

Uveitis literature review 2018

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Disclosures

- RVG serves as
 - Associate Editor of *TVST*
 - Editorial Board Member of *Ophthalmology*
 - Editorial Board Member of *Ophthalmology:Retina*
 - Editorial Board Member of *Ocular Inflammation and Immunology*
- RVG laboratory received research funding in 2018 from:
 - National Eye Institute
 - Research to Prevent Blindness
 - Elasmogen
- Received no direct compensation

Purpose

To bring papers of potential significance and interest to the attention of the AUS membership and guests

Methods

- Literature search for 'uveitis' or 'ocular inflammation' on PubMed
- Limited to English language and added to database in the last year (10/1/17 to 9/30/18)
- Selected ~ 25 papers to discuss briefly based on impact in understanding or managing ocular inflammatory disease

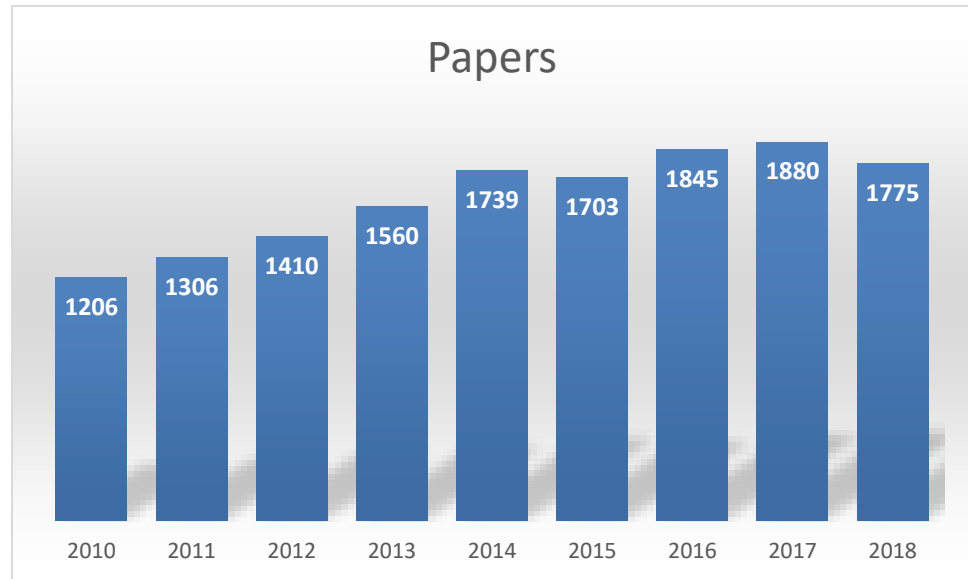
Caveats

- This is a necessarily subjective process
- Less than 2% of the literature can be featured
- All omissions are exclusively my fault and should not be taken personally
- All studies are imperfect: my purpose is to draw attention to the literature, not critique.



Uveitis literature 2017-18

- 1775 papers in English
- 716 human
- 252 reviews
- 13 clinical trials



Most cited uveitis papers from 2016

The NEW ENGLAND JOURNAL of MEDICINE

Zika Virus Infection in Mice Causes Panuveitis with Shedding of Virus in Tears

Jonathan J. Miner,^{1,2,3,4} Abdoulaye Sene,^{5,6} Justin M. Richner,¹ Amber M. Smith,¹ Andrea Santeford,² Norimitsu Ban,² James Weger-Lucarelli,⁶ Francesca Manzella,⁶ Claudia Rückert,² Jennifer Govero,¹ Kevin K. Noguchi,⁶ Gregory D. Ebel,¹ Michael S. Diamond,^{1,2,3,4,7,8} and Rajendra S. Apte^{1,2,3,4}

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⁵Department of Molecular Microbiology

⁶Department of Pathology and Immunology

⁷The Center for Human Immunology and Immunotherapy Programs

⁸Department of Developmental Biology

School of Medicine, Washington University, Saint Louis, MO 63110, USA

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<http://dx.doi.org/10.1016/j.cejep.2016.08.070>

92 citations

ORIGINAL ARTICLE

Adalimumab in Patients with Active Noninfectious Uveitis

Glenn J. Jaffe, M.D., Andrew D. Dick, M.B., B.S., M.D.,
Antoine P. Brézin, M.D., Ph.D., Quan Dong Nguyen, M.D.,
Jennifer E. Thome, M.D., Ph.D., Philippe Kestelyn, M.D., Ph.D., M.P.H.,
Talin Barisani-Asenbauer, M.D., Ph.D., Pablo Franco, M.D.,
Arnd Heiligenhaus, M.D., David Scales, M.D., David S. Chu, M.D.,
Anne Camez, M.D., Nisha V. Kwatra, Ph.D., Alexandra P. Song, M.D., M.P.H.,
Martina Kron, Ph.D., Samir Tari, M.D., and Eric B. Suhler, M.D., M.P.H.

67 citations

...but first, a shameless self-plug for my
colleagues at UW



Use of En Face Swept-Source Optical Coherence Tomography Angiography in Identifying Choroidal Flow Voids in 3 Patients With Birdshot Chorioretinopathy

Kathryn L. Pepple, MD, PhD, Zhongdi Chu, MS, Jessica Weinstein, MD, Marlon R. Munk, MD, PhD, Russell N. Van Gelder, MD, PhD, Ruikang K. Wang, PhD

RESPONSE OF INFLAMMATORY CYSTOID MACULAR EDEMA TO TREATMENT USING ORAL ACETAZOLAMIDE

KATHRYN L. PEPPEL, MD, PhD,* MACKLIN H. NGUYEN, BS,* KAIVON PAKZAD-VAEZI, MD,* KATHLEEN WILLIAMSON, MD,† NAOMI ODELL, MD, MPH,‡ CECILIA LEE, MD, MS,‡ THELLEA K. LEVEQUE, MD, MPH,‡ RUSSELL N. VAN GELDER, MD, PhD*†§



Swept-Source OCT Angiography of Serpiginous Choroiditis

Kaivon Pakzad-Vaezi, MD,¹ Kaver Khakani, PhD,² Zhongdi Chu, MSc,² Russell N. Van Gelder, MD, PhD,^{1,3,4} Ruikang K. Wang, PhD,^{1,2} Kathryn L. Pepple, MD, PhD¹

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ISSN: 0927-3948 print / 1744-5019 online
DOI: 10.1080/09273948.2019.1745758



REVIEW ARTICLE

A Review of the Role of Intravitreal Corticosteroids as an Adjuvant to Antibiotics in Infectious Endophthalmitis

Dawn Ching Wen Ho, Medical Student,¹ Aniruddha Agarwal, MD,^{2,3} Cecilia S. Lee, MD,⁴ Jay Chhablani, MD,⁵ Vishali Gupta, MD,⁶ Manoj Khatri, FRCOphth,⁷ Jayabalan Nirmal, MD,⁸ Carlos Pavesio, FRCOphth,⁹ and Rupesh Agrawal, MD^{1,7,8,9}

Major review

Viral posterior uveitis

Joanne H. Lee¹, Aniruddha Agarwal, MD¹, Padmamalini Mahendradas, MS², Cecilia S. Lee, MD³, Vishali Gupta, MD⁴, Carlos E. Pavesio, FRCOphth⁵, Rupesh Agrawal, MD^{6,7,8,9}

¹Yang Lee Lin School of Medicine, National University of Singapore, Singapore, Singapore
²Department of Vitreoretina and Uveitis, Postgraduate Institute of Medical Education and Research, Chandigarh, India
³Department of Uveitis and Ocular Immunology, Narayana Nethralaya, Bangalore, India
⁴Department of Uveitis, University of Washington, Seattle, Washington, USA
⁵Department of Medical Retina, Moorfields Eye Hospital, NHS Foundation Trust, London, United Kingdom
⁶Department of Ophthalmology, National Healthcare Group Eye Institute, Tan Tock Seng Hospital, Singapore, Singapore



Determinants of Outcomes of Adenoviral Keratoconjunctivitis

Cecilia S. Lee, MD, MS,¹ Aaron Y. Lee, MD, MSCI,¹ Lakshmi Akaleswaran, PhD,¹ David Stroman, PhD,² Kathryn Najafi-Tagol, MD,² Steve Kleiboeker, PhD,³ James Chodosh, MD, MPH,⁴ Amalia Magaret, PhD,^{1,2,3} Anna Wald, MD, MPH,^{2,3,5} Russell N. Van Gelder, MD, PhD,^{1,3,5} on behalf of the BiAYnovation Study Group⁶

Immunology and Microbiology

Comparison of Aqueous and Vitreous Lymphocyte Populations From Two Rat Models of Experimental Uveitis

Kathryn L. Pepple,¹ Leslie Wilson,¹ and Russell N. Van Gelder¹⁻⁵

¹Department of Ophthalmology, University of Washington, Seattle, Washington, United States
²Department of Biological Structure, University of Washington, Seattle, Washington, United States
³Department of Pathology, University of Washington, Seattle, Washington, United States

Received 17 April 2018 | Accepted 21 May 2018
DOI: 10.1080/09273948.2018.1511111



LETTER

Automated three-dimensional cell counting method for grading uveitis of rodent eye in vivo with optical coherence tomography

Woo J. Choi^{1,2} | Kathryn L. Pepple^{3,4} | Ruikang K. Wang^{1,5*}

REVIEW



Cytokines in uveitis

Jessica E. Weinstein and Kathryn L. Pepple

Bajema et al. Journal of Ophthalmic Inflammation and Infection (2017) 7:19
DOI: 10.1186/s12348-017-0137-0

Journal of Ophthalmic Inflammation and Infection

ORIGINAL RESEARCH

Open Access

Tuberculous uveitis: association between anti-tuberculous therapy and clinical response in a non-endemic country

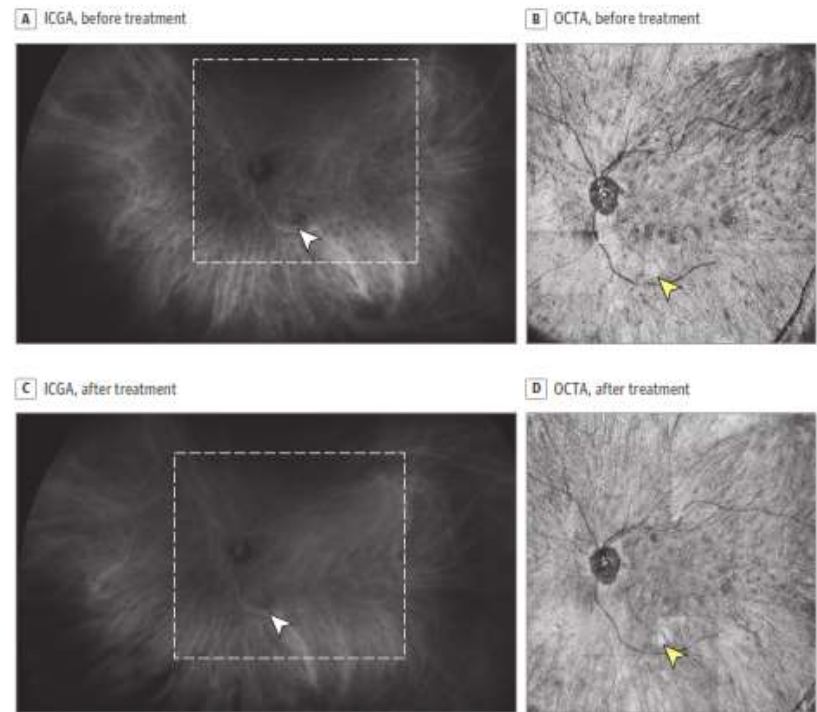
Kristina L. Bajema¹, Kaivon Pakzad-Vaezi², Thomas Hawn¹ and Kathryn L. Pepple^{1,3*}



Use of En Face Swept-Source Optical Coherence Tomography Angiography in Identifying Choroidal Flow Voids in 3 Patients With Birdshot Chorioretinopathy

Kathryn L. Pepple, MD, PhD; Zhongdi Chu, MS; Jessica Weinstein, MD; Marion R. Munk, MD, PhD; Russell N. Van Gelder, MD, PhD; Ruikang K. Wang, PhD

