Developing a Flair for Uveitis

Betty Wang O.D., F.A.A.O.
Orlando VAMC Conference
October 13, 2022

1

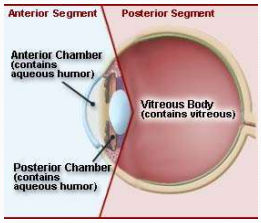
Learning Objectives

- Define uveitis and classify uveitis based on primary site of inflammation.
- List examples of anterior uveitis associated with non-infectious and infectious systemic diseases.
- Compare the symptoms and signs of non-granulomatous uveitis versus granulomatous uveitis.
- Learn how to grade cell and flare using the SUN (The Standardization of Uveitis Nomenclature) and AOA classification schemes.
- Explain when laboratory work up is indicated for anterior uveitis and which labs to order based on the patient's history, review of systems, and clinical exam.
- Discuss various treatment modalities for uveitis and the appropriate follow up schedule.
- List ocular complications from uveitis which can contribute to permanent vision loss.

2

Anterior Uveitis

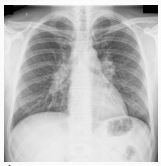
- **Intraocular inflammation of the uveal structures anterior to the vitreous cavity.**[1]
- **Etiology**
  - **Trauma**
  - **Non-Traumatic**
    - 80-90% are associated with a systemic disorder, making accurate diagnosis critical.

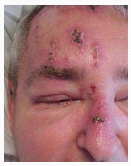


3

Anterior Uveitis

- **Association with systemic diseases**
  - Non-infectious
    - Ankylosing spondylitis
    - Reiter's Syndrome
    - Psoriatic Arthritis
    - IBS (Irritable Bowel Syndrome)
    - Posner Schlossman Syndrome
    - Behcet's
    - VKH (Vogt-Koyanagi-Harada Syndrome)
    - JRA (Juvenile Rheumatoid Arthritis)
    - Lupus
    - Fuch's Heterochromic Cyclitis
    - Sarcoidosis
  - Infectious
    - TB
    - Syphilis
    - HSV
    - HZV
    - Lyme Disease
    - Toxoplasmosis, Toxocariasis, Histoplasmosis





4

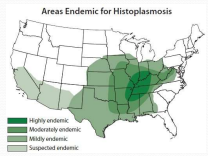
Epidemiology of Uveitis

- **Incidence**
  - Uveitis is the third leading cause of worldwide blindness and currently accounts for approximately 10% of preventable vision loss in the US and up to 15% worldwide. [5,6,7]
  - In the US, uveitis has an estimated prevalence of about 38 cases per 100,000. [7]
  - The incidence is highest in persons between 20-50 years with a peak incidence found in the third decade. [4]

5

Epidemiology of Uveitis

- **Uveitis may affect individuals of any age**
- **Risk Factors**
  - Location
    - Histoplasmosis frequently seen in Ohio and Mississippi River Valleys. [8,9]
    - Lyme disease endemic in northeastern, north central, and western states. [9,10]
  - Gender
    - Higher incidence of uveitis in women than men.
    - Largest differences were seen in older age groups. [7]
  - Sexually transmitted diseases
    - History of syphilis, Reiter's, HIV



6

Classification System

The Standardization of Uveitis Nomenclature (SUN) Working Group Classification System (2005) [11]

- **Anterior Uveitis**
- **Intermediate Uveitis**
- **Posterior Uveitis**
- **Panuveitis**

- **Acute**: inflammation for less than 6 weeks.
- **Chronic**: persistent inflammation over 6 weeks or relapse in less than 3 months after stopping treatment.

7

Table 1 – SUN Working Group anatomic classification of uveitis[6]

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

8

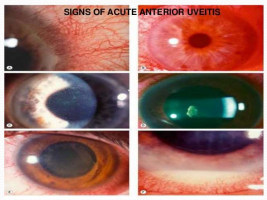
Table 4 – SUN Working Group descriptors in uveitis[6]

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

9

Symptoms and Signs

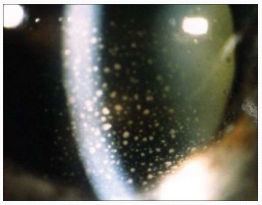
- **Non-granulomatous Anterior Uveitis**
  - Acute onset
  - Circumlimbal conjunctival injection
  - Corneal edema
  - Fine non-granulomatous white KPs
  - Cells and flare
  - Posterior synechiae
  - Variability in intraocular pressure



10

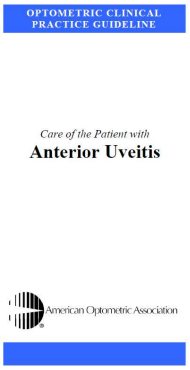
Symptoms and Signs

- **Granulomatous Anterior Uveitis**
  - Acute or gradual onset
  - Circumlimbal conjunctival injection
  - Corneal edema
  - **Granulomatous KPs**
    - "Mutton-fat" large yellow precipitates
  - Cells and flare
  - Posterior synechiae
  - **Iris nodules**
    - Koeppe nodules at the pupillary margin
    - Busacca nodules on the anterior surface
  - Variability in intraocular pressure



11

Clinical Exam



12

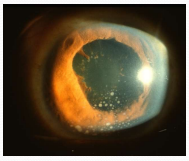
Clinical Exam

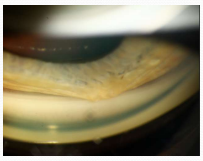
- **Patient History**
  - Symptoms
    - Duration, laterality, onset of symptoms
  - Demographics
    - Age, gender, race
  - Ocular and medical history
    - Prior episodes
    - History of eye trauma or disease
    - Recent infections
    - Fever, malaise, cold sores, shingles, or other skin rash
    - Past history of hospitalization, joint pain, lower back pain
- **Visual Acuity**
- **Pupils**

13

Clinical Exam

- **Slit Lamp/Anterior Segment exam**
  - Conjunctiva
  - Cornea
  - Anterior Chamber
  - Iris
  - Lens
- **Intraocular pressure**
- **Gonioscopy**
- **Posterior Segment**
  - Vitreous
  - Retina
  - Optic nerve





14

OPTOMETRIC CLINICAL PRACTICE GUIDELINE

Care of the Patient with
Anterior Uveitis

American Optometric Association

Table 1
Grading of Flare and Cells*

Grade	Flare	Cells
0	Complete absence	No cells
1+	Faint flare (barely detectable)	5 to 10 cells per field
2+	Moderate flare (iris and lens details clear)	10 to 20 cells per field
3+	Marked flare (iris and lens details hazy)	20 to 50 cells per field
4+	Intense flare (fixed, coagulated aqueous humor with considerable fibrin)	50+ cells per field

15

Table 2 – SUN Working Group grading scheme for anterior chamber cells[6]

Grade	Cells in field[a]
0	<1
0.5+	1–5
1+	6–15
2+	16–25
3+	26–50
4+	>50

a Field size is a 1 mm by 1 mm slit beam.

