“RP” – More Than Just A Single Disease

There are more than 100 forms of hereditary retinal degenerative diseases. An **early and correct diagnosis** is a “ticket for life” and can be very important both for medical care as well as for quality of life and life choices. However, diagnosis is often made very late. For example, the treatable Refsums syndrome is detected on average 11 years after the first visit to the ophthalmologist. The correct diagnosis of the “prognosis range” is also important in order to make informed long-term education and career choices. Furthermore, the types of hereditary forms, particularly syndromal forms, have their **own particular important methods for managing the disease.**

In order to draw attention to the importance of **differential diagnosis**, the **NCL Foundation** and **PRO RETINA Deutschland e. V.** have dedicated themselves to this issue as a joint project. This poster describes different forms of **hereditary retinal degeneration** with their main symptoms and selected findings.

PRO RETINA Deutschland e. V.
Vaalser Str. 108
52074 Aachen
Germany
T: +49 (241) 87 00 18
F: +49 (241) 87 39 61
E: pro-retina@t-online.de

NCL Foundation
Holstenwall 10
20355 Hamburg
Germany
T: +49 (40) 69 666 74 0
F: +49 (40) 69 666 74 69
E: info@ncl-stiftung.de

For additional information, visit:
www.pro-retina.de, www.ncl-foundation.com, www.retinascience.de, www.retnet.org

Authors:
Prof. Dr. med. Ulrich Kellner, Zentrum seltene Netzhauterkrankungen, AugenZentrum Siegburg, MVZ ADTC Siegburg GmbH & RetinaScience, Bonn
Prof. Dr. med. Klaus Rüther, Sankt Gertrauden-Krankenhaus, Berlin
Dr. rer. nat. Frank Stehr, NCL Foundation
Dr. med. Claus Gehrig, PRO RETINA Deutschland e.V.
Dr. rer. medic. Frank Brunsmann, Charité Universitätsmedizin Berlin

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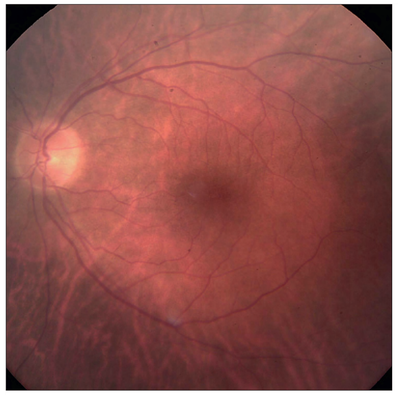
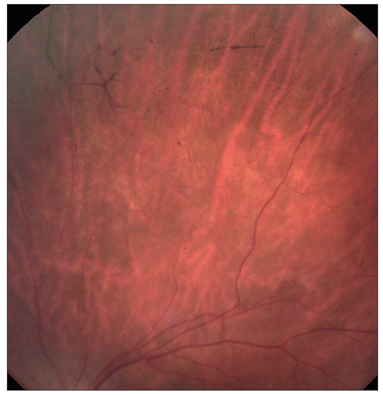
YOUR EYES SEE – YOUR DIAGNOSIS HELPS!





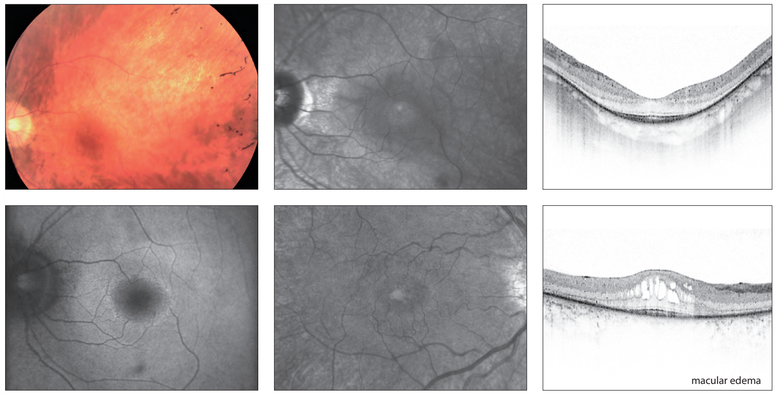
Refsum Syndrome

Refsum syndrome is a very rare autosomal recessively inherited disease associated with mutations in the PEX1-, PEX7-, PHYH- or PXMP3-gene. It mostly begins before age 20. **Visual disturbances** can be the initial symptom. Frequently there are also **neurological diseases** present, such as peripheral neuropathy or ataxia, before eye symptoms appear. **Hearing loss** and **irregular heart rhythm** may occur.

The background of the eye shows changes similar to Retinitis pigmentosa, with constricted peripheral blood vessels recognizable by pigmentation.

Diagnosis is made based on medical history, eye findings, **phytanic acid** in the blood, as well as possibly through a molecular genetic diagnosis.