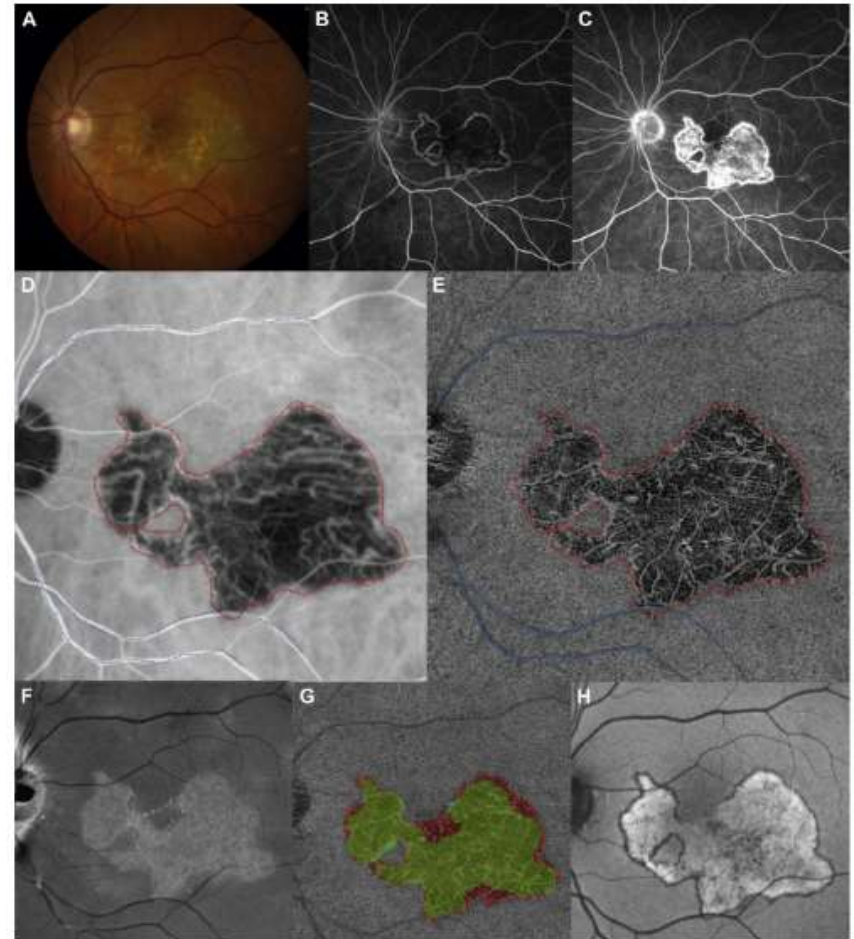
- Compared wide-field SS-OCTA to ICG angiography in 3 patients with BSCR
- Equivalent or higher sensitivity for detection of pathology with OCTA than ICG angiography
- May allow early, non-invasive diagnosis of disease



Swept-Source OCT Angiography of Serpiginous Choroiditis

Kaivon Pakzad-Vaezi, MD,¹ Kosar Khaksari, PhD,² Zhongdi Chu, MSc,² Russell N. Van Gelder, MD, PhD,^{1,3,4}
Ruikang K. Wang, PhD,^{1,2} Kathryn L. Pepple, MD, PhD¹

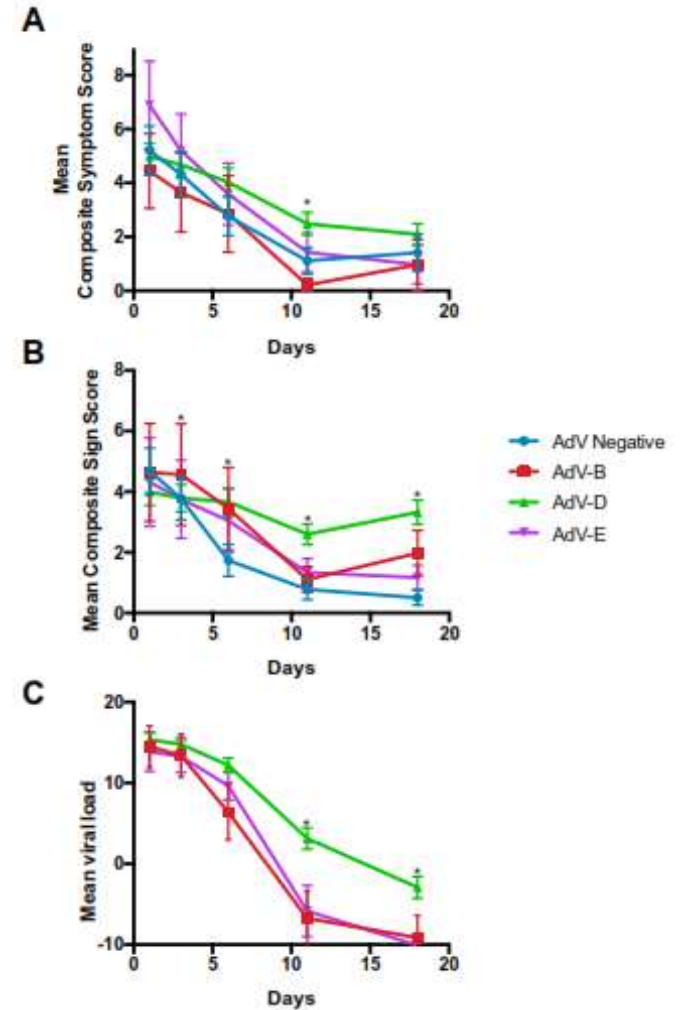
- Used SS-OCTA prototype to look at active and quiescent serpiginous
- Case series of six eyes of three patients
- Choriocapillaris perfusion slab size highly correlated with activity on FAF and FA
- Appeared to have higher sensitivity for active disease than FAF



Determinants of Outcomes of Adenoviral Keratoconjunctivitis

Cecilia S. Lee, MD, MS,¹ Aaron Y. Lee, MD, MSCI,¹ Lakshmi Akileswaran, PhD,¹ David Stroman, PhD,² Kathryn Najafi-Tagol, MD,² Steve Kleiboeker, PhD,³ James Chodosh, MD, MPH,⁴ Amalia Magaret, PhD,^{5,6,7} Anna Wald, MD, MPH,^{7,8,9} Russell N. Van Gelder, MD, PhD,^{1,10} on behalf of the BAYnovation Study Group*

- Prospective study of 500 subjects with EKC
- 22% adenoviral-negative by PCR
- Remarkable diversity of adenoviral type with substantial type B and E
- Outcome strongly influenced by viral type



Comparison of Aqueous and Vitreous Lymphocyte Populations From Two Rat Models of Experimental Uveitis

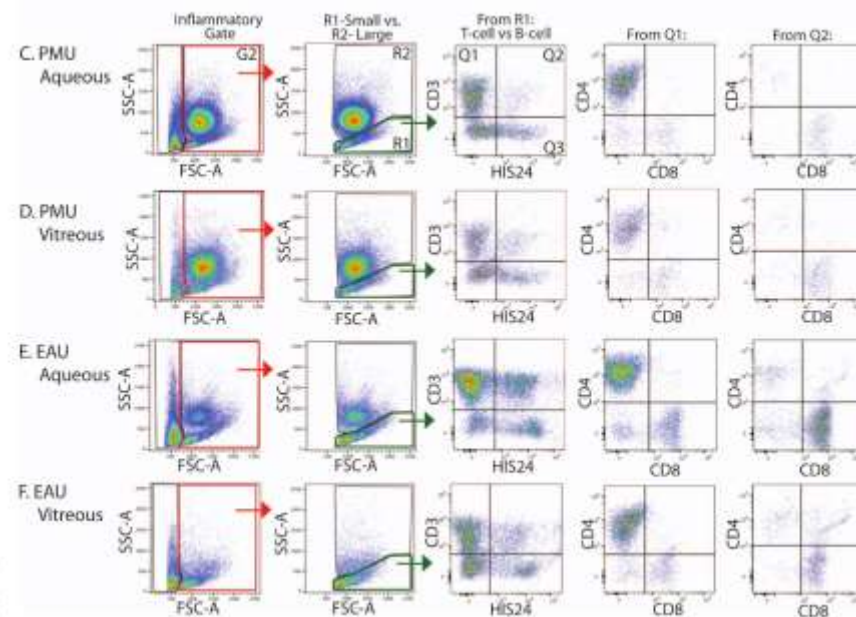
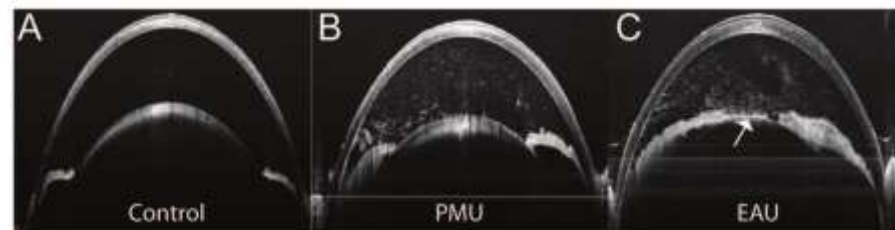
Kathryn L. Pepple,¹ Leslie Wilson,¹ and Russell N. Van Gelder¹⁻³

¹Department of Ophthalmology, University of Washington, Seattle, Washington, United States

²Department of Biological Structure, University of Washington, Seattle, Washington, United States

³Department of Pathology, University of Washington, Seattle, Washington, United States

- Comparison of intraocular lymphocytes in two animal models of uveitis: EAU and PMU
- Both models produce comparable inflammation
- Distinct but overlapping cell infiltrates with surprisingly robust CD4 response in PMU
- May explain chronic uveitis following intraocular infection



Translation



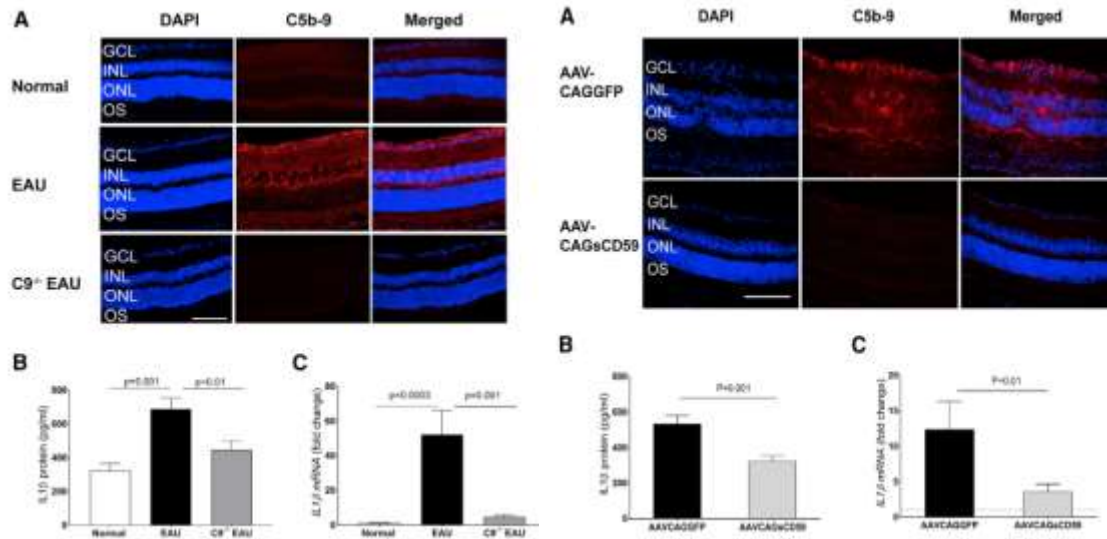
Complement-Mediated Activation of the NLRP3 Inflammasome and Its Inhibition by AAV-Mediated Delivery of CD59 in a Model of Uveitis