16

Table 3 – SUN Working Group grading scheme for anterior chamber flare[6]

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)

17

Anterior Uveitis Associated with Systemic Diseases

18

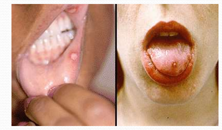
Anterior Uveitis associated with HLA-B27 Conditions

- **All are acute, unilateral, and non granulomatous.**
- **HLA B27**
  - 6% of the US population is HLA B27 positive
  - Cumulative lifetime risk of iritis is 1%.
  - Risk increases to 20-40% if there is joint disease
- **Ankylosing spondylitis**
- **Reiter's syndrome**
- **Inflammatory bowel disease**
- **Psoriatic arthritis**

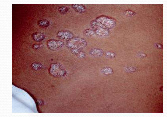
19

Multi-Systemic Disorder Uveitis

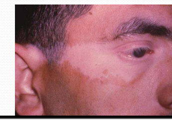
- **Behcet's Disease**
  - Affects young adults in their 20-30s
  - Highest prevalence in Eastern Mediterraneans
  - Triad of oral ulcers, genital ulcers and ocular inflammation
  - Diagnosed by clinical exam of skin lesions and positive Behcet's pathergy test



- **Sarcoidosis**
  - Non-necrotizing granulomatous inflammation
  - Lungs, liver, spleen, skin
  - Diagnosed by granuloma biopsy, chest x-ray, ACE, Lysozyme



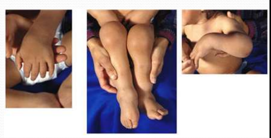
- **Vogt Koyanagi Harada (VKH) Disease**
  - A multisystemic inflammatory and autoimmune disease targeting antigens of melanocytes
  - Vitiligo, Poliosis, Alopecia
  - Hearing loss, tinnitus
  - Headache, nausea, vertigo
  - Diagnosed by clinical exam, auditory exam



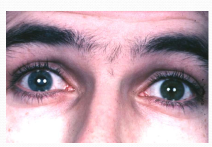
20

Chronic Non-Granulomatous Anterior Uveitis

- **Juvenile Rheumatoid Arthritis**
  - The most common type of arthritis in children under the age of 16.
  - Symptoms: joint pain, swelling, stiffness, fever or swollen lymph nodes in the evenings.
  - 5:1 female to male ratio.
  - Diagnosed by joint x-ray, ANA, negative rheumatoid factor



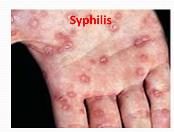
- **Fuch's Heterochromic Iridocyclitis**
  - Chronic unilateral uveitis
  - Asymptomatic
  - Triad of heterochromia, non granulomatous KPs, anterior uveitis
  - Iris can also develop rubeosis and atrophy
  - Diagnosed by clinical exam

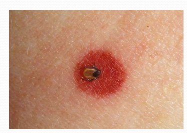


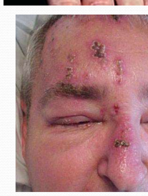
21

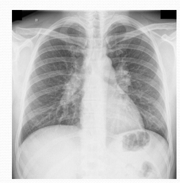
Infectious Uveitis

- **Syphilis**
- **Herpes Simplex Virus**
- **Herpes Zoster Virus**
- **TB**
- **Lyme Disease**









22

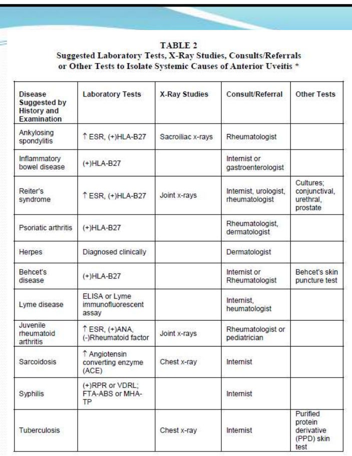
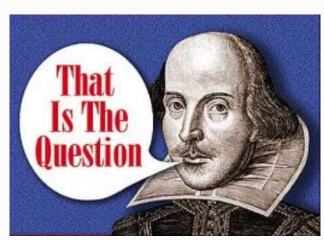


TABLE 2
Suggested Laboratory Tests, X-Ray Studies, Consults/Referrals or Other Tests to Isolate Systemic Causes of Anterior Uveitis *

Disease Suggested by History and Examination	Laboratory Tests	X-Ray Studies	Consult/Referral	Other Tests
Ankylosing spondylitis	↑ ESR, (+)HLA-B27	Sacroiliac x-rays	Rheumatologist	
Inflammatory bowel disease	(+)HLA-B27		Internist or gastroenterologist	
Reiter's syndrome	↑ ESR, (+)HLA-B27	Joint x-rays	Internist, urologist, rheumatologist	Cultures; conjunctival, urethral, prostate
Psoriatic arthritis	(+)HLA-B27		Rheumatologist, dermatologist	
Herpes	Diagnosed clinically		Dermatologist	
Behcet's disease	(+)HLA-B27		Internist or Rheumatologist	Behcet's skin puncture test
Lyme disease	ELISA or Lyme immunofluorescent assay		Internist, heumatologist	
Juvenile rheumatoid arthritis	↑ ESR, (+)ANA, (-)Rheumatoid factor	Joint x-rays	Rheumatologist or pediatrician	
Sarcoidosis	↑ Angiotensin converting enzyme (ACE)	Chest x-ray	Internist	
Syphilis	(+)RPR or VDRL; FTA-ABS or MHA-TP		Internist	
Tuberculosis		Chest x-ray	Internist	Purified protein derivative (PPD) skin test

23

To Workup or not Workup?

