

Update on Central Serous Chorioretinopathy

Steve Bennett
Retina Update 2017



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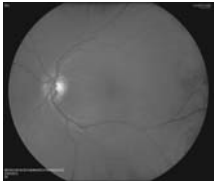
No financial interest

Off label use of Spironolactone, Eplerenone,
Melatonin, Verteporfin, Rifampin

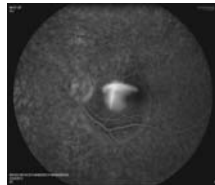


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Classic Central Serous



Young
Anxious
Male

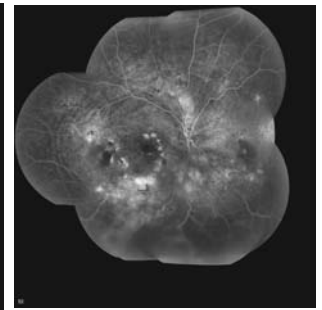
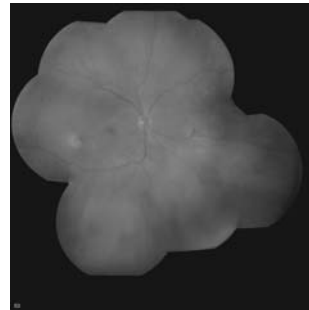


“Smokestack”

Spontaneous
Recovery



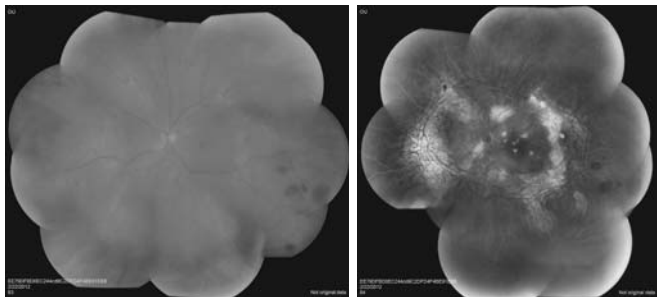
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55 Year Old Woman 20/150 OD
Inferior Exudative Retinal Detachment



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11 Year Course of Repeated Episodes in Spite of
Multiple Therapies
Severe Permanent Vision Loss in Right Eye



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Central Serous Chorioretinopathy

Common Condition
Affects Adults of All Ages
Men and Women
Potentially Severe
Treatable

Valuable Insights
into Ocular Function



The Most Important Part is Under the Surface



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Choroid

Bruch's membrane

Pigment epithelium

Smaller choroidal vessels (choriocapillaris)

Suprachoroid

Larger choroidal vessels

Sclera

Smaller vessels:
Sattler's Layer
(Choriocapillaris)

Larger vessels:
Haller's Layer

Rapid Circulation
Leaky Vessels
Steroid Receptors

Functions to Bring Oxygen
Carry Away Waste
Dissipate Heat

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Can Now Image Choroid Easily

Enhanced Depth Imaging "EDI" OCT
Swept Source OCT

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What is Normal?

Appearance of Choroid Varies with Age, Refractive Error

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Normal Choroidal Thickness Decreases with Myopia

- 10 Myope

- 3 Myope

+5 Hyperope

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Choroidal Thickness Decreases with Age

89 y.o.

28 y.o.

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Temporal Choroid is Thicker than Nasal

31 year old

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Variation in Choroidal Thickness

Decreases with:

High Myopia

Emmetropia: 316, High Myopia: 97

Age

Young Adult: 320, Older than 70: 160

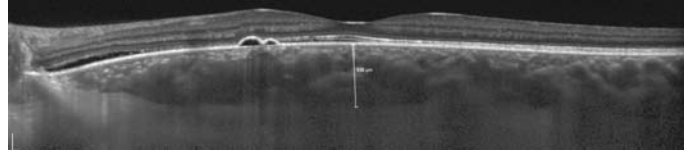


Coscas GJ, ARVO, 2011
Retinal Update 2017

Toyokawa, N, Ophthalmol. Surg. Laser, 2012

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Increased Choroidal Thickness in Central Serous



538 microns

Primarily Haller's Layer



Retinal Update 2015

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Risk Factors for CSC

Steroid use, particularly glucocorticoids, Cushing's Disease

"Stress", type A personality, psychopharmacological medications

Irregular sleep cycle or sleep apnea

Normal menstrual cycles seem protective

Women usually post menopausal or pregnant

Testosterone use is a risk factor



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Steroids and the Eye

The choroid has glucocorticoid and mineralocorticoid receptors, as well as the enzyme 11-beta hydroxysteroid dehydrogenase type 2.

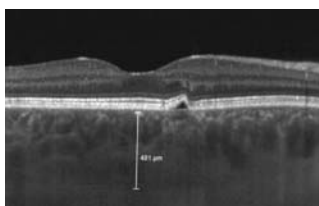
The RPE and choroid have high levels of CYP450 enzymes that metabolize steroid hormones.

High dose corticosteroid or aldosterone induces choroidal vessel dilation and leakage in experimental animals.

