Telomere Biology Disorders (TBDs), including Dyskeratosis congenita, are complex multi-system disorders that cause premature aging of cells and organs. The clinical symptoms of TBDs are varied. A person diagnosed with a TBD may not experience all of the symptoms described below.

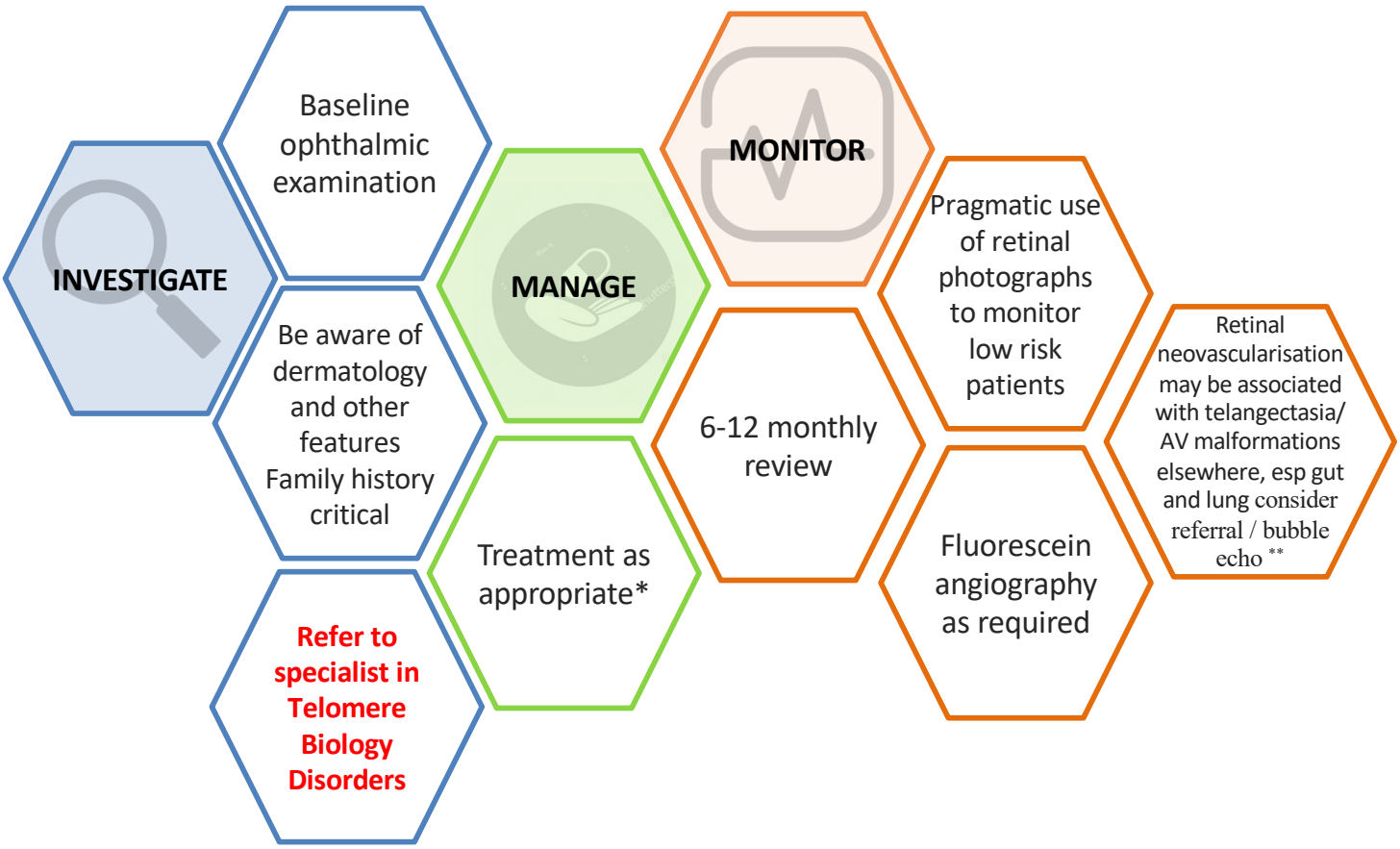
Ophthalmology

Epiphora, lachrymal duct stenosis/absence of tear duct, blepharitis, conjunctivitis, sparse eye lashes/ectropion/entropion/trichiasis, corneal dryness/scarring/ulceration/perforation, retinal vascular changes/atherosclerosis/neovascularisation/proliferation, retinal haemorrhages, exudative retinopathy.

DC variants: Høyeraal-Hreidarsson (HH), Coats Plus (CP), Revesz Syndrome (RS) at high risk of ocular involvement.

Secondary manifestations: Post transplant Graft Versus Host Disease (GVHD) and increased sensitivity to treatments such as corticosteroid or radiation-related changes likely to be more severe e.g. cataract.

Team Telomere Telomere Biology Disorders: Diagnosis and Management Guidelines 2022
https://teamtelomere.org/telomere-biology-disorders-diagnosis-and-management-guidelines-downloads/



Savage SA, Niewisch MR. Dyskeratosis Congenita and Related Telomere Biology Disorders. 2009 Nov 12 [Updated 2023 Jan 19]. In: Adam MP, Mirzaa GM, Pagon RA, et al., editors. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2023. Available from: https://www.ncbi.nlm.nih.gov/books/NBK22301/

*No DC specific treatments currently indicated but danazol/other attenuated androgen, metformin or other telomere-preserving treatments theoretically helpful

** Consider Avastin

This information is based on reports from the medical literature. Please speak to your doctor if you have concerns about TBD.

