781–786.
28. Ganatra JB, Chandler D, Santos C, Kupperman B, Margolis TP. Viral causes of acute retinal necrosis syndrome. *Am J Ophthalmol*. 2000;129:166–172.
29. Wong R, Pavesio CE, Laidlaw DA, Williamson TH, Graham EM, Stanford MR. Acute retinal necrosis: the effects of intravitreal foscarnet and virus type on outcome. *Ophthalmology*. 2010;117:556–560.