A **special diet** can be **therapeutic**, and it is possible an apheresis treatment can positively influence the disease’s progression, which is why early diagnosis is crucial for those affected.



Retinitis Pigmentosa

Retinitis pigmentosa comprises a group of more than 40 similar, but genetically different, diseases with different patterns of inheritance. If this disease is coupled with an **inner-ear hearing loss**, it is called **Usher syndrome**, for which different genes are responsible. The onset and progression of Retinitis pigmentosa and Usher syndrome are very variable. Characteristic signs are first **night blindness**, then a progressive **shrinking of the visual field**, and later **central vision loss**.

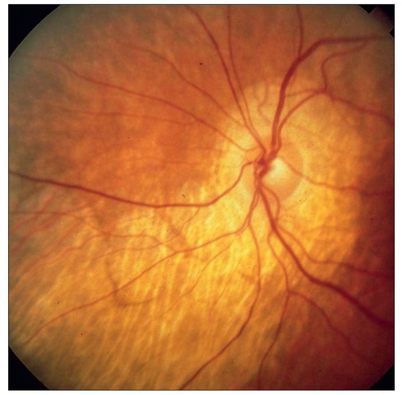
The background of the eye shows highly constricted blood vessels and outward pigmentation.

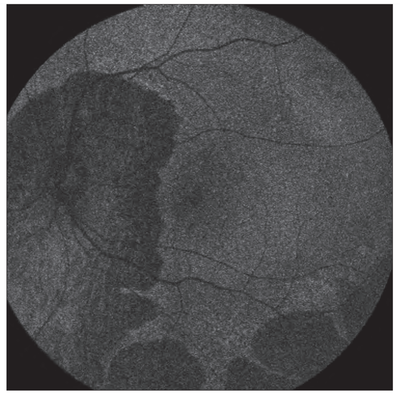
Fundus autofluorescence imaging typically shows a **light ring** of increased intensity at the point of sharpest vision, which is not recognizable in the background of the eye or in a color photo. The ring corresponds to the outer edge of the field of vision.

In a high-resolution OCT, the retinal layers are well preserved in the middle but outside the center become rapidly thinner.

When deciding whether Retinitis pigmentosa or a syndrome is present, the existence of other symptoms is important, and in some cases a molecular genetic diagnosis is necessary.

A causal therapy does not exist at this time, but associated changes such as early cataract formation or macular edema (see OCT) can, like other retinal dystrophies, be treated.





Atrophia Gyrata

Atrophia gyrata is an **autosomal recessively** inherited disease and is associated with mutations in the **ornithine aminotransferase (OAT) gene**. It begins in adolescence first with night blindness, then shows a progressive shrinking of the field of vision, and later central vision loss.

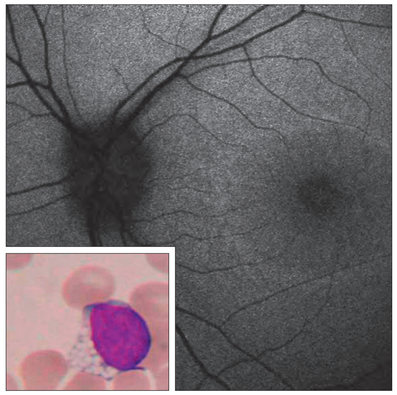
The background of the eye looks similar to that of Choroideremia because of extensive loss of the choroid and of pigment of a light color, but the border between normal and sick tissues are much sharper.

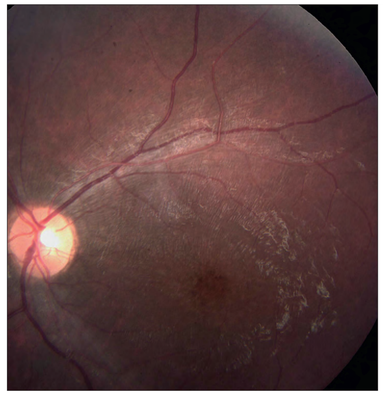
Fundus autofluorescence imaging shows sharply bordered dark areas in areas with complete choroid loss, as well as small changes in the still-functioning areas.

In a high-resolution OCT, retinal layers in areas with choroidal loss are thinned due to the lack of supply.

Diagnosis is made based on the typical retinal findings, the detection of increased **ornithine levels** in the blood as well as possibly through a molecular genetic diagnosis.

With Atrophia gyrata **a dietary therapy** for slowing the disease’s progression is possible, so early diagnosis for those affected is crucial.