Molecular Therapy Vol. 26 No 6 June 2018

Binit Kumar,¹ Siobhan M. Cashman,¹ and Rajendra Kumar-Singh¹

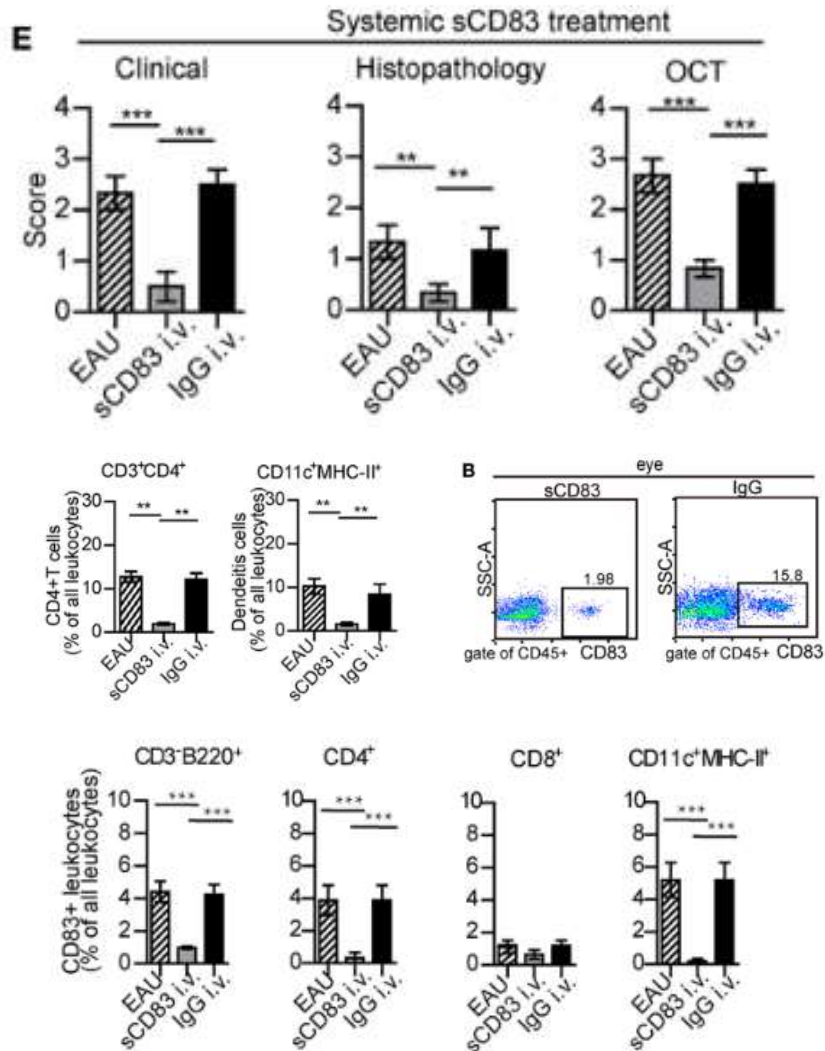
¹Department of Developmental, Molecular and Chemical Biology, Tufts University School of Medicine, Boston, MA 02111, USA

- Studied EAU in wild-type and C9-/- mutant mice
- Found membrane attack complex and NLRP3 inflammasome activated in EAU, and IL1 and Th differentiation dependent on C9
- However, C9-/- mice still had retinal structure and function loss with EAU
- AAV delivery of sCD59 (C9 inhibitor) attenuated NLRP3 inflammasome and EAU pathology



Soluble CD83 Alleviates Experimental Autoimmune Uveitis by Inhibiting Filamentous Actin-Dependent Calcium Release in Dendritic Cells

Wei Lin^{1,2,3*}, Konrad Buscher^{4,5†}, Beibei Wang², Zhichao Fan³, Nannan Song¹, Peng Li¹, Yingying Yue¹, Bingqing Li¹, Culling Li¹ and Hongsheng BF



- Soluble CD83 is extracellular domain of endogenous immunoregulatory factor
- During onset and recovery of EAU, levels rise in aqueous
- Systemic or topical administration of sCD83 protect strongly against EAU (after induction) with induction of tolerogenic dendritic cells
- However, increased mortality after systemic administration



A cell penetrating peptide from SOCS-1 prevents ocular damage in experimental autoimmune uveitis

Chulbul M. Ahmed^a, Michael T. Massengill^b, Emily E. Brown^a, Cristhian J. Idefonso^b, Howard M. Johnson^c, Alfred S. Lewin^{a,c}

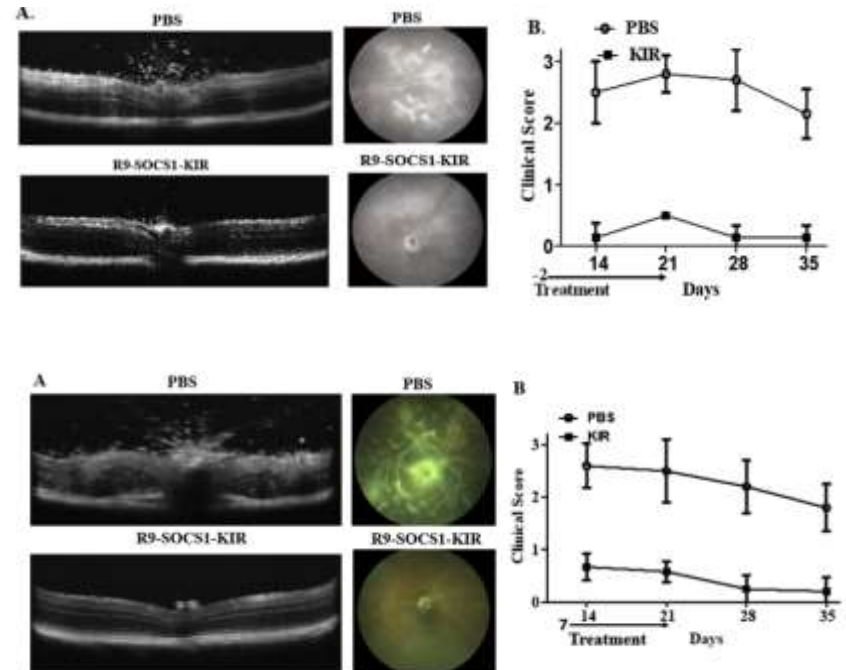
^a Department of Molecular Genetics and Microbiology, University of Florida, Gainesville, FL, 32610 USA

^b Department of Ophthalmology, University of Florida, Gainesville FL, 32610, USA

^c Department of Microbiology and Cell Science, University of Florida, Gainesville, FL, 32611, USA



- Anti-inflammatory peptide that blocks kinase activation of JAK2 and TYK2.
- Attached polyarginine (9) to create cell penetrant peptide
- Protected TNF α and IL-17 damage of ARPE-19 cells
- Topical administration blocked EAU both prophylactically and 7 days after immunization



Autoantibody profiling in intraocular fluid of patients with uveitis

Josianne C. ten Berge^{a,*}, Marco WJ. Schreurs^b, Joost van Rosmalen^c, Aniki Rothova^a

^a Department of Ophthalmology, Erasmus University Medical Center, Rotterdam, The Netherlands

^b Department of Immunology, Erasmus University Medical Center, Rotterdam, The Netherlands

^c Department of Biostatistics, Erasmus University Medical Center, Rotterdam, The Netherlands

Experimental Eye Research 176 (2018) 141–146

- 76 patients with uveitis and 19 cataract samples
- Tested for reactivity to 188 ocular antigens by multiplex immunoassay
- 22 antigens higher reactivity in uveitis than control
- Most notable in post-infectious and MS-associated uveitis
- Anti-tyrosinase weakly associated with CME

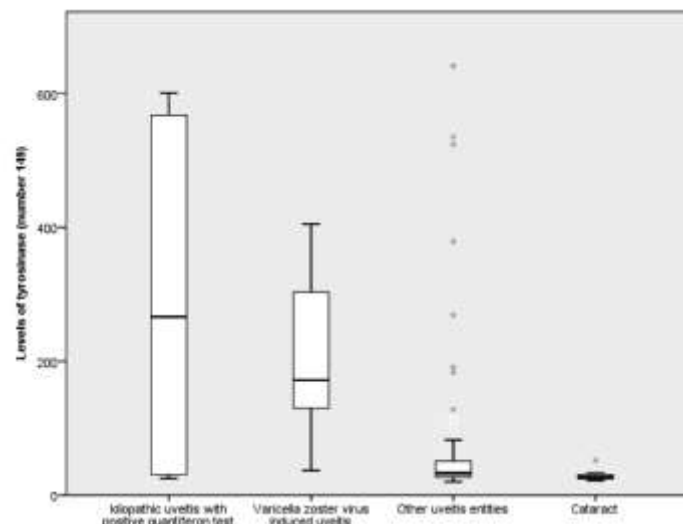


Table 2

Prevalence of anti-ocular antibodies in specific uveitis entities (N = 76) compared to cataract (N = 19)*.

Antigen no.	Antigen name	Short name	p-value**	Fold increase
Varicella zoster virus induced uveitis vs. cataract				
186	G protein-coupled receptor kinase 7	GRK7	< 0.00001	31.7
80	Neural retina-specific leucine zipper protein	NRL	< 0.00001	11.3
149	Tyrosinase	TYR	< 0.00001	6.4
104	Retinol-binding protein 3	RBP3	< 0.00001	5.6
Multiple sclerosis associated uveitis vs. cataract				
102	Guanine nucleotide-binding protein G(I)/G(S)/G(O) subunit gamma-T2	GNGT2	< 0.00001	25.1
107	Retina and anterior neural fold homeobox protein 2	RAX2	< 0.00001	12.3
33	Recoverin	RCVRN	< 0.00001	8.5
153	Retinal-specific ATP-binding cassette transporter	ABCA4	< 0.00001	5.4
87	Fructose-bisphosphate aldolase C	ALDOC	< 0.00001	5.23
Idiopathic uveitis with positive quantiferon test vs. cataract				
149	Tyrosinase	TYR	< 0.00001	18.1
164	Retinoschisin	RS1	< 0.00001	8.3
11	Oxygen-regulated protein 1	RP1	< 0.00001	7.8
143	Cbp/p300-interacting transactivator 1	CITED1	< 0.00001	7.7

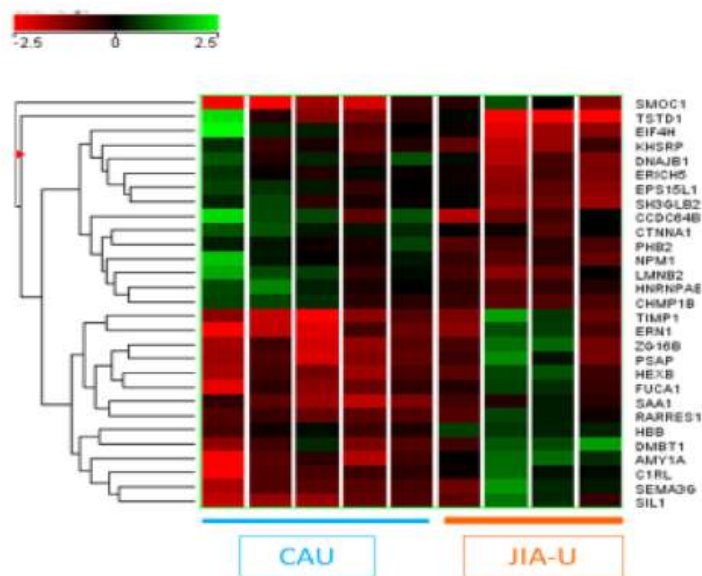
ORIGINAL RESEARCH

Open Access



Discovery of tear biomarkers in children with chronic non-infectious anterior uveitis: a pilot study

Sheila T. Angeles-Han^{1,2*}, Steven Yeh³, Purnima Patel³, Duc Duong⁴, Kirsten Jenkins⁵, Kelly A. Rouster-Stevens^{5,6}, Mekibib Altaye^{8,2}, Ndate Fall^{1,2}, Sherry Thornton^{1,2}, Sampath Prhalad^{5,6,7} and Gary N. Holland⁹



- Pilot study examining GC-Mass Spec of tears for cytokines involved in JIA
- Nine eyes of seven subjects with either JIA-uveitis or chronic idiopathic uveitis
- Found patterns indicative of JIA or chronic disease, including elevated S100A8/A9 and elevated TIMP in JIA
- Further work needed for validation

Potential Diagnosis of Vitreoretinal Lymphoma by Detection of *MYD88* Mutation in Aqueous Humor With Ultrasensitive Droplet Digital Polymerase Chain Reaction

Laura S. Hiemcke-Jiwa, MD; Ninette H. ten Dam-van Loon, MD; Roos J. Leguit, MD; Stefan Nierkens, PhD; Jeannette Ossewaarde-van Norel, PhD; Joke H. de Boer, PhD; Floor F. Roholl, BSc; Roel A. de Weger, PhD; Manon M. H. Huibers, PhD; Jolanda D. F. de Groot-Mijnes, PhD; Jonas J. W. Kuiper, PhD

JAMA Ophthalmol. doi:10.1001/jamaophthalmol.2018.2887
Published online July 19, 2018.

