Telomere Biology Disorders (TBD), including Dyskeratosis Congenita (DC), are complex, genetic, multi-system disorders that cause premature aging of cells and organs. The clinical symptoms of TBDs are varied and may require multi-disciplinary diagnosis and management

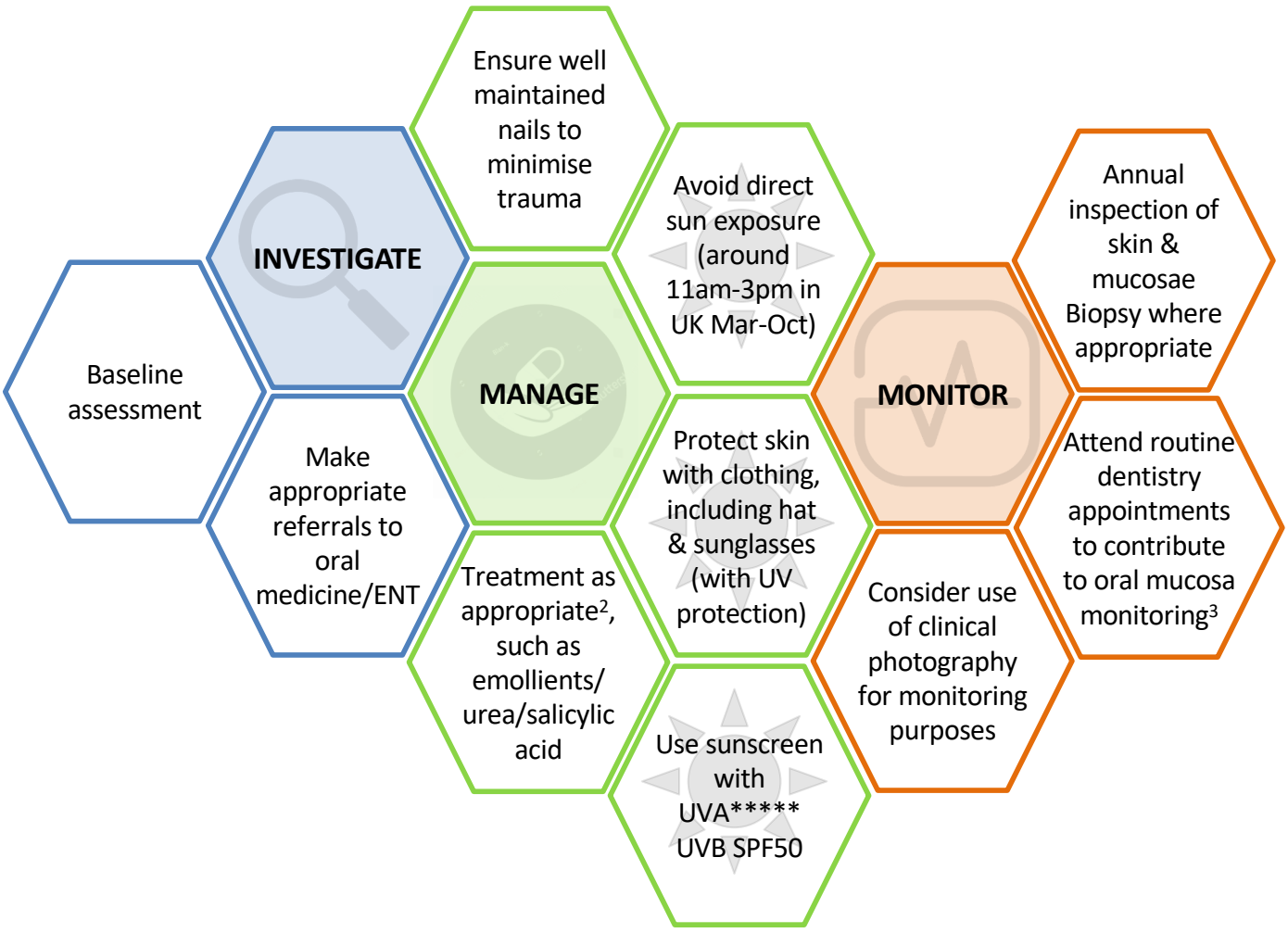
Dermatology [1]

Nails: Dystrophic/ridged/split/absent/hypoplastic finger & toenails.