Neuronal Ceroid Lipofuscinosis

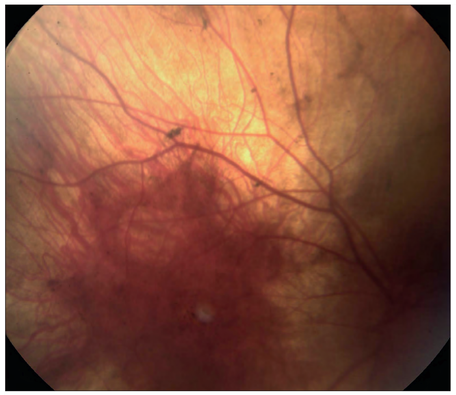
Neuronal Ceroid Lipofuscinoses are rare **autosomal recessively** inherited diseases counted among lysosomal storage diseases. The onset of vision impairment in the **juvenile form** is associated with mutations in the **CLN3 gene** and usually begins in the first decade of life. As it progresses, the disease causes a halt in development, then a degeneration of development with the loss of learned functions caused by the **death of nerve cells**, ending in **premature death** usually during the 2nd decade of life.

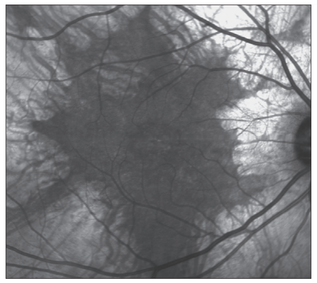
The background of the eye frequently shows changes similar to Retinitis pigmentosa, but in the beginning a **bull’s eye maculopathy** can also be observed. The frequently encountered glittering surface of the retina with folds occurs as a secondary change in many retinal dystrophies, and is not characteristic of a particular disease.

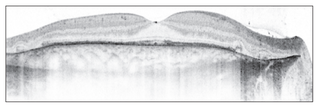
Fundus autofluorescence imaging shows a ring of higher intensity as in Retinitis pigmentosa.

Diagnosis is made based on medical history, retinal findings, as well as through a molecular genetic diagnosis. Moreover, one can see in a routine blood sample in the cytoplasm many lymphocytes with numerous large light vacuoles (see photo, kindly provided by Dr. A. Schulz).

A causal therapy does not exist at this time. The disease’s progression places high demands upon the parents of affected children, so an early diagnosis and consultation is essential.







Choroideremia

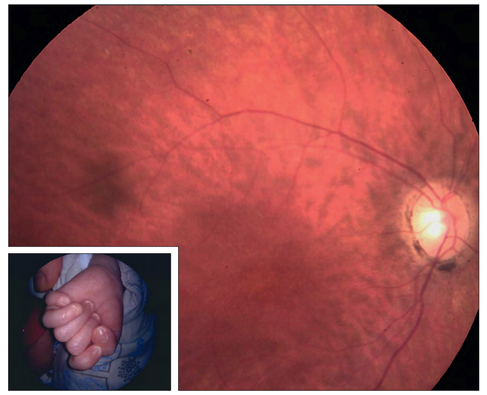
Choroideremia is an **x-linked** hereditary disease associated with mutations in the **CHM gene** and primarily affects men. Women typically show retinal changes, but see well in almost all cases. Men notice in youth first a **night blindness**, a **progressive shrinking of the field of vision**, and then central vision loss.

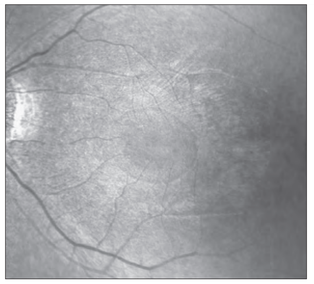
The background of the eye shows – because of the extensive loss of the choroid and pigment – a light color, with the darker-colored areas being those that are still functioning.

Fundus autofluorescence imaging shows sharply defined dark areas in regions of total choroid loss as well as **spotty changes** in the still-functioning areas.

In a high resolution OCT, the retinal layers are thinned in areas of choroidal loss due to lack of supply.

Diagnosis is based on the typical retinal findings, the findings of the mother, as well as possibly through a molecular genetic diagnosis. A causal therapy does not exist at this time.





Bardet-Biedl Syndrome

Bardet-Biedl Syndrome comprises at least 12 clinically similar, but genetically different, diseases. The mode of inheritance is autosomal recessive with variable manifestations of individual symptoms. The expression of retinal changes is variable and can be similar to Retinitis pigmentosa, but can also progress similarly to a rod-and-cone dystrophy.

A frequent sign of this syndrome is a **6th finger or toe** that is often removed at birth and soon forgotten in the child’s medical history.

The background of the eye can show variable changes, in this case **narrowed vessels** as in Retinitis pigmentosa. Fundus autofluorescence imaging and high-resolution OCT are also variable.

Diagnosis is made based on a medical history of **other symptoms** (possibilities are: developmental delays, obesity, underdevelopment of the reproductive organs, kidney changes) as well as through a molecular genetic diagnosis.

A causal therapy for eye changes is not possible, but the **other affected organs** require appropriate therapy according to the severity, making an **early diagnosis** essential for those affected.