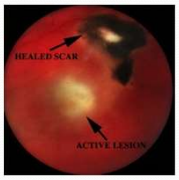


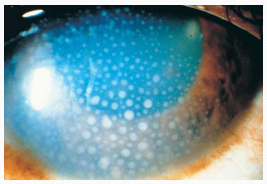
24

- **Situations when laboratory work up is not necessary**
  - First episode of unilateral, non-granulomatous uveitis with a history and exam not suggestive of systemic disease
  - Uveitis in the setting of known systemic disease
    - Pre-diagnosed infections: Syphilis, TB, Lyme
    - Pre-diagnosed inflammatory conditions: Sarcoidosis
  - Clinical findings are classic for a diagnosis
    - HSV, HZV, Fuch's Heterochromic Iridocyclitis

25

- **Situations when laboratory work up is indicated**
  - Recurrent episodes of unilateral, non-granulomatous uveitis
  - Bilateral uveitis
  - Posterior uveitis
  - Granulomatous uveitis





26

Supplemental Testing

- **Laboratory Testing**
  - Venereal Disease Research Laboratory (VDRL) and/or Rapid plasma reagin (RPR).
    - The VDRL and RPR are nonspecific serology tests for syphilis.
  - Fluorescent treponemal antibody absorption (FTA-ABS) and/or microhemagglutination assay for antibodies to Treponema pallidum (MHA-TP)
    - Specific treponemal tests
    - A false-positive FTA-ABS may be associated with various other conditions.
  - Purified protein derivative (PPD) skin test
  - Human leukocyte antigen - B27 (HLA-B27)
  - Antinuclear antibody (ANA)
  - CBC with differential
  - Erythrocyte sedimentation rate (ESR)
  - Angiotensin-Converting Enzyme (ACE)

27

Supplemental Testing

- **Lab Tests continued..**
  - HIV Test
  - Toxoplasmosis titers
  - Tococara titers
  - Lyme titers
- **Imaging Studies**
  - Sacroiliac Joint X-Ray
  - Ankle or Knee X-Rays
  - Chest X-Ray

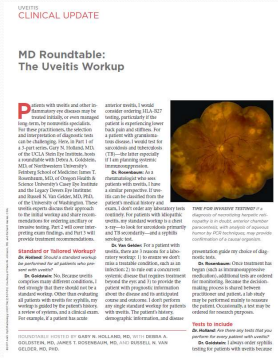
28

Table 3
Suggested Workup for Bilateral, Granulomatous or Recurrent Anterior Uveitis with No Indication of a Systemic Cause *

- Complete blood count (CBC)
- Erythrocyte sedimentation rate (ESR)
- Antinuclear antibody test (ANA)
- Rapid plasma reagin (RPR) or venereal disease research laboratory (VDRL)
- Fluorescent treponemal antibody absorption (FTA-ABS) or microhemagglutination assay for antibodies to Treponema pallidum (MHA-TP)
- Purified protein derivative (PPD) and anergy panel
- Chest x-ray for sarcoidosis and tuberculosis
- Lyme titer in endemic areas
- Consider HLA-B27 testing

29

The Uveitis Workup


UVEITIS
CLINICAL UPDATE

MD Roundtable:
The Uveitis Workup

- **Uveitis Clinical Update published in EyeNet March 2017**
- **Dr. Gary N. Holland MD of the UCLA Stein Eye Institute**
- **Roundtable discussion with 3 uveitis specialists to discuss their approach to the uveitis work up.**

30

Standard or Tailored Workup?

- ***Dr. Holland:*** *Should a standard workup be performed for all* patients who present with uveitis?

- The consensus among all three uveitis specialists…
  - There is not a standard work up
  - Directed by patient's history, review of systems, and the clinical exam
  - Evaluate all patients with uveitis for syphilis.
  - For a patient with granulomatous disease, test for sarcoidosis and tuberculosis
    - The latter especially if planning systemic immunosuppression.

31

Tests to Omit

- ***Dr. Holland:*** *Are there laboratory tests that are not useful in the evaluation of patients with nonspecific intraocular inflammation?*

- Lab tests that are not useful
  - ANA in adults (SLE is a clinical diagnosis)
    - However has significant prognostic information for JRA associated uveitis
  - ACE and lysozyme (debatable)
    - Low sensitivity and specificity
    - ACE and lysozyme can suggest granulomatous disease, but do not allow for definitive diagnosis
  - Lyme
    - Extremely rare cause of only uveitis and approximately 10% of the population is positive
  - Rheumatoid factor
    - Rheumatoid arthritis does not cause anterior uveitis

32

Thoughts & Discussion

33

Treatment and Follow up

- **Mild uveitis**
  - Cyclopentolate, 1% (t.i.d.) or homatropine, 5% (b.i.d.-t.i.d.)
  - Prednisolone, 1% (b.i.d.-q.i.d.)
  - Oral aspirin or ibuprofen, 2 tablets (q.4h)
  - Consider beta blockers if IOP is elevated
  - Re-evaluate 4-7 days (or p.r.n. if worsening)

- **Moderate uveitis**
  - Homatropine, 5% (q.i.d.) or scopolamine, 0.25% (b.i.d.)
  - Prednisolone, 1% (q.i.d.)
  - Oral aspirin or ibuprofen, 2 tablets (q.4h)
  - Consider beta blockers if IOP is elevated
  - Sunglasses
  - Advise patient carefully (e.g., pain, course, compliance)
  - Re-evaluate 2-4 days (or p.r.n)

34

Treatment and Follow up

- **Severe uveitis**
  - Atropine, 1% (b.i.d.-t.i.d.) or homatropine, 5% (q.4h)
  - Prednisolone, 1% (q.2-4h)
  - Oral aspirin or ibuprofen, 2 tablets (q.3-4h)
  - Consider beta blockers if IOP is elevated
  - Sunglasses
  - Advise patient carefully
  - Re-evaluate 1-2 days

- **Additional considerations/reminders**
  - Shake steroid suspensions well before using.
  - May use dexamethasone or fluorometholone steroid ointments at bedtime.
  - Aspirin is contraindicated in the presence of concurrent hyphema.
  - Avoid prostaglandins

35

Follow up

- **Follow Up Exams**
  - Between 1-7 days, depending on severity
  - VA, IOP, slit lamp, A/C exam
  - DFE is needed if not completed initially or if clinical appearance is worsening