- Retrospective analysis of *MYD88* PCR mutation analysis by droplet digital PCR in VRL and uveitis
- 96 samples from 63 patients, 23 with VRL
- L265P mutation detected in 17/23 with VRL and 0/40 with uveitis
- PPV = 100%; NPV 0.87
- Vitreous yields slight better than aqueous; generally concordant

Table 2. *MYD88* L265P Analysis ddPCR in Vitreous Fluid and Aqueous Humor of Patients With Vitreoretinal Lymphoma or Uveitis

Result	Samples, No. (%)	
	Patients With Vitreoretinal Lymphoma	Patients With Uveitis
Vitreous fluid		
Patients	19 (49)	20 (51)
Total samples	21 (51)	20 (49)
Positive for <i>MYD88</i> L265P	16 (76)	0
Negative for <i>MYD88</i> L265P	5 (24)	20 (100)
Aqueous humor		
Patients	21 (46)	25 (54)
Total samples	27 (49)	28 (51)
Positive for <i>MYD88</i> L265P	11 (41)	0
Negative for <i>MYD88</i> L265P	16 (59)	28 (100)

Abbreviations: ddPCR, droplet digital polymerase chain reaction; *MYD88*, myeloid differentiation primary response gene 88.

MYD88 L265P MUTATION DETECTION IN THE AQUEOUS HUMOR OF PATIENTS WITH VITREORETINAL LYMPHOMA

RETINA 00:1-6, 2018

ELISABETTA MISEROCCHI, MD,* ANDRÉS J. M. FERRERI, MD,† CHIARA GIUFFRÈ, MD,*
 MARIA G. CANGI, PhD,‡ ILARIA FRANCAVIGLIA, MS,‡ TERESA CALIMERI, MD,†
 MAURILIO PONZONI, MD,‡ LORENZA PECCIARINI, MS,‡ FRANCESCO M. BANDELLO, MD,*
 GIULIO M. MODORATI, MD*

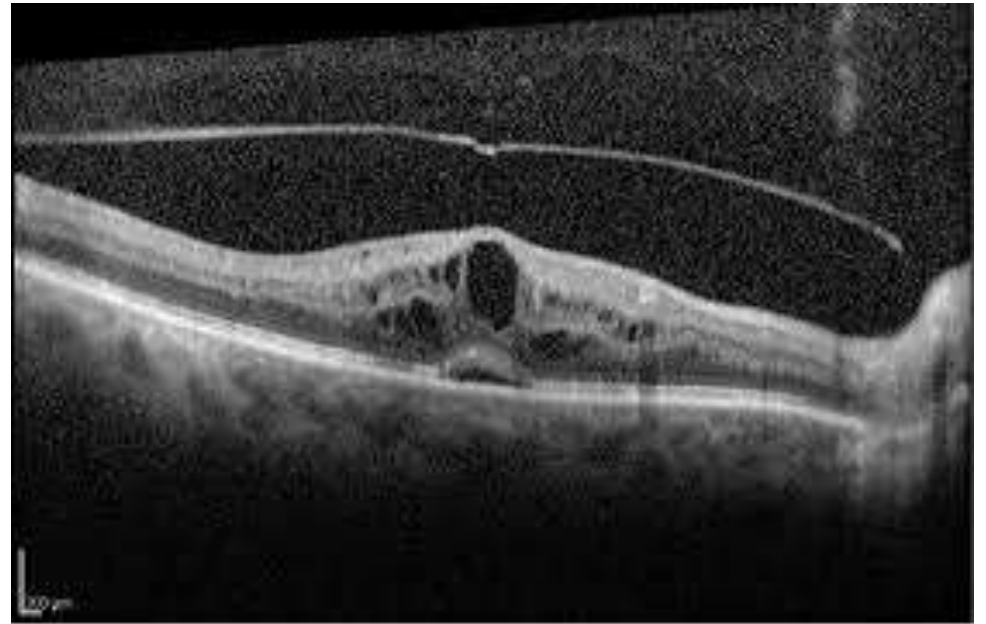
- 8 patients with bilateral vitreoretinal lymphoma, 6 patients with uveitis control
- 8/8 vitreous biopsies positive for L265P mutation; 6/8 aqueous positive
- 0/6 controls positive

Table 2. MYD88 Mutation Analysis in Aqueous and Vitreous Samples and Cytological Diagnosis of Lymphoma in the Vitreous and the Brain

PT	MYD88 (L265P)				Cytology/Histology		
	Aqueous		Vitreous		Vitreous		Brain
	RE	LE	RE	LE	RE	LE	
1	Negative	Negative	Not performed	Not performed	Positive	Not performed	Positive
2	Positive	Positive	Not performed	Not performed	Not performed	Negative	Positive
3	Positive	Positive	Positive	Positive	Positive	Negative	Not performed
4	Positive	Negative	Positive	Not performed	Positive	Not performed	Not performed
5	Positive	Negative	Positive	Not performed	Positive	Not performed	Not performed
6	Negative	Negative	Not performed	Positive	Not performed	Positive	Positive
7	Positive	Positive	Positive	Positive	Positive	Positive	Positive
8	Positive	Not performed	Positive	Not performed	Positive	Not performed	Not performed

LE, left eye; PT, patient; RE, right eye.

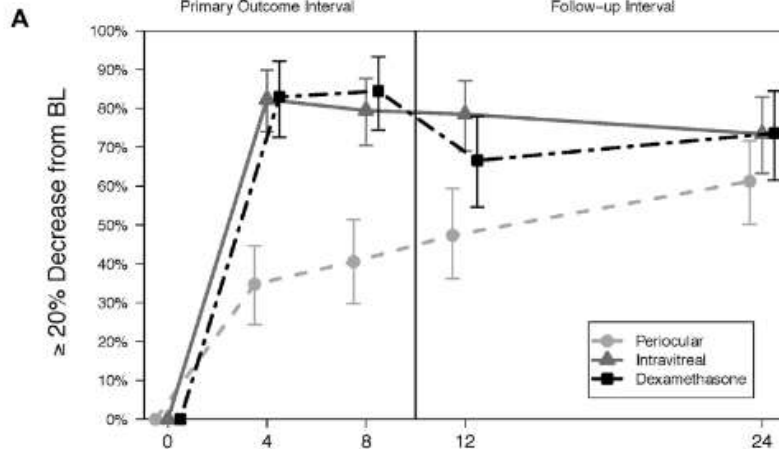
C A N
Y O U
S E E
M E ?



Periocular Triamcinolone vs. Intravitreal Triamcinolone vs. Intravitreal Dexamethasone Implant for the Treatment of Uveitic Macular Edema: The PeriOcular vs. INTravitreal corticosteroids for uveitic macular edema (POINT) Trial

The Multicenter Uveitis Steroid Treatment Trial Research Group*

Writing Committee: Jennifer E. Thorne, MD, PhD,^{1,2} Elizabeth A. Sugar, PhD,^{2,3} Janet T. Holbrook, PhD,² Alyce E. Burke, MPH,² Michael M. Altaweel, MD,⁴ Albert T. Vitale, MD,⁵ Nisha R. Acharya, MD, MS,^{6,7} John H. Kempen, MD, PhD,^{8,9,10} Douglas A. Jabs, MD, MBA^{2,11,12}

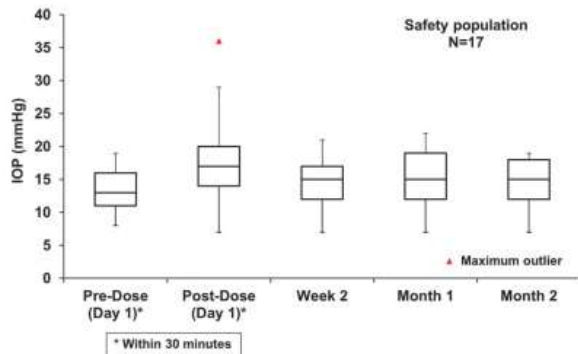
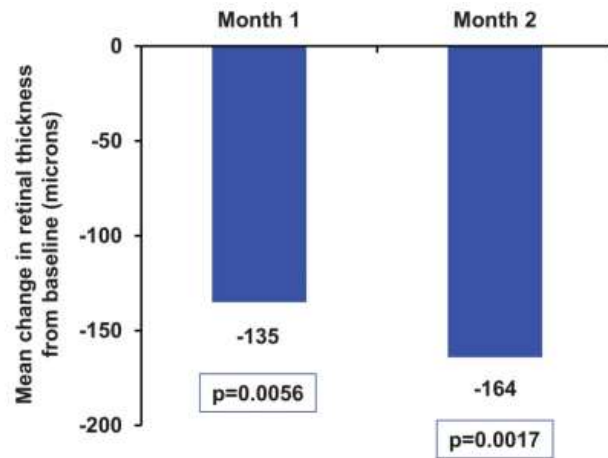


- Prospective RCT comparing periocular triamcinolone, intravenous triamcinolone, or intravitreal dexamethasone implant for uveitic macular edema
- 235 eyes of 192 patients
- All groups showed improvement
- Periocular injection showed slowest and least improvement
- Risk of IOP elevation > 24 mm Hg greater in intravitreal groups than in periocular groups.

SUPRACHOROIDAL INJECTION OF TRIAMCINOLONE ACETONIDE, CLS-TA, FOR MACULAR EDEMA DUE TO NONINFECTIOUS UVEITIS

A Randomized, Phase 2 Study (DOGWOOD)

STEVEN YEH, MD,* SHREE K. KURUP, MD,† ROBERT C. WANG, MD,‡ C. STEPHEN FOSTER, MD,§¶**
GLENN NORONHA, PhD,†† QUAN DONG NGUYEN, MD, MSc,‡‡ DIANA V. DO, MD‡‡
FOR THE DOGWOOD STUDY TEAM



- Randomized, controlled phase 2 study of suprachoroidal delivery of triamcinolone for uveitic edema
- Two doses (4 mg and 0.8 mg), primary outcome central subfield thickness
- 22 patients enrolled
- Significant reduction in central subfield thickness
- Minimal effect on IOP

Difluprednate for the Treatment of Uveitic Cystoid Macular Edema

Am J Ophthalmol 2018;191:14-22.