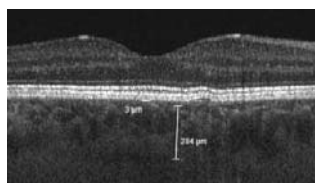


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High dose prednisone
(60 mg/day)
481 microns



5 months
Off Steroids
284 microns

33 Year Old Woman with Inflammatory Kidney Disease



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Steroids and Central Serous

Corticosteroids induce choroidal thickening.

Corticosteroids can cause Central Serous.

Steroid blocking agents might be used as treatment.



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Many Cases are Mild and Resolve Spontaneously

Often no treatment is indicated.

First acute episode of central serous in a young patient of less than 3 months duration: usually observe without treatment.



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Consider Treatment

Severe vision loss

Occupational need for excellent binocular vision

Chronic sub-retinal fluid (3-6 months)

Repeated episodes

Older patient



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Risk Factors for Prolonged Sub-retinal Fluid

Sub-foveal choroidal thickness greater than 500 microns

PED higher than 50 microns at leakage site

Age greater than forty

Daruich et.al. Retina 2017



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Multiple Treatment Options



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Thermal Laser

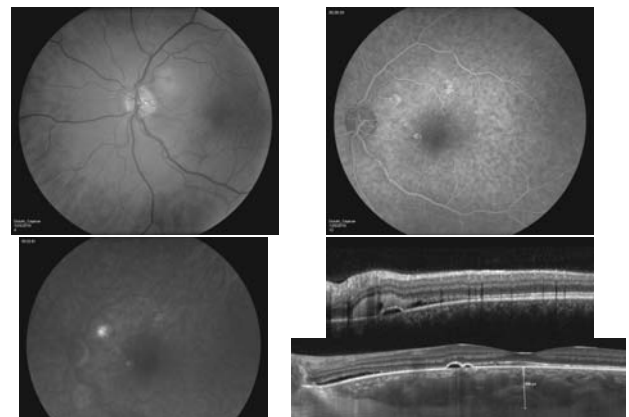
Focal leak away from foveal center

Fluid extends into the center

Very light treatment directly to leak

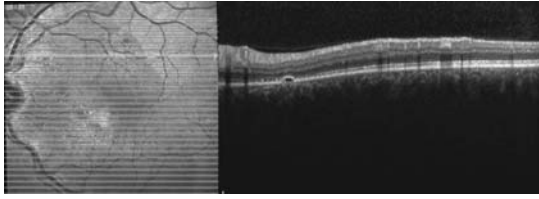


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45 y.o. Heavy Equipment Operator

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One Month After Laser

Corticosteroid Antagonists

Small case series have reported benefit in using several antagonists to corticosteroids.

Ketoconazole, mifepristone, finasteride, rifampin.

Rifampin is CYP450 inducer, increases metabolism of steroid hormones.

I have seen benefit from rifampin in several patients, but concern over side effects of long term use limit appeal.

Spirolactone

Non-selective antagonist to aldosterone.

Some cross antagonism to glucocorticoid, androgen and progesterone receptors.

Must monitor renal function and potassium levels.

Hormonal side effects: gynecomastia, decreased libido, menstrual irregularity. Must not be used in pregnancy.

Used off label for treatment of acne in women.

Side effects uncommon at low doses.

Spirolactone

Dosage range 25 mg to 200 mg/day, typically use 25 mg/day for CSC.

Low cost.

Work with primary care doctor, particularly in the elderly.

Trimethoprim/sulfamethoxazole, ACE inhibitors, and NSAIDs may increase the effect on potassium levels.

Eplerenone

Selective inhibitor of aldosterone. Less effect on other hormones than spironolactone.

Less strong, fewer hormonal side effects.

Typical dose 50 mg/day.

Metabolized by P4503A4 system, and effect may be increased by inhibitor drugs (amifostine, cyclosporine, fluconazole, itraconazole, ketoconazole, mifepristone, clarithromycin, tacrolimus, bactrim, voriconazole).

Randomized Controlled Study (Crossover) Of Spirolactone for Central Serous

16 patients randomized to spironolactone 50/mg day or placebo, treated for one month, and switched.

Statistically significant reduction in sub-retinal fluid and choroidal thickness.

Bousquet, E. et al. Retina 2015

Pooled Data (282 Eyes) of Eyes Treated with Aldosterone Antagonists

71% of treated eyes showed some objective improvement.

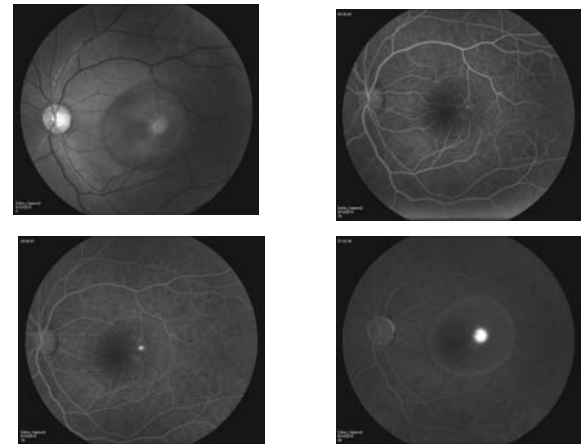
46.5% complete resolution of sub-retinal fluid.