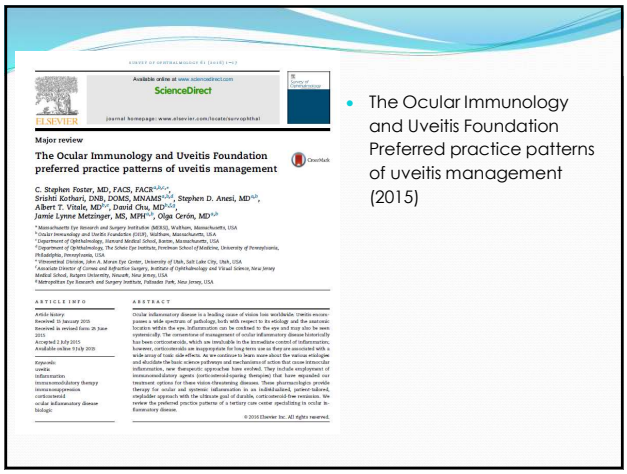
- **Medications and Tapering**
  - Cycloplegic agents can be discontinued when symptoms are improving and flare is absent.
  - Continue steroid dosing until cells are minimal or absent.
    - Taper regimen varies
    - Example if the patient is using steroids qid for 1 week, then taper should be weekly (tid x 1 week, bid x 1 week, qd x 1 week, then stop).

36

Clinical Degree of Anterior Uveitis *,*

Mild	Moderate	Severe
Mild to moderate symptoms	Moderate to severe symptoms	Moderate to severe symptoms
VA 20/20 to 20/30	VA from 20/30 to 20/100	VA ≤20/100
Superficial circumcorneal flush	Deep circumcorneal flush	Deep circumcorneal flush
No KPs	Scattered KPs	Dense KPs
Trace to 1+ cells and flare	1-3+ cells and flare Miotic, sluggish pupil Mild posterior synechiae Mild iris swelling	3-4+ cells and flare Sluggish or fixed pupil Posterior synechiae (fibrous) Boggy iris (no crypts)
IOP reduced < 4 mmHg	IOP reduced 3-6 mm Hg	Raised IOP
	Anterior virtreous cells	Moderate to heavy anterior cells

37



Major review

The Ocular Immunology and Uveitis Foundation preferred practice patterns of uveitis management

- The Ocular Immunology and Uveitis Foundation Preferred practice patterns of uveitis management (2015)

38

"The cornerstone of medical therapy should ***include corticosteroids, as well as topical cycloplegics and mydriatics*** *when appropriate. To achieve durable corticosteroid-free remission or cure of the disease, a long-term stepladder approach is used, involving initiation of aggressive therapy for the specific disease process and severity, and advancement up the ladder to other modalities as needed"*

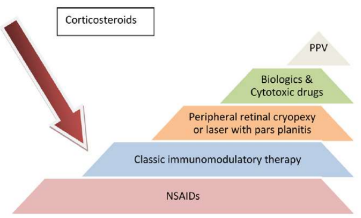


Fig. 1 – The stepladder approach. PPV, pars plana vitrectomy; NSAIDs, nonsteroidal anti-inflammatory drugs.

39

Mydriatic and Cycloplegic Agents

- Beneficial for breaking or preventing the formation of posterior synechiae and for relieving photophobia and pain secondary to ciliary spasm.

40

Corticosteroids

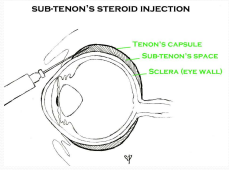
- **The mainstay of uveitis therapy**
  - Should be used in the acute management of active uveitis, not as a long-term therapy strategy.
- **Dose and duration**
  - Tailored to the patient
  - Start therapy with a high dose of corticosteroids and taper according to the clinical response rather than starting at a lower dose and escalating therapy.

41

Corticosteroids

- **Topical**
  - Effective primarily for anterior uveitis
  - May have beneficial effects on vitritis. or macular edema in patients who are pseudophakic, aphakic, or post vitrectomy.

- **Periocular**
  - Intermediate or posterior uveitis, or for those with cystoid macular edema.
  - Administered as a depot injection
    - Transseptal (orbital floor) route
    - Sub-Tenon approach directed into the superotemporal or inferotemporal quadrant.



42

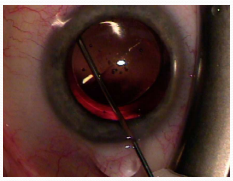
Corticosteroids

- **Periocular**
  - Indications
    - A more posterior effect is needed
    - Patient is non compliant or poor responsive to topical or systemic treatment.
  - Complications
    - Periorbital hemorrhage, globe perforation, orbital fat prolapse, and blepharoptosis.
  - Contraindications
    - Patients with necrotizing scleritis
    - Established steroid responders

43

Corticosteroids

- **Intravitreal**
  - Indications
    - Acute inflammation recalcitrant to periocular injections
    - A bridge to corticosteroid-sparing systemic IMT.
  - Complications
    - Greater risk of developing cataract or secondary glaucoma.
    - Sterile endophthalmitis, or "pseudoendophthalmitis" from crystallization, may occur in up to 1% of patients and requires extensive anti-inflammatory therapy.



44

Corticosteroids

- **Sustained release devices: Corticosteroid implants**
  - Administered by intravitreal injection or by surgical fixation to sclera through a pars plana approach
  - Indications
    - Patients with severe or recalcitrant unilateral or bilateral noninfectious uveitis
    - Patients who have failed or are intolerant of systemic corticosteroids or IMT.
  - Complications
    - Greater risk of developing cataract or secondary glaucoma.
  - They are not viewed as first-line therapy options, though their utilization may be individualized per patient preference.

45

46

Nonsteroidal Anti-inflammatory Drugs (NSAIDS)

- **Mechanism of Action**
  - Inhibiting cyclooxygenase (isoforms 1 and 2 or 2 alone), and reduce the synthesis of prostaglandins that mediate inflammation
  - Indications
    - Postoperative inflammation
    - CME, including CME which persists after the uveitis has resolved
  - Side effects
    - Gastric ulceration, gastrointestinal bleeding, hypertension, nephrotoxicity, and hepatoxicity

47

Other Systemic Treatments

- **Immunomodulatory therapy**
  - Antimetabolites
  - Inhibitors of T-lymphocytes signaling modifiers

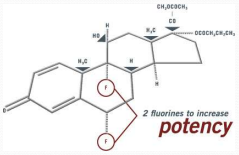
48

Durezol vs Other Steroids

49

Durezol

- **History**
  - The first topical steroid developed in 1973 for the treatment of ocular inflammation
  - A difluorinated derivative of prednisolone
    - Increases the penetrance across the cornea
    - Increases glucocorticoid receptor affinity, which enhances its anti-inflammatory ability. [12]
- **Labeled Indication**
  - Treatment of postoperative inflammation
  - Recommended dosing regimen is one drop, two to four times daily throughout the first two weeks post-op, followed by two times daily for a week with tapering thereafter. [13]



50

Better than other topical steroids?