JULIE M. SCHALLHORN, KATHERINE M. NIEMEYER, ERICA N. BROWNE,
PARTH CHHETRI, AND NISHA R. ACHARYA

- Retrospective study of 72 eyes of 58 patients with uveitic CME
- 43 eyes treated with difluprednate only had CST decrease by 17%
- Risk of IOP elevation > 24 ~20% by 90 days treatment

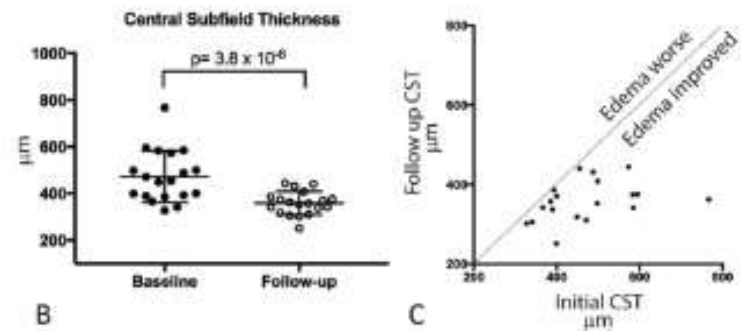
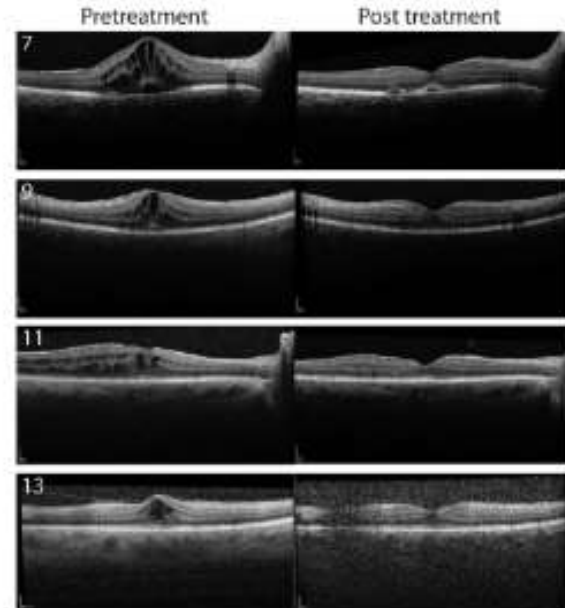
% Change CST

Baseline		-		-		-		-
Day 30	39	-17% (-7% to -33%)	24	-6% (-17% to -2%)	-20% (3%)	<.001	-7% (4%)	.04
Day 60	26	-13% (-6% to -43%)	16	-4% (-9% to 4%)	-21% (3%)	<.001	-2% (5%)	.70
Day 90	10	-26% (-11% to -53%)	15	-17% (-5% to -35%)	-25% (6%)	<.001	-17% (4%)	<.001

RESPONSE OF INFLAMMATORY CYSTOID MACULAR EDEMA TO TREATMENT USING ORAL ACETAZOLAMIDE

KATHRYN L. PEPPE, MD, PhD,* MACKLIN H. NGUYEN, BS,* KAIVON PAKZAD-VAEZI, MD,*
KATHLEEN WILLIAMSON, MD,* NAOMI ODELL, MD, MPH,* CECILIA LEE, MD, MS,*
THELLEA K. LEVEQUE, MD, MPH,* RUSSELL N. VAN GELDER, MD, PhD*†‡

- Retrospective study of 19 eyes of 16 subjects with recalcitrant CME
- Only medication modification addition of acetazolamide
- VA improved from 20/57 to 20/37
- Central subfield improved from 471 μm to 358 μm

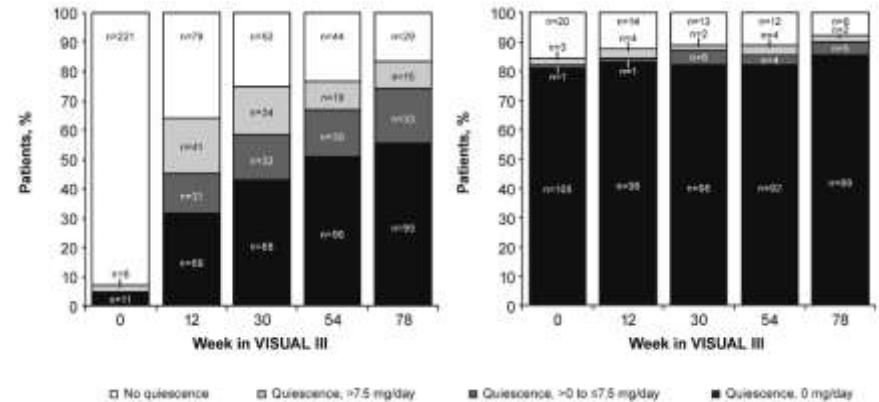




Safety and Efficacy of Adalimumab in Patients with Noninfectious Uveitis in an Ongoing Open-Label Study: VISUAL III

Eric B. Suhler, MD, MPH,¹ Alfredo Adán MD, PhD,² Antoine P. Brézin, MD, PhD,³ Eric Fortin, MD,⁴ Hiroshi Goto, MD,⁵ Glenn J. Jaffe, MD,⁶ Toshikatsu Kaburaki, MD,⁷ Michal Kramer, MD,⁸ Lyndell L. Lim, MBBS, FRANZCO,⁹ Cristina Muccioli, MD, MBA,¹⁰ Quan Dong Nguyen, MD, MSc,¹¹ Joachim Van Calster, MD,¹² Luca Cimino, MD,¹³ Martina Kron, PhD,¹⁴ Alexandra P. Song, MD, MPH,¹⁵ Jianzhong Liu, MD,¹⁵ Sophia Pathai, MBBS, PhD,¹⁶ Anne Camez, MD,¹⁴ Ariel Schlaen, MD,¹⁷ Mirjam E.J. van Velthoven, MD, PhD,¹⁸ Albert T. Vitale, MD,¹⁹ Manfred Zierhut, MD, PhD,²⁰ Samir Tari, MD, MBA,¹⁵ Andrew D. Dick, MBBS, MD²¹

Ophthalmology 2018;125:1075-1087



- Phase III open label extension study from Visual I/II
- Number with inactive uveitis increased from 35% at entry to 74% at week 78
- Steroid use reduced in active group from 13 mg/d to 3 mg/d
- Significant AE profile but no significant difference from initial trials
- Suggests durable effect for most patients treated with adalimumab

Table 2. Adverse Events (Safety Data Set)

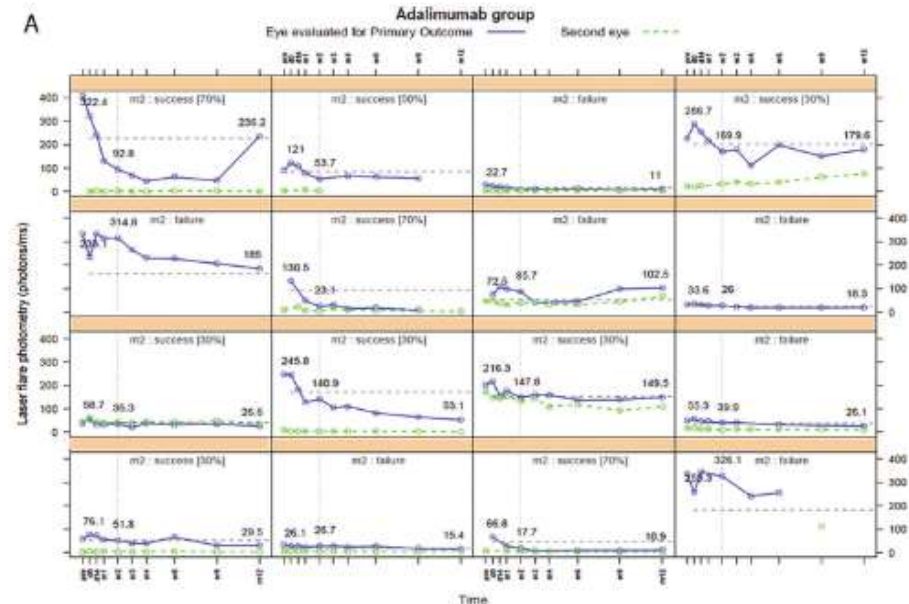
	Events (Events/100 PY) N = 424; PY = 953.7
Any AE	4043 (423.9)
AEs leading to death	4 (0.4)
Accidental death	1 (0.1)
B-cell lymphoma	1 (0.1)
Brain abscess	1 (0.1)
Metastatic pancreatic carcinoma	1 (0.1)
AEs leading to discontinuation	82 (8.6)
Serious AEs	157 (16.5)
Infections	787 (82.5)
Serious infections	38 (4.0)
Opportunistic infections (excluding oral candidiasis and tuberculosis)	5 (0.5)
Tuberculosis	16 (1.7)
Active	1 (0.1)
Latent	15 (1.6)
Allergic reactions	30 (3.2)
Malignancies	12 (1.3)
Non-melanoma skin cancer	6 (0.6)
Lymphoma	1 (0.1)
Other*	5 (0.5)
Sarcoidosis [†]	4 (0.4)
Vasculitis [‡]	8 (0.8)
Liver events including liver failure	10 (1.1)
Demyelinating disorders	5 (0.5)

ADJUVITE: a double-blind, randomised, placebo-controlled trial of adalimumab in early onset, chronic, juvenile idiopathic arthritis-associated anterior uveitis

Pierre Quartier,^{1,2,3,4} Amandine Baptiste,⁵ Véronique Despert,⁶ Emma Allain-Launay,⁷ Isabelle Koné-Paut,⁸ Alexandre Belot,^{4,9} Laurent Kodjikian,¹⁰ Dominique Monnet,^{3,11} Michel Weber,¹² Caroline Elie,⁵ Bahram Bodaghi,¹³ On behalf of the ADJUVITE Study Group

To cite: Quartier P, Baptiste A, Despert V, et al. *Ann Rheum Dis* 2018;**77**:1003–1011.

- RCT for patients with JIA-uveitis and inadequate response to MTX
- 31 patients
- Used laser flare photometry as outcome marker
- At month 2, 9/16 responders to adalimumab vs 3/15 on placebo



Interobserver Agreement Among Uveitis Experts on Uveitic Diagnoses: The Standardization of Uveitis Nomenclature Experience

DOUGLAS A. JABS, ANDREW DICK, JOHN T. DOUCETTE, AMOD GUPTA, SUSAN LIGHTMAN, PETER MCCLUSKEY, ANNABELLE A. OKADA, ALAN G. PALESTINE, JAMES T. ROSENBAUM, SOPHIA M. SALEEM, JENNIFER THORNE, AND BRETT TRUSKO, FOR THE STANDARDIZATION OF UVEITIS NOMENCLATURE WORKING GROUP

- Study to evaluate interobserver agreement on uveitis diagnosis
- 5766 cases for 25 diseases evaluated by expert committees
- Overall kappa statistic 0.39, ranging from 0.23 (toxoplasma retinitis) to 0.79 (CMV anterior uveitis)
- Consensus could be achieved in 99% of cases after discussion
- Agreement among uveitis experts re: diagnosis is moderate at best
- Strongly suggest need for validated disease criteria

Disease	No. of Cases Submitted	Online Voting Results		
		Mean κ	SD	Range κ 's
Cytomegalovirus anterior uveitis	112	0.79	0.15	0.51–1.00
Herpes simplex anterior uveitis	250	0.32	0.14	0.00–0.56
Varicella zoster anterior uveitis	163	0.58	0.10	0.35–0.87
Fuchs uveitis syndrome	249	0.44	0.13	0.16–0.65
Juvenile idiopathic arthritis chronic uveitis	251	0.29	0.16	–0.02 to 0.64
Spondylitis/human leukocyte antigen-B27-associated uveitis	251	0.47	0.11	0.27–0.71
Tubulointerstitial nephritis with uveitis	125	0.54	0.22	0.16–0.87
Pars planitis	308	0.32	0.15	–0.04 to 0.63
Intermediate uveitis, non-pars planitis type	209	0.49	0.09	0.27–0.67
Multiple sclerosis associated uveitis	183	0.44	0.08	0.31–0.62
Acute posterior multifocal placoid pigment epitheliopathy	149	0.44	0.12	0.17–0.84
Birdshot chorioretinitis	257	0.36	0.09	0.20–0.57
Multiple evanescent white dot syndrome	95	0.39	0.12	0.10–0.75
Multifocal choroiditis with panuveitis	251	0.30	0.13	0.02–0.58
Punctate inner choroiditis	250	0.52	0.08	0.32–0.70
Serpiginous choroiditis	157	0.37	0.19	–0.02 to 0.69
Serpiginous-like tuberculous choroiditis	104	0.28	0.15	–0.02 to 0.55
Acute retinal necrosis	252	0.43	0.18	0.13–0.61
Cytomegalovirus retinitis	251	0.27	0.16	0.07–0.65
Syphilitic uveitis	250	0.47	0.12	0.15–0.68
Toxoplasmic retinitis	213	0.23	0.14	0.03–0.53
Tuberculous uveitis	254	0.24	0.16	0.01–0.58
Behçet disease	248	0.36	0.13	0.15–0.61
Sarcoid uveitis	383	0.56	0.15	0.23–0.86
Sympathetic ophthalmia	149	0.31	0.12	0.07–0.51
Vogt-Koyanagi-Harada disease, early	224	0.45	0.14	0.16–0.72
Vogt-Koyanagi-Harada disease, late	177	0.42	0.14	0.13–0.68
Overall	5766	0.39	0.14	–0.04 to 1.00