Side effects in 8% eplerenone and 22% spironolactone (gynecomastia and elevated potassium each in about 1% of patients).

Rahimy,E et. al. Retinal Physician, 2016

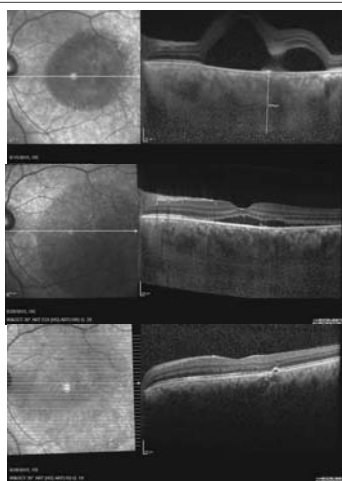


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37 y.o. man 20/200

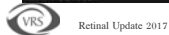
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Initial OCT

2 weeks Spironolactone

6 weeks Spironolactone



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Melatonin for Chronic Central Serous

13 patients with chronic CSC, 8 randomized to 3mg TID, 5 to placebo for one month.

87% of treated patients improved, 37% complete resolution of sub-retinal fluid.

No changes in control group.

Gramajo,A, Eye, 2015



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Melatonin for Central Serous

Daytime sleepiness can be a problem at dose used in study.

Response more limited.

I do try, and will continue 3mg at bedtime, particularly if history of sleep problems or shift work.

No FDA oversight of supplements.



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Verteporfin PDT for Central Serous

Affects choroid and causes choroidal thinning

Can treat larger areas with little risk of vision loss

Has shown effectiveness in many series

One time treatment



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Verteporfin PDT for Central Serous: Newer Protocols

- Halved dose of drug
- Halved fluence (laser intensity)
- Halved time of light exposure
- All reported good improvement rates with low side effect rate in short term follow up



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Verteporfin PDT for Central Serous: Problems

- Cost of drug: over \$2000 per dose.
- Insurance coverage for non-FDA approved use.
- Concern of long term RPE or choriocapillaris atrophy.
- Low risk of severe vision loss at time of treatment seen in AMD treatment. Lack of large prospective studies at any of the dosage regimens.



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My Treatment Protocol for CSC

- Observe first episode for 3 months unless severe or occupational needs for bilateral vision
- Avoid corticosteroids: Oral, nasal sprays, joint injections, skin ointments
- Consider Cushing's Disease
- Treat sleep problems: Shift work, sleep apnea
- Consider Melatonin: 3 mg at bedtime



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My Treatment Protocol for CSC

- Focal leak away from fovea: Thermal laser.
- Diffuse leak under fovea, good health and normal renal function: Consider mineralocorticoid antagonist such as spironolactone 25 mg/day.
- Poor candidates or failures of Spironolactone: Offer PDT.



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Spectrum of Related Diseases: Thick Choroid

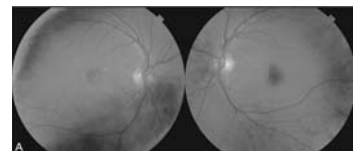
- Central Serous Chorioretinopathy
- Pachychoroid Pigment Epitheliopathy
- Pachychoroidal Neovascularopathy
- Polypoidal Choroidal Vasculopathy

Warrow et. al. Retina 2013

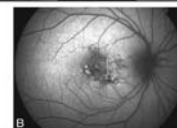


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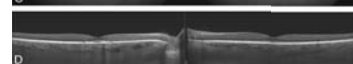
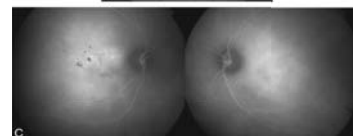
Pachychoroid
Pigment
Epitheliopathy



Often
Asymptomatic



Warrow et al
Retina 2013



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Pachychoroidal Neovascularopathy

Older patient

Neovascularization under the RPE occurring over areas of choroidal thickening

Lack of drusen

Reduced fundus tessellation

“Double Layer Sign” of RPE consistent with type 1 choroidal neovascularization

Pang and Freund, Retina 2015



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Pachychoroidal Neovascularopathy

Common

Difficult to differentiate from exudative AMD

Less responsive to typical anti-VEGF therapy

May respond to combination therapy or PDT



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Few Drusen
RPE changes
Reduced Tessellation

74 y.o. man
20/50 OS
1 month blurring and distortion

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Initial OCT

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Diagnosis: Pachychoroidal Neovascularopathy

Treated with one dose of anti-VEGF

Spironolactone 25 mg/day after checking electrolytes

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1 month 20/20, dry

No further Anti-VEGF
Continued spironolactone
6 months still dry

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Summary

Central Serous Chorioretinopathy often resolves without treatment, but can be severe, prolonged, and vision threatening.

Multiple treatments are available, including oral medications. Mineralocorticoid blocking agents appear promising.



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Summary

Older patients with thickened choroid may develop choroidal neovascularization. These patients may be part of a spectrum of disease that includes Central Serous Chorioretinopathy.



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