Please contact us. We welcome your feedback.

ADVOCACY EDUCATION SUPPORT

Telomere Biology Disorders (TBD) affect progenitor stem cell production and cell replication in multiple organ systems. Dyskeratosis Congenita (DC) is a severe TBD presenting in early childhood with a clinical triad of nail dysplasia, oral leukoplakia, and abnormal skin pigmentation, associated with bone marrow failure. Mutations in ACD, TINF2, CTC1, DKC1, DCLRE1B, NHP2, NOP10, NPM1, POT1, RPA1, STN1, TCAB1, PARN, RTEL1, TERT, TERC, MDM4, ZCCHC8 WRAP53 genes, all involved in telomere maintenance, have been identified in patients with a spectrum of clinical manifestations including pulmonary fibrosis, emphysema, cryptogenic liver cirrhosis, lacrimal duct, oesophageal and urethral stenosis, avascular necrosis of hips and shoulders, periodontal disease, an increased predisposition to epithelial and hematologic malignancies plus premature greying of hair. Classical DC is characterized by extremely short telomeres but different gene mutations in telomere maintenance genes can produce variable phenotypes, differing in severity, in childhood or later into adulthood. Severe Dyskeratosis Congenita /Telomere Biology Disorder variants Høyeraal-Hreidarsson Syndrome (HH), Revesz Syndrome (RS) and Coats' Plus Syndrome (CPS) may present with serious ocular problems. Some of these complications have also been reported in individuals with other TBDs. Common findings include punctal stenosis with epiphora, entropion, and trichiasis. Retinal changes may not be rare and warrant close evaluation.

In a cross-sectional study, 75 patients (2001-2007) with an Inherited Bone Marrow Failure Syndrome and 121 of their first-degree relatives had complete ophthalmic investigations. In the 28 patients with DC, abnormalities of the lacrimal drainage system (29%) were the most prevalent findings, followed by retinal abnormalities (pigmentary changes, retinal neovascularization, retinal detachment, exudative retinopathy) in 21%, cicatricial entropion with trichiasis and blepharitis in seven percent each, sparse eyelashes and congenital cataract in three and a half percent each.

Tsilou ET, Giri N, Weinstein S, Mueller C, Savage SA, Alter BP. Ocular and orbital manifestations of the inherited bone marrow failure syndromes: Fanconi anemia and dyskeratosis congenita. Ophthalmology. 2010 Mar;117(3):615-22. Doi:10.1016/j.optha.2009.08.023

Team Telomere Telomere Biology Disorders: Diagnosis and Management Guidelines 2022. Chapter 7. Opthalmic Manifestations. https://teamtelomere.org/telomere-biology-disorders-diagnosis-and-management-guidelines-downloads/

CASE STUDIES

Condition	Ocular findings	Reference
Autosomal dominant DC	Bilateral retinal vasculopathy and proliferative retinopathy with vitreous hemorrhage in the right eye, in the absence of pancytopenia.	Vaz-Pereira S, Pacheco PA, Gandhi S, Kulasekararaj AG, Marsh JC, Pal B, Mufti GJ. Bilateral retinal vasculopathy associated with autosomal dominant dyskeratosis congenita. Eur J Ophthalmol. 2013 Sep-Oct;23(5):772-5. doi: 10.5301/ejo.5000297.
DC	Two siblings presenting with exudative retinopathy, thrombocytopenia, and macrocytosis with markedly shortened telomeres and a previously unreported, inherited mutation in TERT, c.2603A>G.	Sharma A, Myers K, Ye Z, D'Orazio J. Dyskeratosis congenita caused by a novel TERT point mutation in siblings with pancytopenia and exudative retinopathy. Pediatr Blood Cancer. 2014 Dec;61(12):2302-4. doi: 10.1002/pbc.25161.
HH (DKC1 mutation)	Sclerotic retinal vessels and peripheral non-perfusion and neovascularisation.	Allingham MJ. Bilateral Proliferative Retinopathy Associated With Hoyeraal-Hreidarsson Syndrome, a Severe Form of Dyskeratosis Congenita. Ophthalmic Surg Lasers Imaging Retina. 2016 Apr 1;47(4):366-8. doi: 10.3928/23258160-20160324-11.
Coats Plus Syndrome (CPS)	Vitreous haemorrhage and peripheral retinal arteriovenous anastomosis.	Mansukhani S, Ho ML, Gavrilova RH, Mohney BG, Quiram PA, Brodsky MC. Cerebroretinal microangiopathy with calcifications and cysts (CRMCC) or "Coats Plus": when peripheral retinal vasculature signals neurologic disease. J AAPOS. 2017 Oct;21(5):420-422. doi: 10.1016/j.jaapos.2017.04.015.
DC	Siblings diagnosed with familial exudative vitreoretinopathy managed with laser photocoagulation. Eight years later, both developed pancytopenia secondary to bone marrow failure. Both had severely shortened telomere length caused by a missense mutation in the gene encoding reverse transcriptase component of telomerase.	Thanos A, Todorich B, Hypes SM, Yonekawa Y, Thomas B, Randhawa S, Drenser KA, Trese MT. RETINAL VASCULAR TORTUOSITY AND EXUDATIVE RETINOPATHY IN A FAMILY WITH DYSKERATOSIS CONGENITA MASQUERADING AS FAMILIAL EXUDATIVE VITREORETINOPATHY. Retin Cases Brief Rep. 2017 Winter;11 Suppl 1:S187-S190. doi: 10.1097/ICB.0000000000000430.