Medical Malpractice in Uveitis: A Review of Clinical Entities and Outcomes

Ashvini K. Reddy, MD¹, Stephanie B. Engelhard, BA², Christopher T. Shah, MD², Austin J. Sim, BA³, and Jennifer E. Thorne, MD, PhD^{1,4}

- Retrospective review of malpractice settlements
- Lawsuits related to uveitis searched from 1930-2014.
- 25 total cases
- Viral retinitis most common diagnosis
- 64% of findings favored defendant
- 7/25 suits resolved by settlement with mean indemnity of ~\$725,000

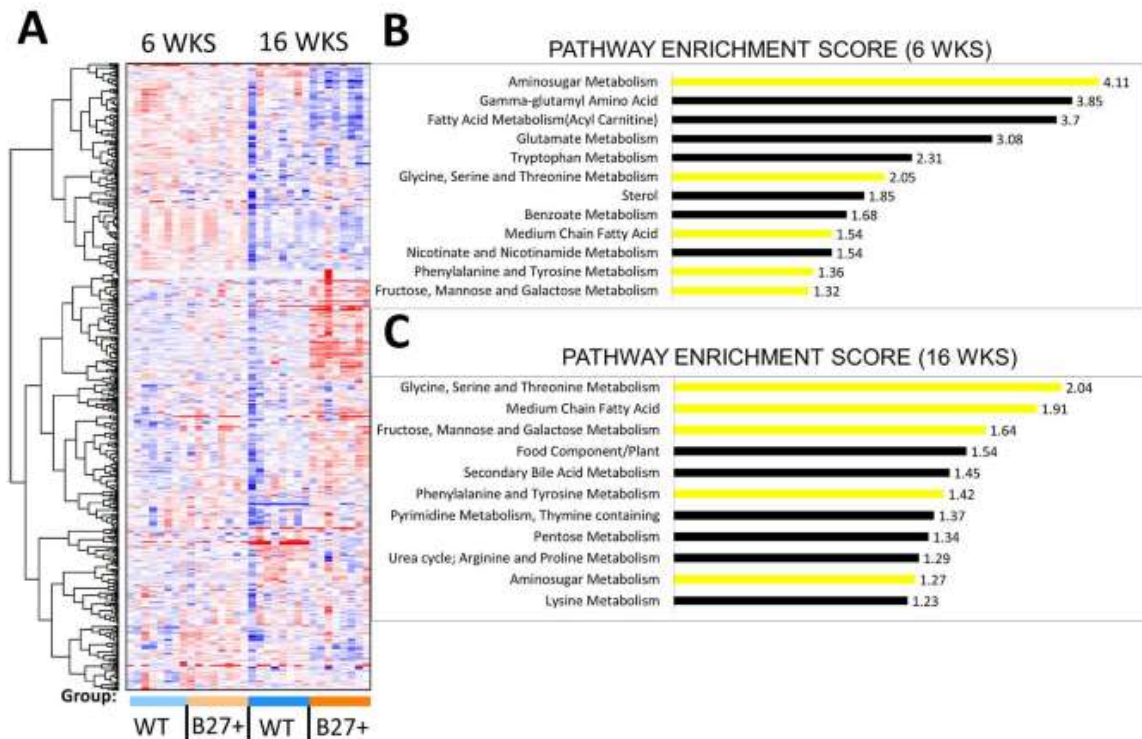
Ophthalmic Subspecialty	Minimum	Maximum	Mean
General	146 ^a	6,746,539	984,466
Pediatric	170,316	1,323,277	880,993
Glaucoma	285,577	3,020,022	1,099,668
Retina	57,469	42,061,690	3,852,137
Cornea	2,970	9,196,441	1,126,389
Neuro-ophthalmology	10,489	14,733,366	1,906,059
Oculoplastics	35,083	8,493,086	978,039
Oncology	192,190	1,261,538	670,086
Uveitis	127,837	2,021,887	797,052
Unknown	48,818	1,359,010	659,348
Traumatic	40,202	1,032,167	596,915

The Scoop on Poop



Intestinal Metabolites Are Profoundly Altered in the Context of HLA-B27 Expression and Functionally Modulate Disease in a Rat Model of Spondyloarthritis

Mark Asquith,¹ Sean Davin,¹ Patrick Stauffer,¹ Claire Michell,¹ Cathleen Janowitz,¹ Phoebe Lin,¹ Joe Ensign-Lewis,² Jason M. Kinchen,³ Dennis R. Koop,¹ and James T. Rosenbaum⁴



- Follow-up to previous work showing intestinal microbiome altered in B27 transgenic rats
- HPLC-MS characterization of 582 metabolites
- More than half significantly altered at 16 weeks
- Administration of propionate (short chain fatty acid); resulted in reduced inflammation



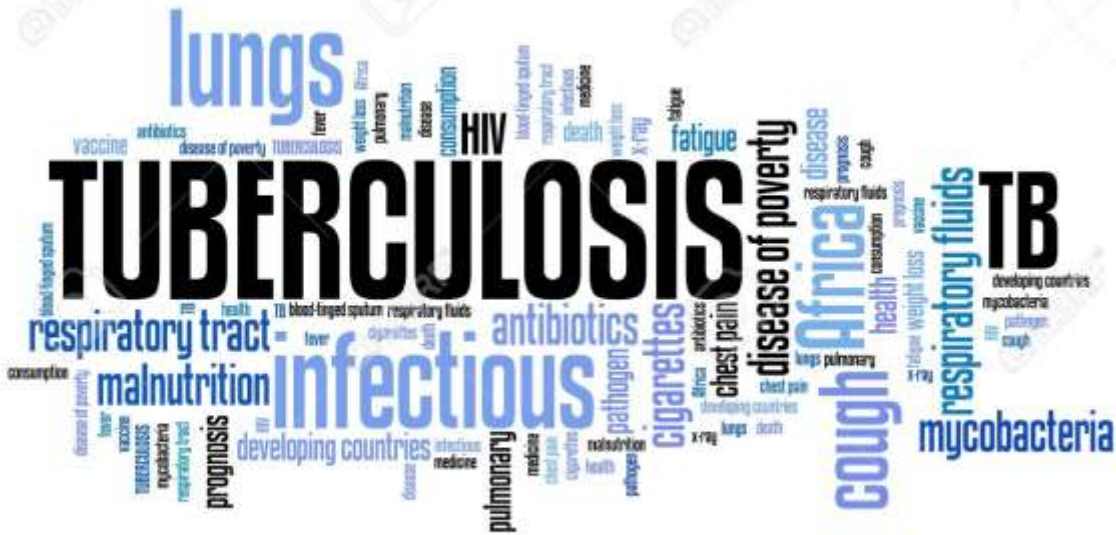
Fecal transplants in spondyloarthritis and uveitis: ready for a clinical trial?

Rene Y. Choi^a, Mark Asquith^b, and James T. Rosenbaum^{a,b,c}

UVEITIS IN SPONDYLOARTHRITIS A MICROBIOME-DRIVEN DISEASE?

KEY POINTS

- Intestinal dysbiosis occurs in various subsets of SpA.
- SpA-related uveitis may be due to a gut microbiome regulated increase in intestinal permeability.
- Therapeutic modalities targeting the intestinal microbiome could be a future approach to treating SpA.



Distinguishing Uveitis Secondary to Sarcoidosis From Idiopathic Disease

Cardiac Implications

Yong Seop Han, MD; Erick Rivera-Grana, MD; Sherveen Salek, MD; James T. Rosenbaum, MD

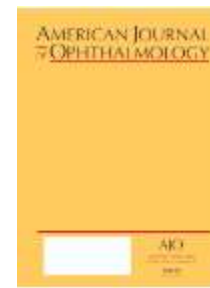
- Do we need to distinguish sarcoid uveitis from idiopathic disease?
- Studied 249 patients, 179 referred for idiopathic uveitis
- 53 underwent chest CT; 19 had presumptive sarcoid diagnosis made.
- Additional 14 patients previously diagnosed with sarcoid -> 33 total sarcoid patients

- EKG obtained in 14/33
- 9/14 had abnormal EKG
- 4/9 with paroxysmal ventricular tachycardia requiring defibrillator
- Suggest that patients older 40 with history of idiopathic uveitis be evaluated by chest CT and/or EKG

Manifestation of CS followed by definitive diagnosis by cardiac MRI and PET	VT	PVCs and VT	PVCs, VT, and cardiomyopathy	Complete AV block and VT
Surgical management for CS	ICD	ICD	Cardiac ablation ICD	Pacemaker ICD
Other systemic manifestations of sarcoidosis	Pulmonary, glandular, splenic involvement	Pulmonary	Pulmonary	Pulmonary, neurosarcoidosis

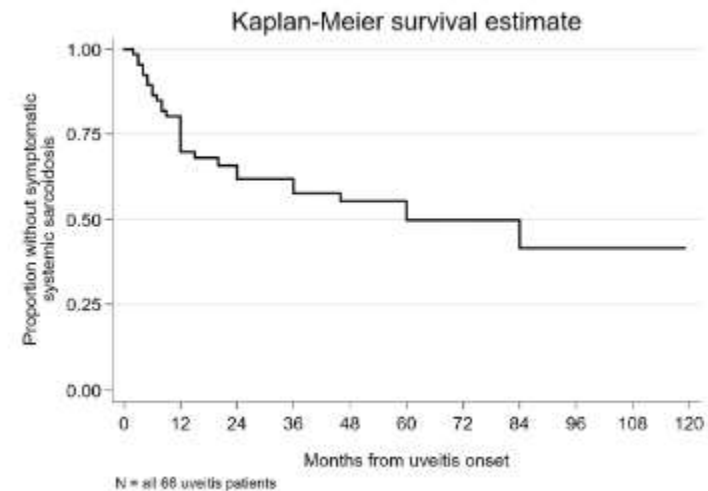
Sarcoidosis related uveitis: Clinical presentations, disease course and rates of systemic disease progression after uveitis diagnosis

Shirley Ma BMedSci, MBBS^{1,3,4}, Sophie L Rogers BSc(Hons), MEpi¹, Anthony J Hall MD, FRANZCO^{2,3}, Lauren Hodgson¹, Jessica Brennan¹, Richard Stawell MBBS, FRANZCO^{2,4}, Lyndell L Lim DMedSci, FRANZCO^{1,2,4}



10.1016/j.ajo.2018.09.013

- Retrospective review of 143 patients with uveitis and sarcoidosis
- Determined rate of development of symptomatic systemic sarcoid from uveitis onset
- Uveitis presenting complaint in 79%.
- 20% developed symptomatic systemic sarcoid with median time 12 months
- No ocular predictors of systemic disease
- Suggests clinically significant systemic sarcoidosis can develop late in patients presenting with ocular disease

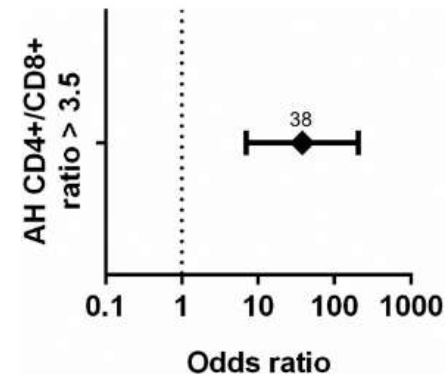
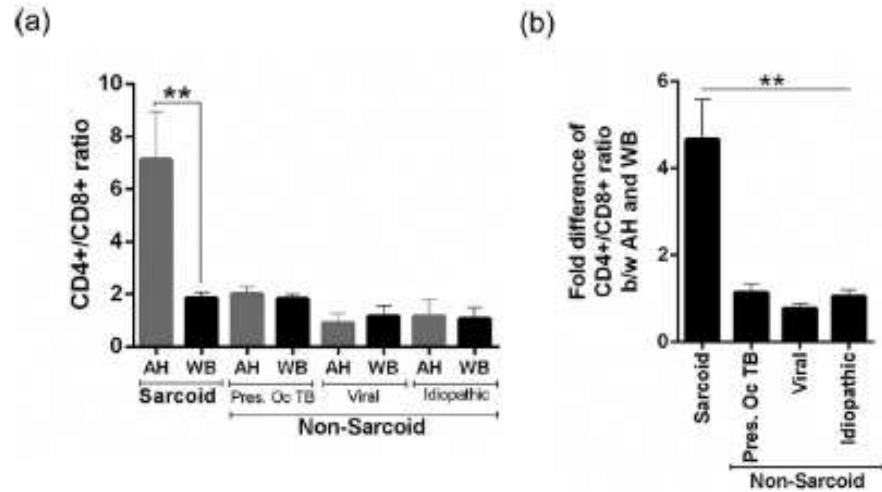


