# Clinical, experimental, and genetic studies on the etiology of central serous chorioretinopathy

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| **Ethical review** | Approved WMO |
| **Status** | Recruiting |
| **Health condition type** | Retina, choroid and vitreous haemorrhages and vascular disorders |
| **Study type** | Observational invasive |

## Summary

### ID

NL-OMON42212

**Source**
ToetsingOnline

**Brief title**
Studies on the etiology of central serous chorioretinopathy

### Condition

- Retina, choroid and vitreous haemorrhages and vascular disorders

**Synonym**
central serous chorioretinopathy

**Research involving**
Human

### Sponsors and support

**Primary sponsor:** Leids Universitair Medisch Centrum
**Source(s) of monetary or material Support:** Ministerie van OC&W,Gisela Thier Fellowship

## Intervention

**Keyword:** central serous chorioretinopathy, etiology

## Outcome measures

**Primary outcome**

1) Genetic analysis and ophthalmological examination in a CSC patient cohort, and in known families with CSC.

* Exome sequencing in patients with familial CSC could reveal genes with a different expression, as compared to healthy controls. These genes could give a clue in studying the aberrant gene expression levels in patients with sporadic CSC. Purpose of study is elucidate the etiology of CSC.

2) Analysis of serum complement activity in CSC patients and in a healthy control group.

* Complement activity in patients and in controls will be compared.

3) Endocrinological analysis of cortisol and testosterone exposure and sensitivity in CSC patients and in controls.

* Purpose of study is to find possible endocrinological abnormalities in CSC patients.

4) Analysis of the retinal phenotype and choroidal thickness in patients with Cushing*s syndrome, Conn*s syndrome, patients who receive solumedrol (a corticosteroid) during acute rejection of a renal transplant, or post renal transplantation patients who receive corticosteroids. Comparison of these

results to a control group of patients which do not show hypercortisolism will

be done.

* Purpose of study is to find abnormalities in retinal phenotype and choroidal

thickness in the several patient groups.

### Secondary outcome

Secondary study parameters are non-applicable.

## Study description

### Background summary

Central serous chorioretinopathy (CSC) is a specific and relatively common early-onset form of macular degeneration, that often occurs in patients in the professional active age range. This eye disease can present as an acute or a chronic disease.
CSC is a specific form of macular degeneration, in which there is an accumulation of fluid under the retina, which causes a detachment of the neuroretina.This fluid accumulation under the retina appears to be caused by a dysfunction of the retinal pigment epithelium (RPE) as a result of hyperpermeability and swelling of the underlying vascular layer of the eye, the choroid. A prolonged neuroretinal detachment in the macula leads to permanent central visual loss due to photoreceptor atrophy. Such a loss of visual acuity, with image distortion, loss of colour and contrast vision may have a high impact on a patient*s personal and professional life. Early diagnosis and treatment is desirable to try to improve the visual outcome and quality of life. After all, long-term follow-up studies have shown that the natural course of chronic CSC often results in permanent visual loss.
An association between severe psychosocial stressful events and CSC has been found, especially in patients with poor coping mechanisms. Both endogenous and exogenous Cushing*s syndrome are associated with CSC. Although little is known about the causes of CSC, circumstantial evidence suggests that the immune system may participate in the etiology of CSC, since CSC can occur in various immune-mediated diseases such as membranoproliferative glomerulonephritis and systemic lupus erythematosus. In age-related macular degeneration, a disease that shows overlapping features with CSC, complement activation has also been found to play an important role. Several studies have found increased serum complement activation in age-related macular degeneration. With the study we hope to learn more about the etiology of CSC.

## Study objective

The key objectives of this study are to identify both the genetic background and pathophysiological mechanisms that underlie CSC. To achieve this we will:
1) Perform genetic analysis and ophthalmological examination in a cohort of sporadic CSC patients and a database of families with CSC to assess the role of genetic factors and possible genotype-phenotype correlations in CSC.
2) Assess whether there is evidence of serum complement activation in CSC.
3) Analyse possible abnormalities in endocrinological factors in CSC, such as cortisol and testosterone levels and sensitivity to these hormones in CSC patients.
4) Perform ophthalmological examination of the retinal phenotype and choroidal thickness in individuals at risk of developing CSC, including patients with Cushing*s syndrome, Conn*s syndrome, patients who receive solumedrol (a corticosteroid) during acute rejection of a renal transplant, and post kidney transplantation patients receiving corticosteroids.

## Study design

1) Genetic analysis and ophthalmological examination in a cohort of sporadic CSC patients, in known families with CSC, and in a healthy control group.
* Genetic case-control study.