- **Postoperative inflammation**
  - Durezol has been shown to be clinically comparable to the very potent agent betamethasone, with an equal likelihood of a steroid response.
  - Due to its enhanced bioavailability and clinical potency, Durezol tends to need less frequent dosing than other topical steroids.[14]

ARVO Annual Meeting Abstract | May 2007

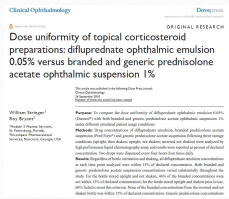
Efficacy and Safety Results of a Phase III Study of Difluprednate Ophthalmic Emulsion(DFBA), 0.05% in Postoperative Inflammation

M. Ohji, Y. Tano, T. Hida, T. Sekiya, T. Ogawa, DFBA Study Group

51

Increased Bioavailability of Durezol

- Lipid emulsion has a smaller particle size
- Provides uniform medication concentration
- Eliminates the need for shaking before use
- **Dose uniformity of topical corticosteroid preparations by Stringer et al (2010)** [15]
  - Study of dose-drop uniformity
  - Durezol vs both the branded and generic versions of prednisolone acetate 1%
  - Results: Durezol was within 10% of the label claim, regardless of whether the bottle was stored inverted or upright, or shaken before testing.[5]
  - Concentrations of prednisolone acetate varied by bottle storage and shaking.


Clinical Ophthalmology

ORIGINAL RESEARCH

Dose uniformity of topical corticosteroid preparations: difluprednate ophthalmic emulsion 0.05% versus branded and generic prednisolone acetate ophthalmic suspension 1%

52

Treating Anterior Uveitis

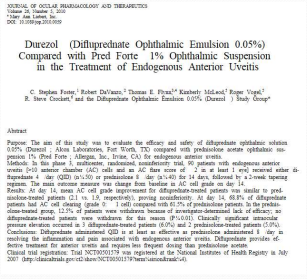
- **Phase III non-inferiority study of difluprednate ophthalmic emulsion (DFBA), 0.05% in the treatment of anterior uveitis**
  Ohno et al (2007) [16]

- Large anterior uveitis trial of 136 patients
- Difluprednate q.i.d. was found to be similar to betamethasone q.i.d., and was significantly better at clearing inflammation in patients with more severe inflammation.
- The incidence of steroid-related elevation in intraocular pressure is approximately 3%, which is similar to that of other topical steroids.

53

Treating Anterior Uveitis

- **Durezol® (Difluprednate Ophthalmic Emulsion 0.05%) Compared with Pred Forte® 1% Ophthalmic Suspension in the Treatment of Anterior Uveitis**
  Foster et al (2010) [17]


JOURNAL OF OCULAR PHARMACOLOGY AND THERAPEUTICS

Durezol (Difluprednate Ophthalmic Emulsion 0.05%) Compared with Pred Forte 1% Ophthalmic Suspension in the Treatment of Endogenous Anterior Uveitis

Abstract

- 90 patients
- Difluprednate q.i.d. was as effective as prednisolone acetate eight times/day
- No patient who was treated with difluprednate q.i.d. had to be withdrawn due to lack of efficacy and given rescue therapy (prednisolone acetate 16 times/day)
- 12.5% of the patients being treated with prednisolone eight times/day had to be withdrawn and were given the double-dosing rescue therapy.

54

Cost Considerations

Durezol

Winn-Dixie		$180.06 with free coupon
Costco	$217 est cash price	$180.06 with free coupon
Walmart	$207 est cash price	$183.35 with free discount
Kroger Pharmacy	$200 est cash price	$185.04 with free coupon
Safeway	$241 est cash price	$185.67 with free coupon
Kmart		$186.74 with free coupon
CVS Pharmacy	$214 est cash price	$190.03 with free coupon
Target (CVS)	$214 est cash price	$190.03 with free coupon

Generic Prednisolone acetate 1%

Walmart	$41 est cash price	$22.17 with free discount
Walgreens	$60 est cash price	$25.90 with free coupon
CVS Pharmacy	$53 est cash price	$27.67 with free coupon
Target (CVS)	$53 est cash price	$27.67 with free coupon
Costco		$35.94 estimated cash
Kroger Pharmacy	$48 est cash price	$41.04 with free coupon
Kmart		$42.02 with free coupon
Safeway	$55 est cash price	$42.47 with free coupon

55

Cost Considerations

Durezol

Winn-Dixie		$180.06 with free coupon
Costco	$217 est cash price	$180.06 with free coupon
Walmart	$207 est cash price	$183.35 with free discount
Kroger Pharmacy	$200 est cash price	$185.04 with free coupon
Safeway	$241 est cash price	$185.67 with free coupon
Kmart		$186.74 with free coupon
CVS Pharmacy	$214 est cash price	$190.03 with free coupon
Target (CVS)	$214 est cash price	$190.03 with free coupon

Brand Predforte Suspension 1%

Winn-Dixie		$146.27 with free coupon
Costco		$146.27 with free coupon
Walmart		$147.63 with free discount
Kroger Pharmacy		$149.46 with free coupon
Safeway		$150.97 with free coupon
Kmart		$151.63 with free coupon
CVS Pharmacy	$175 est cash price	$153.29 with free coupon
Target (CVS)		$153.29 with free coupon

56

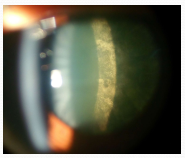
Cost Considerations VA Pharmacy

MEDICATION	DRUG MESSAGE	SUPPLIED	COST
Ophthalmic Corticosteroids			
DIFLUPREDNATE 0.05% OPH EMULSION	CONSULT REC EXC OPTH & OPTOMETRY	5ML	$ 13.56
PREDNISOLONE ACETATE 1% OPH SUSP		5ML	$ 13.75
DEXAMETHASONE NA PHOSPHATE 0.1% OPH SOLN		5ML	$ 22.71
FLUOROMETHOLONE 0.1% OPH SUSP		5ML	$ 38.27
FLUOROMETHOLONE 0.1% OPH OINT	2ND LINE; FLUOROMETHOLONE 0.1% OPH SUSP PREF	3.5GM	$ 67.63
NSAID			
DICLOFENAC NA 0.1% OPH SOLN	**PREFERRED AGENT**	5ML	$ 1.81
KETOROLAC TROMETHAMINE 0.5% OPH SOLN	CONSULT REQ EXC EYE CLINIC;2ND LINE TO DICLOFENAC	5ML	$ 2.75
KETOROLAC TROMETHAMINE 0.4% OPH SOLN	CONSULT REQ EXC EYE CLINIC;2ND LINE TO DICLOFENAC - **USE 0.5%**	5ML	**$ 20.60**