- Case control study of 61 patients with uveitis (21 with sarcoid)
- CD4/CD8 ratio in aqueous and blood determined by flow cytometry.
- Mean ratio in AH 6.3 in sarcoid compared with 1.6 in non-sarcoid
- Ratio > 3.5 had odds ratio of 38 of being associated with sarcoidosis
- Bayesian utility less as PPV 0.26 and NPV 0.73

ORIGINAL ARTICLE

Increased Aqueous Humor CD4+/CD8+ Lymphocyte Ratio in Sarcoid Uveitis

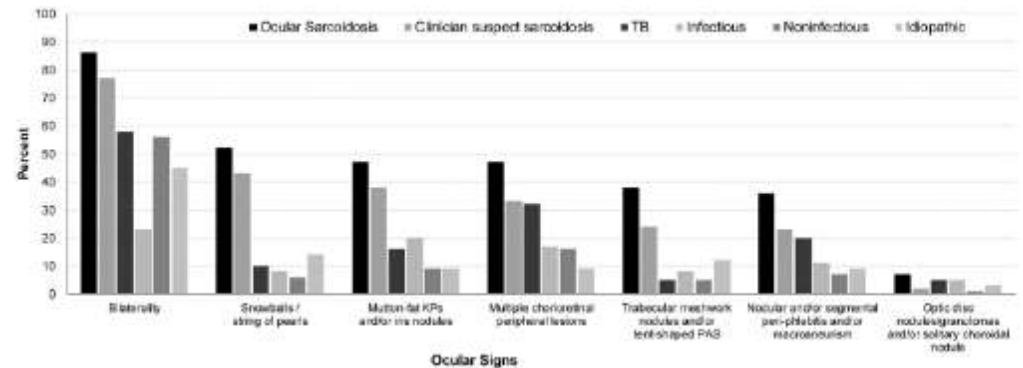
Namita Dave, MS¹⁺, Priyanka Chevour, MSC²⁺, Padmamalini Mahendradas, DNB¹, Anitha Venkatesh, DNB¹, Ankush Kawali, DNB³, Rohit Shetty, FRCS PHD¹, Arkasubhra Ghosh, PHD^{2,3}, and Swaminathan Sethu²



Distinguishing Features of Ocular Sarcoidosis in an International Cohort of Uveitis Patients

Nisha R. Acharya, MD, MS,^{1,2} Erica N. Browne, MS,¹ Narsing Rao, MD,³ Manabu Mochizuki, MD, PhD,⁴ for the International Ocular Sarcoidosis Working Group*

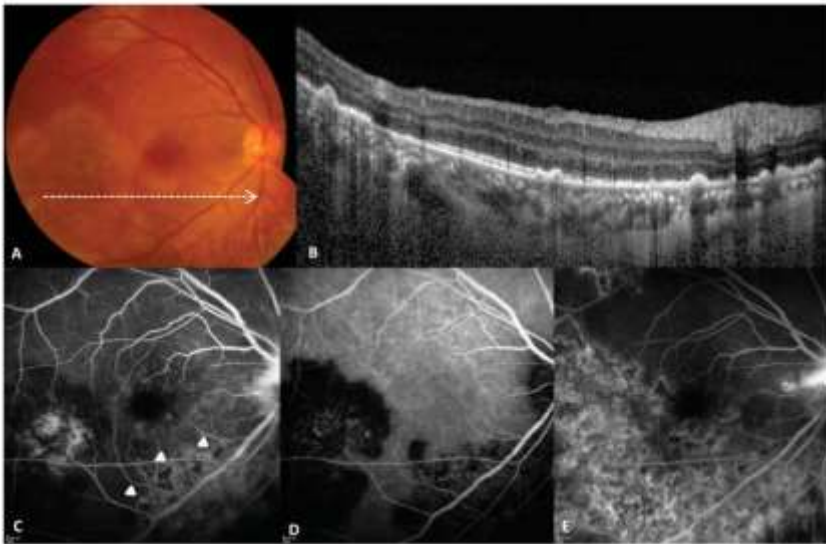
- Validation study of 884 uveitis patients, 30% with likely sarcoid
- 180/264 met IWOS criteria
- Signs with highest predictive values were bilaterality, snowballs, mutton fat KP, iris nodules
- ACE/lysozyme elevated in 62%
- Current criteria need revision; certain signs (elevated LFT) not useful



VITREOUS TREPONEMAL ANTIBODY AS A SUPPLEMENTARY TEST TO SEROLOGY FOR THE CONFIRMATION OF SYPHILITIC CHORIORETINITIS

RETINAL CASES & BRIEF REPORTS 0:1–4, 2017

Sukhum Silpa-archa, MD, BBA,* Janine M. Preble, MS,† C. Stephen Foster, MD,
FACS‡§¶



- Describes two cases of possible syphilitic choroiditis with vitreous FTA-Abs and RPR
- One case positive for both but with negative serum RPR responded well to PCN therapy
- Second case (figure) negative for FTA-Abs and RPR did not respond to PCN; diagnosed with serpiginous and responded to IMT

Global Variations and Challenges With Tubercular Uveitis in the Collaborative Ocular Tuberculosis Study

Rupesh Agrawal,¹⁻³ Dinesh Visva Gunasekeran,^{1,2,4} Dhananjay Raje,⁵ Aniruddha Agarwal,⁶ Quan Dong Nguyen,⁷ Onn Min Kon,⁸ Carlos Pavesio,² and Vishali Gupta⁶; for the Collaborative Ocular Tuberculosis Study Group

¹National Healthcare Group Eye Institute, Tan Tock Seng Hospital, Singapore

²Moorfields Eye Hospital, National Health Service Foundation Trust, London, United Kingdom

³Singapore Eye Research Institute, Singapore

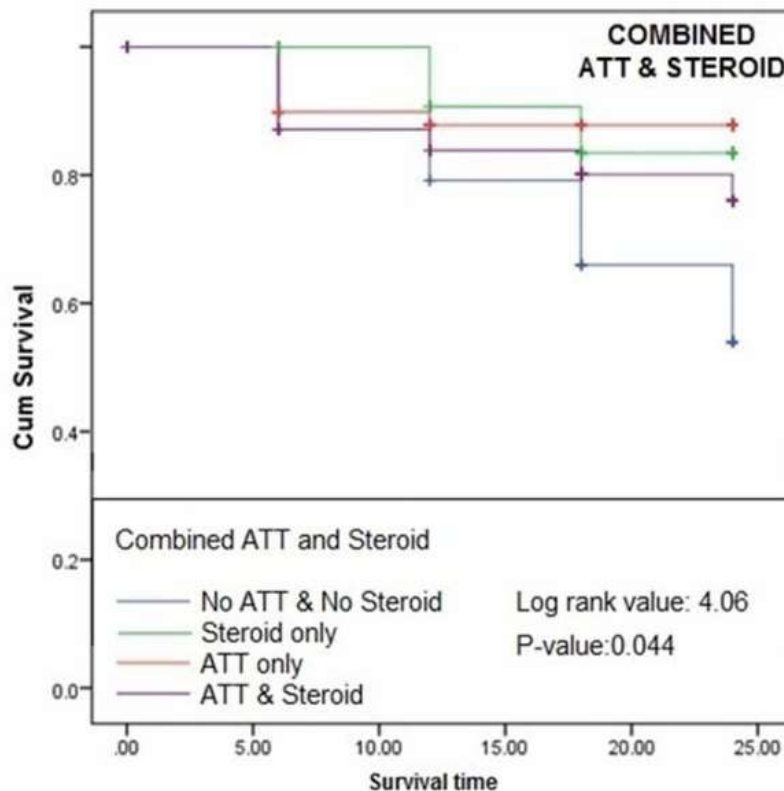
⁴School of Medicine, National University of Singapore, Singapore

⁵MDS Bio-Analytics, Nagpur, India

⁶Advanced Eye Centre, Postgraduate Institute of Medical Education and Research, Chandigarh, India

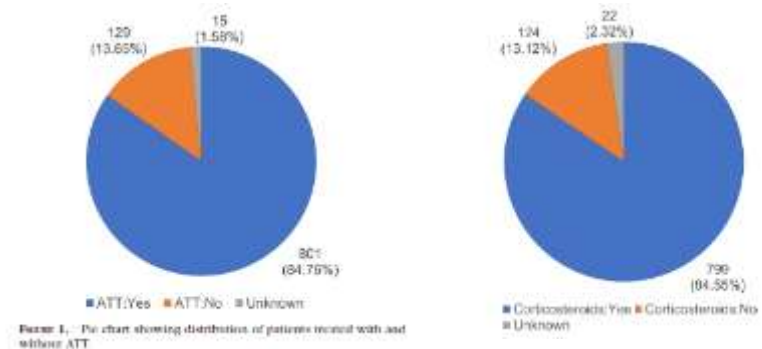
⁷Byers Eye Institute, Stanford University, Palo Alto, California, United States

⁸Chest and Allergy Clinic, St. Mary's Hospital, Imperial College Healthcare National Health Service Trust, London, United Kingdom



IOVS 2018;59:4162-4171

- International collaboration on ocular tuberculosis
- Retrospective study of 945 patients with presumed TB uveitis
- Primary outcome = treatment failure/recurrent disease/inability to taper steroid
- Majority of patients without signs, symptoms, or radiographic evidence of TB
- African, Hispanic, and immigrant status associated with worse outcomes
- No significant effect of treatment with steroid or ATT on primary outcome

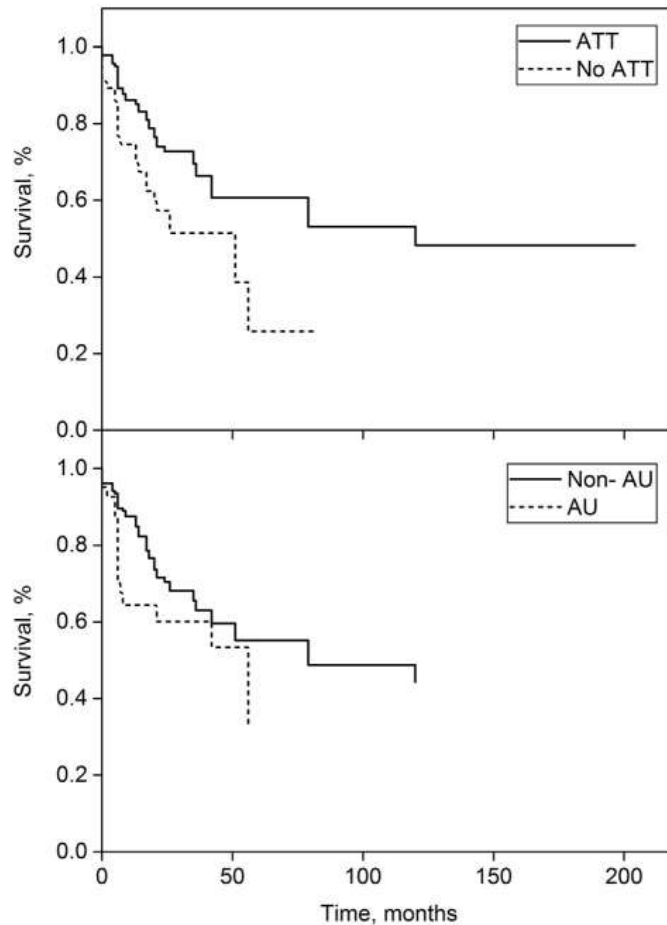


Effect of Antituberculous Therapy on Uveitis Associated With Latent Tuberculosis



(Am J Ophthalmol 2018;190:164–170.)