2) Analysis of serum and plasma complement activity in CSC patients and in a healthy control group.
* Analysis of serum and plasma complement factors.

3) Cross-sectional endocrinological analysis of cortisol and testosterone exposure- and sensitivity in CSC patients and in controls.
* Both cross-sectional (treated CSC patients in remission) and prospective (de novo patients with active CSC) evaluation of cortisol and testosterone exposure- and sensitivity. These results will be compared to a control group of patients, matched for blood pressure and diabetes/glycosylated haemoglobin.

4) Detailed evaluation of the retinal phenotype and choroidal thickness in patients with documented endogenous corticosteroid excess (Cushing*s syndrome), primary hyperaldosteronism (Conn*s syndrome) or exogenous corticosteroid excess (post kidney transplantation patients who receive corticosteroids) will be performed. These results will be compared to a control group of patients, matched for blood pressure and diabetes/glycosylated haemoglobin, without corticosteroid overexposure. Also assessment of intrinsic differences in glucocorticoid sensitivity between patients will be performed, using blood samples.
* Both cross-sectional and prospective

## Study burden and risks

The only invasive procedure, which will be performed in some of the patients participating within this study, is a venepuncture. This procedure has a minimal risk on the development of pain, a subcutaneous edema, of a phlebitis. The other procedures, which will be performed within this study, are part of standard clinical care.

## Contacts

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## Trial sites

### Listed location countries

Netherlands

## Eligibility criteria

**Age**
Adults (18-64 years)
Elderly (65 years and older)

### Inclusion criteria

All participants will be aged above 18 years.;1) Genetic analysis and ophthalmological examination in a CSC patient cohort, and in known families with CSC.
* Sporadic CSC: CSC patients who visit or visited the outpatient clinic of the Department of Ophthalmology in either the Leiden University Medical Center or the Rotterdam Eye Hospital.
* Familial CSC: CSC patients, who have at least one family member in whom CSC has been

detected. ;2) Analysis of serum complement activity in CSC patients and in a healthy control group.
* CSC patients who visit the outpatient clinic of the Department of Ophthalmology in the Leiden University Medical Center. Per patient a control will be recruited. For example, the husband or wife of each CSC patient who visits the outpatient clinic of the department of Ophthalmology.;3) Endocrinological analysis of cortisol and testosterone exposure and sensitivity in CSC patients and in controls.
* CSC patients who visit the outpatient clinic of the Department of Ophthalmology in the Leiden University Medical Center will be referred to the outpatient clinic of the Department of Endocrinology. ;4) Analysis of the retinal phenotype and choroidal thickness in patients with Cushing*s syndrome, Conn*s syndrome, patients who receive solumedrol (a corticosteroid) during acute rejection of a renal transplant, or post renal transplantation patients who receive corticosteroids.
* Patients with Cushing*s syndrome or Conn*s syndrome who visit or visited the outpatient clinic of the Department of Endocrinology and are willing to take part in this study.
* Patients receiving solumedrol during acute rejection of a renal transplant, or post renal transplantation patients who receive corticosteroids, who visit or visited the outpatient clinic of the Department of Nephrology and are willing to take part in this study.

### Exclusion criteria

For our study no exclusion criteria are applicable.

## Study design

### Design

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| Study type: | Observational invasive |
| Intervention model: | Other |
| Allocation: | Non-randomized controlled trial |
| Masking: | Open (masking not used) |
| Control: | Active |
| Primary purpose: | Basic science |

### Recruitment

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| Recruitment status: | Recruiting |
| Start date (anticipated): | 01-05-2015 |

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| Enrollment: | 825 |
| Type: | Actual |

## Ethics review

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| Approved WMO Date: | 10-04-2015 |
| Application type: | First submission |
| Review commission: | METC Leiden-Den Haag-Delft (Leiden)<br>metc-ldd@lumc.nl |

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| Approved WMO Date: | 21-07-2015 |
| Application type: | Amendment |
| Review commission: | METC Leiden-Den Haag-Delft (Leiden)<br>metc-ldd@lumc.nl |

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| Approved WMO Date: | 23-02-2016 |
| Application type: | Amendment |
| Review commission: | METC Leiden-Den Haag-Delft (Leiden)<br>metc-ldd@lumc.nl |

## Study registrations

### Followed up by the following (possibly more current) registration

No registrations found.

### Other (possibly less up-to-date) registrations in this register

No registrations found.

## In other registers

| Register | ID |
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| CCMO | NL50816.058.14 |