57

Ocular Complications

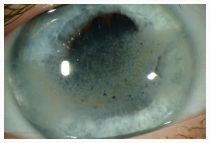
- **Cataract development**
  - Chronic inflammation
  - Prolonged topical steroid use
- **Secondary Glaucoma**
  - Inflammatory cells blocking aqueous outflow
  - Pupillary block from posterior synechia
  - Angle closure from peripheral anterior synechia
  - Elevated IOP from topical steroid use
  - Neovascular glaucoma from rubeosis

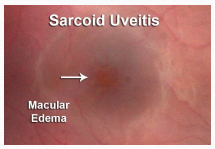


58

Ocular Complications

- Phthisis bulbi
- Hypotony
- Band keratopathy
- Cataracts
- Glaucoma
- Macular edema
- Retinopathy
- Retinal detachments
- **Intermediate uveitis, posterior uveitis, and panuveitis are responsible for most visually threatening conditions.**





59

Conclusions

- Anterior uveitis is defined as intraocular inflammation of the uveal structures anterior to the vitreous cavity.
- In non-traumatic etiologies, 80-90% are associated with a systemic non-infectious or infectious disorder, making accurate diagnosis and treatment critical.
- Laboratory work up is indicated for recurrent episodes of unilateral, non-granulomatous uveitis, bilateral uveitis, posterior uveitis or granulomatous uveitis with no prior diagnosis of systemic disease.
- The cornerstone of medical therapy should include corticosteroids and topical cycloplegics/mydriatics.
- Difluprednate has been shown in some studies to be as effective as prednisolone acetate with better patient compliance and less dosing required to achieve the same results.
- Serious ocular complications including cataract development, secondary glaucoma, corneal edema, macular edema can occur without appropriate and prompt treatment.

60

Apply What You've Learned

- **Three cases**
- **Participation encouraged**

61

Case 1

62

M.A. 35 year old Caucasian Male

- **CC:** Sudden onset of redness, pain (5/10), irritation, and tearing OD
  - Symptoms started 3 days ago
  - Worsening with light sensitivity today
  - Mild blur in distance vision
  - No symptoms OS

63

Ocular and Medical History

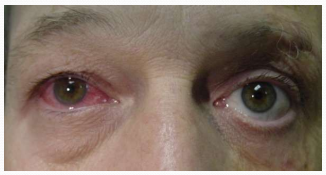
- **Ocular History**
  - Refractive error OU
    - Daily disposable CL wear
    - Reports compliance with replacement schedule
  - Patient reports having a "red eye" OS a few years ago and was treated with drops for a few weeks.
  - History of blunt trauma right eye 10 years ago
- **Medical history**
  - Unremarkable to the patient's knowledge
  - No history of diabetes, hypertension, high cholesterol, or arthritis.

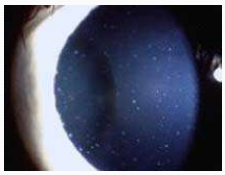
64

Clinical Exam

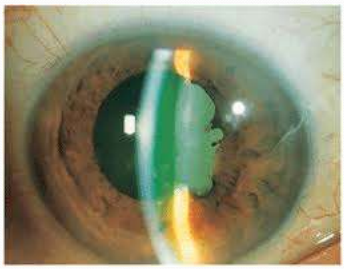
- **BCVA cc:** OD 20/25, OS 20/20
- **Confrontation fields:** FTFC all 4 quads OD & OS
- **EOMs:** full movement in all fields of gaze OD & OS
- **Pupils:** Round and reactive, - APD OU
- **Anterior segment :**
  OD: 2+ diffuse injection of conjunctiva, chemosis, 1+cell and flare
  OS: normal
- **Intraocular pressures:** OD 11, OS 16 mm Hg

65





66



67

Clinical Exam

- **Lens:** OD: posterior synechiae temporal, OU: 1+ NS
- **Vitreous:** syneresis, -pigment, -cell OU
- **Optic Nerve:** pink, healthy rims, distinct margins OU
- **C/D:** 0.35/0.30
- **Vessels:** normal OU
- **Posterior Pole:** normal OU
- **Peripheral Retina:** flat and intact OU

68

Narrowing Down Differentials

- **Site of inflammation?**
- **Granulomatous or Non-granulomatous?**
- **Pertinent systemic disease?**
  - Recent infections?
  - Fever, malaise, cold sores, shingles, or other skin rash?
- **Laterality?**
- **Past episodes?**

69

Differential Diagnoses?

70

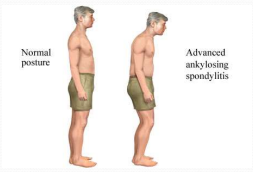
Additional information or testing?

- **Labs**
  - RPR or VDRL: non reactive
  - FTA-ABS or MHA-TP: non reactive
  - Rheumatoid factor: negative
  - ACE: normal
  - PPD Skin Test: normal
  - ANA: normal
  - Rheumatoid factor: normal
  - HIV: negative
  - CBC: normal
  - HLA-B27: positive
- **Associated systemic symptoms?**
  - Back pain for 4 months with stiffness, unable to bend at night and early morning
  - Pain improves with exercise

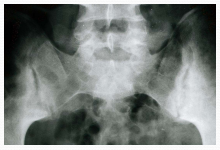
71

Additional information or testing?

- **Referral to Rheumatology**
  - Pain and tenderness along the back, hips, and sacroiliac joints.
  - Limitation of spinal mobility in all directions.



- **X-Rays**
  - Chest: normal/clear
  - Sacroiliac joint: thinning of the sacroiliac joint and/or fusion of several joints.



