Genetic Testing
Clinical genetic testing can confirm the diagnosis, and is available to assess genetic risk in family members for prenatal counseling. The Norrie gene, *NDP*, consists of three exons and codes for a protein of 133 amino acids. Disease-causing mutations in *NDP* can be detected in the majority of male cases by direct sequencing. In cases where clinical suspicion of Norrie disease could not be confirmed through DNA analysis, other genes that have been associated with similar clinical conditions should be investigated (*FZD4*, *LRP5*, *TSPAN12*).

Treatment
By the time the disease is first noticed, irreversible total retinal detachment usually already occurred. However, patients who have not completely lost their vision may be treated with surgery or laser therapy very early in life. Hearing loss can be treated with hearing aids and cochlear implants. Counseling, behavioral or pharmacologic management and care by special education professionals can assist with improvement of behavioral abnormalities and cognitive difficulties. Men with Norrie disease may need varying degrees of assistance from family, friends and caretakers, but can live a full and rewarding life. For further information, please feel free to contact the Norrie Disease Association (NDA) or any of the associated professionals indicated on the back of this brochure.
**Clinical Features**

The first visible symptom typically is a white pupillary reflex (leukocoria; pseudoglioma). The disease is highly variable (even within a family), and additional ocular signs can include an avascular retinal periphery, vitreoretinal haemorrhages, retinal folding, exudative and/or tractional retinal detachment, and persistent fetal vasculature. Later, shrinkage of the eye bulb (phthisis bulbi) can be observed, and the lens becomes cataractous. The cornea, iris, ciliary body and/or retinal pigment epithelium may be affected by the disease. In addition to the ocular signs, most Norrie males experience the onset of progressive hearing loss during late childhood or early adolescence, initially affecting high frequencies. Further, up to half of the patients exhibit cognitive impairments or behavioral abnormalities that can include autism-like features. A few patients can have epileptic seizures. There may be increased risk of peripheral vascular abnormalities (e.g. venous insufficiency).

**Differential Diagnosis**

Several other human diseases can be easily confused with Norrie disease, including: retinoblastoma, primary retinal dysplasia, persistent hyperplastic primary vitreous, retinopathy of prematurity, retinal dysplasia of Reese, Coats’ disease, X-linked juvenile retinoschisis, osteoporosis pseudoglioma syndrome, and especially familial exudative vitreoretinopathy (FEVR). This latter disease has been associated with mutations in four different genes (NDP, FZD4, LRP5, TSPAN12) to date. Thus, clinical genetic testing is essential for the proper diagnosis.

**Research**

Research continues to reveal more about how these genetic mutations cause the clinical features of Norrie disease and to explain the biological factors that lead to blindness, hearing loss, and characteristic features in cognition and behavior. With increased understanding of these issues, we hope to learn how to improve prevention or treatment of the clinical symptoms and to better support the patients and families affected by Norrie disease.

The high similarity between ND and FEVR has lead to the discovery that the gene products of the associated genes (NDP, FZD4, LRP5, TSPAN12) interact with each other in the so-called canonical Wnt-pathway. Mutations in one of these genes cause blood vessel defects, which appear to be the common mechanism underlying the different clinical symptoms.

**Norrie Disease Association**

The Norrie Disease Association (NDA) is a diverse organization eager to serve individuals with ND, as well as their families, social circles, educators, employers, and medical professionals. We are working to expand our collective knowledge of ND by facilitating collaboration among these groups. Our vision is to become the primary resource and advocate for the international ND community. The NDA depends entirely on volunteers and member donations to operate, and its list of services will expand as the organization grows. Learn more at: [www.norriedisease.org](http://www.norriedisease.org)