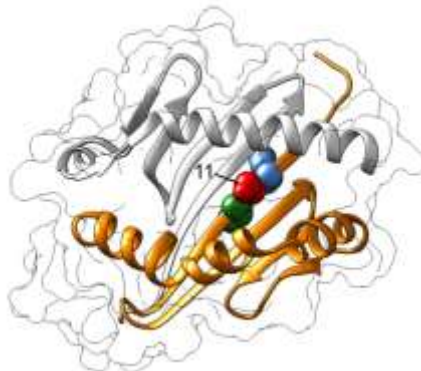
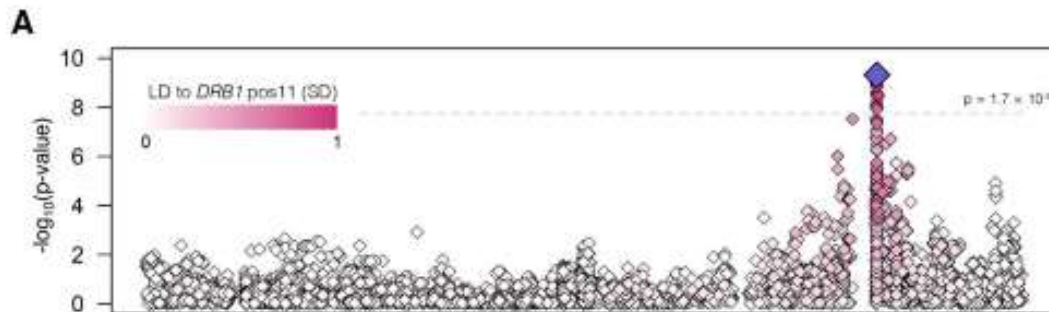
OREN TOMKINS-NETZER, BELINDA C.S. LEONG, XIAOZHE ZHANG, SUE LIGHTMAN, AND PETER J. MCCLUSKEY, FOR THE SYDNEY-LONDON LATENT OCULAR TB STUDY GROUP



- Retrospective cohort analysis of 199 eyes of 129 patients with uveitis and latent TB
- 69% received antitubercular therapy
- Overall 35% with recurrence of uveitis
- Odds ratio of recurrence with ATT = 0.47
- Treated eyes recurred at median 122 months vs 51 months with no treatment

Identification of an Amino Acid Motif in HLA-DR β 1 That Distinguishes Uveitis in Patients With Juvenile Idiopathic Arthritis

Anne-Mieke J. W. Haasnoot,¹ Marco W. Schilham,² Sylvia Kamphuis,³ Petra C. E. Hissink Muller,² Arnd Heiligenhaus,⁴ Dirk Foell,⁵ Kirsten Minden,⁶ Roel A. Ophoff,⁷ Timothy R. D. J. Radstake,¹ Anneke I. Den Hollander,⁸ Tjitske H. C. M. Reinards,² Sanne Hiddingh,¹ Nicoline E. Schalijs-Delfos,² Esther P. A. H. Hoppenreijns,⁸ Marion A. J. van Rossum,⁹ Carine Wouters,¹⁰ Rotraud K. Saurenmann,¹¹ J. Merlijn van den Berg,¹² Nico M. Wulfraat,¹ ICON-JIA Study Group, Rebecca ten Cate,² Joke H. de Boer,¹ Sara L. Pulit,¹³ and Jonas J. W. Kuiper¹



- Analysis of 576 patients with JIA (from 2 cohorts), 214 with uveitis by GWAS
- High linkage with presence of serine at position 11 of HLA-DR β 1 (OR 2.6) which was specific to girls.
- Amino acid in peptide binding domain
- Likely affects antigen binding and presentation

Running head: CARRA consensus treatment plans for anterior uveitis

Title: Childhood Arthritis and Rheumatology Research Alliance consensus treatment plans

for juvenile idiopathic arthritis-associated and idiopathic chronic anterior uveitis

- Group of pediatric rheumatologists, ophthalmologists, and lay members
- Developed two consensus treatment plans with >95% consensus for treatment of JIA-associated uveitis
- Identified areas for further research within consortium



REVIEW

Open Access

Methotrexate in juvenile idiopathic arthritis: advice and recommendations from the MARAJIA expert consensus meeting



Giovanna Ferrara^{1†}, Greta Mastrangelo^{2†}, Patrizia Barone³, Francesco La Torre⁴, Silvana Martino⁵, Giovanni Pappagallo⁶, Angelo Ravelli⁷, Andrea Taddio⁸, Francesco Zulian⁹, Rolando Cimaz^{2*}  On behalf of the Rheumatology Italian Study Group

- The Rheumatology Italian Study Group consensus recommendations
- PICO based evidence-based literature assessment
- MTX is first line treatment
- CBC/LFT monitoring every 4-8 weeks initially, then q12-16 weeks
- Dose of 10-15 mg/m²/week
- SQ treatment preferred
- **MTX may be discontinued after 6 months of stable remission**
- Folic acid 1 mg/day
- MTX + anti-TNF for recalcitrant cases



OPEN ACCESS

EXTENDED REPORT

Consensus-based recommendations for the management of uveitis associated with juvenile idiopathic arthritis: the SHARE initiative

Tamas Constantin,¹ Ivan Foeldvari,² Jordi Anton,³ Joke de Boer,⁴ Severine Czitrom-Guillaume,⁵ Clive Edelsten,⁶ Raz Gepstein,⁷ Arnd Heiligenhaus,^{8,9} Clarissa A Pilkington,¹⁰ Gabriele Simonini,¹¹ Yosef Uziel,¹² Sebastian J Vastert,¹³ Nico M Wulfraat,¹³ Anne-Mieke Haasnoot,⁴ Karoline Walscheid,⁸ Annamária Pálinkás,¹ Reshma Pattani,⁶ Zoltán Györgyi,¹ Richárd Kozma,¹ Victor Boom,¹⁴ Andrea Ponyi,¹ Angelo Ravelli,¹⁵ Athimalaipet V Ramanan¹⁶

- European consortium generating recommendations for management of JIA
- Used evidence-based consensus methodology
- 22 recommendations with >80% agreement
- Methotrexate is first choice for systemic IMT
- Non-Etanercept anti-TNF is second line
- Recommend 2 years of inactive disease off topicals before IMT holiday
- Consider tocilizumab, rituximab, and abatacept as 3rd line treatment

Association of Hypovitaminosis D With Increased Risk of Uveitis in a Large Health Care Claims Database

JAMA Ophthalmol. 2018;136(5):548-552.

Lucia Sobrin, MD, MPH; Lynn K. Stanwyck, BS; Wei Pan, MS; Rebecca A. Hubbard, PhD;
John H. Kempen, MD, PhD; Brian L. VanderBeek, MD, MPH, MSCE

- Retrospective case control analysis of claims data from 558 noninfectious uveitis cases and 2790 controls
- All had vitamin D levels drawn within 1 year
- Patients with normal vitamin D levels had odds ratio 0.79 for uveitis compared with controls
- Effect more pronounced in black patients (OR 0.49)

TABLE 3. Unadjusted and Adjusted Logistic Regression Results

Variable	No. of Patients	Odds Ratio (95% CI)	P Value
Unadjusted logistic regression			
Vitamin D level			
<20 ng/dL	587	1 [Reference]	.03
≥20 ng/dL	2761	0.78 (0.62-0.98)	
Adjusted logistic regression^a			
Vitamin D level			
<20 ng/dL	587	1 [Reference]	.04
≥20 ng/dL	2761	0.79 (0.62-0.99)	
Vitamin D blood draw month			
April-October	1864	1 [Reference]	.39
November-March	1484	1.08 (0.90-1.30)	
Geographic region			
Northeast	713	1 [Reference]	.18
Southeast	1903	1.31 (1.02-1.67)	
West	717	1.16 (0.86-1.56)	
Unknown	9	0.91 (0.20-4.11)	
Adjusted race/ethnicity-stratified logistic regression^{a,b}			
Vitamin D level in white patients			
<20 ng/dL	265	1 [Reference]	.40
≥20 ng/dL	1757	0.87 (0.62-1.47)	
Vitamin D level in black patients			
<20 ng/dL	150	1 [Reference]	.004
≥20 ng/dL	402	0.49 (0.30-0.80)	
Vitamin D level in Hispanic patients			
<20 ng/dL	51	1 [Reference]	.10
≥20 ng/dL	111	0.60 (0.33-1.10)	

Association of Low Vitamin D Levels with Noninfectious Uveitis and Scleritis

Ocular Immunology & Inflammation, 2018; 00(00): 1–8

Stephanie M. Llop, MD*, Samaneh Davoudi, MD*, Lynn K. Stanwyck, BS, Shaleen Sathe, BA, Lisa Tom, MD, Tina Ahmadi, BS, Lindsay Grotting, MD, George N. Papalioidis, MD, and Lucia Sobrin, MD, MPH

Department of Ophthalmology, Harvard Medical School, Massachusetts Eye and Ear Infirmary, Boston, Massachusetts, USA

- Retrospective case-control study of 333 uveitis cases, 103 scleritis cases, and 329 controls
- Odds ratio 1.92 for uveitis for low vitamin D levels ($p < 0.0003$)
- Primarily factor for anterior uveitis and scleritis
- 5% lower risk for every 1 U increased vitamin D level

	Univariate		Multivariate*	
	OR (95% CI)	<i>p</i> -value	OR (95% CI)	<i>p</i> -value
Anterior uveitis (223 cases vs. 329 controls)	1.77 (1.25–2.51)	0.001	1.92 (1.31–2.82)	0.001
Idiopathic anterior uveitis (156 cases vs. 298 controls)	2.04 (1.38–3.03)	3.85×10^{-4}	2.16 (1.42–3.30)	3.57×10^{-4}
Intermediate uveitis (22 cases vs. 329 controls)	1.31 (0.54–3.15)	0.552	1.16 (0.43–3.07)	0.772
Idiopathic intermediate uveitis (10 cases vs. 298 controls)	1.26 (0.35–4.57)	0.723	1.47 (0.38–5.67)	0.573
Posterior uveitis (23 cases vs. 329 controls)	1.73 (0.74–4.04)	0.206	1.86 (0.77–4.51)	0.167

competition outstanding
distinguished manager
creative unusual individual
colorful object nature leader
original many idea business
forward
unique
concept different boss success solitude creativity group direction healthy
distinct special leadership uniqueness individuality
independent contrast difference inspiration standout strategy
education courage

Ophthalmic Images

Ocular Inflammation Associated With Fibers From Eyelash Extensions

Mohammad Samir Dowlut, MBChB, FRCOphth; Yousry Ahmed, MBChB; Angela Knox, FRCOphth



Figure. The white arrowheads indicate linear subconjunctival fibers and the associated localized hyperemia.

A woman in her 40s with a history of using eyelash extensions/fibers (Moodstruck 3D Fiber Lashes +; Younique) presented with redness, irritation, and pain in her right eye. An examination revealed several fibers (approximately 1 mm long) overlying the conjunctiva, with at least 6 in the subconjunctival space.

The patient's eyes were too tender for removal of the subconjunctival foreign bodies at slitlamp. These fibers are described as being made from nylon and enriched with several chemicals (propylene glycol, squalane, tocopheryl).¹

She was prescribed a course of topical chloramphenicol, 0.5%, and dexamethasone, 0.1%, 4 times daily. Three days later she was still symptomatic, and the fibers were subsequently removed in the operating room under a local anesthetic (Figure). Nylon is inert; however, the chemicals presumably caused the localized reaction. The patient's symptoms resolved following the removal of the fibers while continuing the course of topical chloramphenicol and dexamethasone for 2 weeks.

Copy-editor of the year award

Effectiveness and safety of *Glycyrrhizae* Decoction for Purging Stomach-Fire in Behcet disease patients

Study protocol for a randomized controlled and double-blinding trail

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Background: Behcet disease (BD) is a worldwide-occurred autoimmune disorder and currently lack of optional successful treatment. An ancient traditional Chinese medical formula called *Glycyrrhizae* Decoction for Purging Stomach-Fire (GDPSF) was recorded and nowadays has been observed to be effective for BD patients. However, the strict randomized controlled and double-blinding trail is needed to further assess this alternative medicine.

Thank you!