72

Final Diagnosis

- **Acute non-granulomatous anterior uveitis OD 2' ankylosing spondylitis**
  - +HLA B27
  - +Sacroiliac joint X-Ray findings
  - Unilateral and alternating (prior history left eye)

73

Treatment and Follow up Plan

- **Rx: Cyclogyl tid OD**
- **Rx: Predforte 1 % q2hr OD**
  - Shake bottle well prior to instillation
  - 0 refills
- **Refer to rheumatology for treatment/management of AS**
  - Systemic steroids, NSAIDS, immunomodulators.
  - Physical therapy
- **Next follow up?**

74

Case 2

75

B.L. 62 year old Latino Male

- **CC:** Red painful left eye for 1 week
  - Severe pain, 8/10 level
  - Started acutely 1 week ago with worsening symptoms
  - Accompanying symptoms: photophobia, tearing, blurred vision

76

Ocular and Medical History

- **Ocular History**
  - Last eye exam 1 year ago
  - Refractive error OU
  - Incipient cataracts OU
- **Medical history**
  - Diabetes Type 2, -insulin
    - Last A1c: 6.2%
  - Hypertension
    - Blood pressure: 118/74 mmHg, right arm, seated
    - Pulse: 78 bpm
  - High Cholesterol

77

Clinical Exam

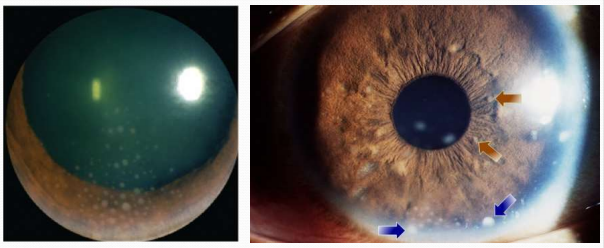
- **BCVA cc:** OD 20/20, OS 20/30
- **Confrontation fields:**
  OD: full in all quadrants
  OS: full in all quadrants
- **Pupils:**
  OD: 4mm dark/3mm light, rrl , -RAPD
  OS: 4mm dark/4mm light, slow to constrict to light, near reflex intact, -RAPD
- **EOMs:**
  OD: full movement in all fields of gaze
  OS: full movement in all fields of gaze

78

Clinical Exam

- **Slit lamp**
  - **Lids/lashes/adnexa**
    - OD/OS: unremarkable
  - **Conjunctiva**
    - OD normal
    - OS 2+ injection bulbar conj with circumlimbal flush
  - **Cornea**
    - OD clear
    - OS scattered large granulomatous KPs
  - **Anterior chamber**
    - OD deep and quiet
    - OS 2+ cells, 1+ flare
  - **Iris**
    - OD normal
    - OS nodular lesions near the pupillary border

79



80

Clinical Exam

- **Intraocular pressures:** OD 11, OS 10 mm Hg
- **Lens:** 1+ NS OU
- **Vitreous:** syneresis, -pigment, -cell OU
- **Optic Nerve:** pink, healthy rims, distinct margins OU
- **C/D:** 0.20/0.20
- **Vessels:** normal OU
- **Posterior Pole:** normal OU
- **Peripheral Retina:** flat and intact OU

81

Narrowing Down Differentials

- **Site of inflammation?**
- **Granulomatous or Non-granulomatous?**
- **Pertinent systemic disease?**
  - Recent infections?
  - Fever, malaise, cold sores, shingles, or other skin rash?
- **Laterality?**
- **Past episodes?**

82

Differential Diagnoses?

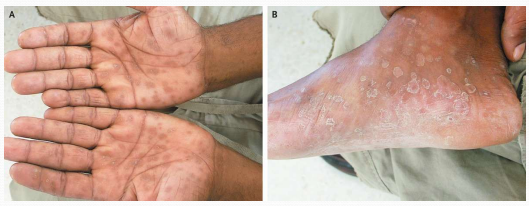
83

Additional information or testing?

- **Labs**
  - RPR: reactive
  - FTA-ABS: reactive
  - Rheumatoid factor: negative
  - ACE: normal
  - PPD Skin Test: normal
  - ANA: normal
  - Rheumatoid factor: normal
  - HIV: negative
  - CBC: normal
  - HLA-B27: negative
- **Associated systemic symptoms?**
  - Swollen lymph nodes
  - Fever,malaise, sore throat for the past week
  - Skin rash on palms and soles

84

Additional information or testing?



85

Final Diagnosis

- **Acute granulomatous anterior uveitis OS 2' syphilis infection**
  - +RPR, +FTA-ABS and associated systemic signs

86

Treatment and Follow up Plan

- **Rx: Homatropine 5% tid OS**
- **Rx: Predforte 1 % q2hr OS**
  - Shake bottle well prior to instillation
  - 0 refills
- **Refer to PCP or infectious disease for treatment/management of syphilis infection**
  - Penicillin G 2.4 million units intramuscularly (IM) in a single dose
  - Oral doxycycline, oral erythromycin, or IM ceftriaxone sodium
- **Next follow up?**

87

Case 3

88

J.D. 55 year old Caucasian Male

- **CC: Eye redness, pain and hazy vision OS x 5 days**
  - Pain of 6/10 OS
  - Gradual onset, worsening
  - Accompanying symptoms: light sensitivity
  - Patient reports this has happened three times in the same eye with "high eye pressure"

89

Ocular and Medical History

- **Ocular History**
  - Last eye exam 6 months ago, no prior records
  - History of laser surgery in the left eye
  - Early cataracts both eyes
- **Medical history**
  - Hypertension
  - High Cholesterol
  - Asthma

90

Clinical Exam

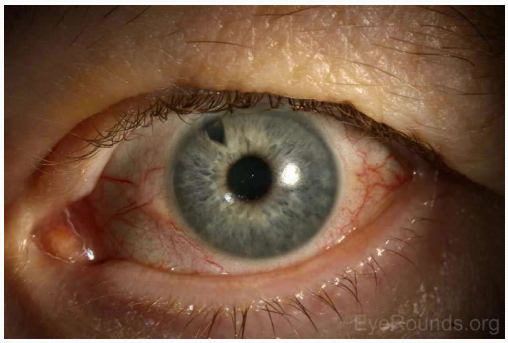
- **BCVA cc:** OD 20/20, OS 20/40-2 PH NI
- **Confrontation fields:**
  OD: full in all quadrants
  OS: full in all quadrants
- **Pupils:**
  OD: 3mm dark/2mm light, rrl , -RAPD
  OS: 4mm dark/4mm light, fixed pupil, -RAPD by reverse
- **EOMs:**
  OD: full movement in all fields of gaze
  OS: full movement in all fields of gaze