Skin: Lacy reticular/hypo/hyper pigmentation (may be more pronounced on sun exposed areas and flexures), mucosal leukoplakia (early onset), telangiectasia, thin skin, loss of fingerprints, hyperkeratosis (exacerbated by physical factors such as cold, repeated trauma or other irritation), hyperhidrosis / hypohidrosis, increased risk of squamous cell carcinoma at young age.

Hair: Alopecia, hair thinning, early greying of hair. Abnormal eye lash growth can cause corneal damage (see Ophthalmology Information Sheet).

Secondary manifestations: Post transplant Graft Versus Host Disease (GVHD) may mimic the features listed above.



[1] Dyskeratosis congenita. NEJM Images in Clinical Medicine. 2017, n engl j med 376;15. DOI:10.1056/NEJMicm1613081
[2] No DC specific treatments currently indicated
[3] Local dental practitioners may need to be made aware of the increased risk of SCC in TBD.

We value your feedback. Please contact us.

ADVOCACY EDUCATION SUPPORT

This information is based on medical literature. Please see your doctor if you have concerns about TBD

Telomere Biology Disorders (TBD), including Dyskeratosis Congenita (DC),have variable phenotypes depending on the genes involved and other epigenetic factors. Telomere length is used as a diagnostic tool. Clinical manifestations include bone marrow failure, liver cirrhosis, pulmonary fibrosis, increased risk of head and neck and genitourinary cancers and immunological features. [1,2] A diagnostic feature can be the "classic triad' of reticulate skin pigmentation, nail dystrophy, and oral leukoplakia but these mucocutaneous features can present individually in combination with the above. [3]

Sixty patients with a genetic diagnosis of DC were included in a longitudinal cohort study and the presence of 'triad' features were extracted from dermatology records and photographs.
The 'classical triad' features and 8 additional mucocutaneous findings (adermatoglyphia, palmoplantar hyperkeratosis, hyperhidrosis, premature greying, scalp or eyelash hair loss, epiphora, and lash irritation/blepharitis) are described. The complete clinical triad manifested in only 37% of patients and 10% lacked all triad features. The study concluded that severe mucocutaneous phenotypes, as defined by the number of triad features and additional findings, are associated with higher-risk genotypes and poorer prognosis compared with milder mucocutaneous phenotypes. Careful detection and monitoring of all mucocutaneous features of DC [TBD] is recommended to enable early referral, confirmatory testing, and appropriate multi-disciplinary clinical management. [4]

Ratnasamy *et al* describe the diagnostic and genetic work up and pedigree analysis in a case study of a patient presenting with recurrent febrile episodes and reticulate skin pigmentation interspersed with hypopigmented macules involving the face, neck and extremities, hyperkeratosis of palms and soles, nail dystrophy, leukoplakia of the tongue, premature graying of hair, watery eyes and dental caries. Several of his male relatives were affected with a similar condition. The authors suggest that 'primary care physicians, dentists, and dermatologists should be vigilant enough to diagnose this rare condition in their clinical practice, where patients may present with recurrent febrile illnesses, dental problems, and skin or nail changes for routine evaluation'. [5]

1 Savage SA. Dyskeratosis congenita 2009 (updated 2019 Nov 21) in Adam MP, Ardinger HH, Pagon RA *et al.,* Eds. Gene Reviews® [internet] Seattle (WA): University of Washington Seattle; 1993-1019. Bookshelf URL https://ncbi-nlm.nih.gov/books/

2 Mangaonkar AA and Patnaik MM. Short Telomere Syndromes in Clinical Practice: Bridging Bench and Bedside Mayo Clin Proc. July 2018;93(7):904-916 https://doi.org/10.1016/j.mayocp.2018.03.020

3 Niewisch MR & Savage SA (2019) An update on the biology and management of dyskeratosis congenita and related telomere biology disorders. Expert Review of Hematology, 12:12, 1037-1052, DOI: 10.1080/17474086.2019.1662720

4 Ward SC *et al*. Beyond the triad: Inheritance, mucocutaneous phenotype, and mortality in a cohort of patients with dyskeratosis congenita. J Am Acad Dematol. 2018 Volume 78, Issue 4, Pages 804–806 https://www.jaad.org/article/S0190-9622(17)32543-4/pdf

5 Ratnasamy V *et al*. Dyskeratosis congenita with a novel genetic variant in the DKC1 gene: a case report. BMC Medical Genetics (2018) 19. Article number: 85. https://bmcmedgenet.biomedcentral.com/articles/10.1186/s12881-018-0584-y