91

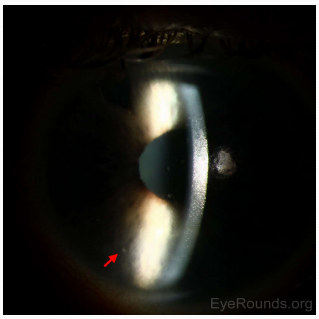
Clinical Exam

- **Slit lamp**
  - **Lids/lashes/adnexa**
    - OD/OS: unremarkable
  - **Conjunctiva**
    - OD nasal pinguecula
    - OS diffuse 1+ injection, nasal pinguecula
  - **Cornea**
    - OD clear
    - OS diffuse microcystic edema, cluster of small keratic precipitates (KP) inferonasally
  - **Anterior chamber**
    - OD deep and quiet
    - OS few cells (2-3 cells seen/view), no flare
  - **Iris**
    - OD blue iris, few flat nevi
    - OS blue iris, patent PI sup/nasal, mild irregularity of the pupil

92



93



94

Clinical Exam

- **Intraocular pressures:** OD 12, OS 42 mm Hg
- **Gonioscopy (4 mirror):** OU CBB all 4 quads, 1+ TM pigment, +PAS temporal OS
- **Lens:** OD: 1+ NS, OS: 1+ NS, PS at 11:00, mild pigment on the anterior capsule
- **Vitreous:** syneresis, -pigment, -cell OU
- **Optic Nerve:** pink, healthy rims, distinct margins OU
- **C/D:** 0.30/0.40
- **Vessels:** normal OU
- **Posterior Pole:** normal OU
- **Peripheral Retina:** flat and intact OU

95

Narrowing Down Differentials

- **Site of inflammation?**
- **Granulomatous or Non-granulomatous?**
- **Pertinent systemic disease?**
  - Recent infections?
  - Fever, malaise, cold sores, shingles, or other skin rash?
- **Laterality?**
- **Past episodes?**

96

Differential Diagnoses?

97

Additional information or testing?

- **Labs**
  - RPR: negative
  - FTA-ABS: negative
  - Rheumatoid factor: negative
  - ACE: normal
  - PPD Skin Test: normal
  - ANA: normal
  - Rheumatoid factor: normal
  - HIV: negative
  - CBC: normal
  - HLA-B27: negative
- **Associated systemic symptoms?**
  - negative

98

Final Diagnosis

- **Anterior uveitis OS 2' Posner-Schlossman Syndrome**
  - Anterior uveitis with high IOP
    - No signs of HSV or HZV
    - Lab work up normal
    - History of recurrent episodes
    - No iris heterochromia, iris transillumination defects, stellate KP, or iris/angle neovascularization

99

Treatment and Follow up Plan

- **Administer IOP lowering drops in office**
  - **Which class?**
- **Rx: Predforte 1 % qid OS**
  - Shake bottle well prior to instillation
  - 0 refills
- **Rx: Which IOP lowering medication?**
- **Next follow up?**

100

References

1. Weinberg RS. Anterior uveitis. Ophthalmol Clin North Am 1993; 6(1):23-8.

2. Schlaegel TF. Essentials of uveitis. Boston: Little, Brown & Co.,1969.

3. Rothova A, van Veenendaal W, Linssen A, et al. Clinical features of acute anterior uveitis. Am J Ophthalmol 1987; 103(2):137-45.

4. Schlaegel TF, O'Connor GR. Current aspects of uveitis: general considerations. Int Ophthalmol Clin 1977; 17(3):1-42.

5. Darrell RW, Wagener HP, Kurland LT. Epidemiology of uveitis. Incidence and prevalence in a small urban community. Arch Ophthalmol. 1962;68:502e14

6. Goldstein H. The reported demography and causes of blindness throughout the world. Adv Ophthalmol. 1980;40:1e99

7. Gritz DC, Wong IG. Incidence and prevalence of uveitis in Northern California; the Northern California Epidemiology of Uveitis Study. Ophthalmology. 2004;111:491e500, discussion 500.

8. Schlaegel TF, O'Connor GR. Current aspects of uveitis: general considerations. Int Ophthalmol Clin 1977; 17(3):1-42.

9. Heiden D, Nozik RA. A systematic approach to uveitis diagnosis.Ophthalmol Clin North Am 1993; 6(1):13-22.

10. Winterkorn JM. Lyme disease: neurologic and ophthalmic manifestations. Surv Ophthalmol 1990; 35(3):191-204.

101

References

11. Jabs DA, Nussenblatt RB, Rosenbaum JT. Standardization of Uveitis Nomenclature (SUN) Working Group. Standardization of uveitis nomenclature for reporting clinical data. Results of the First International Workshop. Am J Ophthalmol.2005;140:509e16

12. Bikowski J, Pillai R, Shroot B. The position not the presence of the halogen in corticosteroids influences potency and side effects. J Drugs Dermatol. 2006 Feb;5(2):125-30.

13. Korenfeld MS, Silverstein SM, Cooke DL, et al. Difluprednate ophthalmic emulsion 0.05% for postoperative inflammation and pain. J Cataract Refract Surg. 2009 Jan;35(1):26-34.

14. Ohji M. Efficacy and safety results of a phase III study of difluprednate ophthalmic emulsion (DFBA), 0.05%, in postoperative inflammation. Presented at ARVO Annual Meeting, May 6-10, 2007; Ft Lauderdale, Fla.: poster B807, program 3903.

15. Stringer W, Bryant R. Dose uniformity of topical corticosteroid preparations: difluprednate ophthalmic emulsion 0.05% versus branded and generic prednisolone acetate ophthalmic suspension 1%. Clin Ophthalmol. 2010 Oct 5;4:1119-24.

16. Ohno S. Phase III non-inferiority study of difluprednate ophthalmic emulsion (DFBA), 0.05% in the treatment of anterior uveitis. Presented at ARVO Annual Meeting, May 6-10, 2007; Ft Lauderdale, Fla.: poster B808, program 3904.

17. Foster CS, Davanzo R, Flynn TE, et al. Durezol (Difluprednate Ophthalmic Emulsion 0.05%) compared with Pred Forte 1% ophthalmic suspension in the treatment of endogenous anterior uveitis. J Ocul Pharmacol Ther. 2010 Oct;26(5):475-83.

102