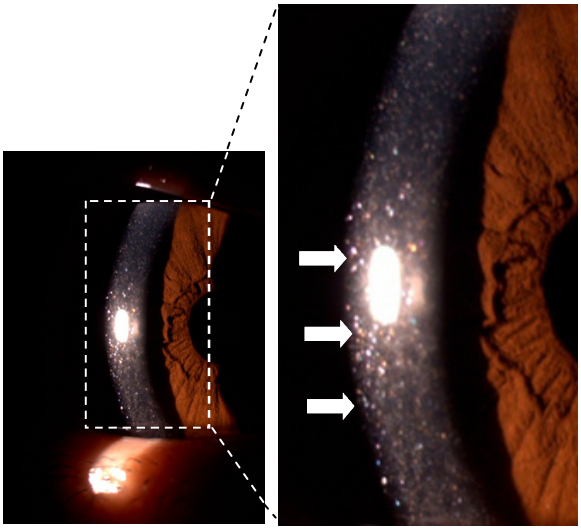
(*Refer to page 179*)

Answer: Cystinosis

The presence of multiple polychromatic crystals (**Panel**) involving the stroma is pathognomonic for Cystinosis in the setting of Fanconi's syndrome. [1] *(For differential diagnosis of multiple polychromatic crystals, refer to Supplementary Text).*

Cystinosis is a rare autosomal recessive metabolic disorder that causes the amino acid cystine, to accumulate in the kidneys, eyes, liver, muscles, pancreas, brain and the white blood cells. The major clinical manifestation of cystinosis is renal failure.

Cystinosis is caused by mutations in the gene CTNS (cystinosin lysosomal cystine transporter gene). The CTNS gene provides instruction for making a protein called cystinosin. This cystinosin specifically moves the amino acid cystine out of lysosome.



Enlarged image showing multiple polychromatic spots-crystals (some of which indicated by white arrows) of Cystinosis.

Cystinosis occurs with a frequency of approximately one in 100,000 to 200,000 and has been found worldwide in all ethnic groups. [1] Depending on the age at presentation and the degree of disease severity, three clinical forms of cystinosis are recognised [2]: **A)** Nephropathic infantile form, which is the most frequent and severe form of the disease, **B)** Nephropathic juvenile form, synonyms: intermediate cystinosis, late onset form, adolescent form, and **C)** Non-Nephropathic adult form; synonyms: benign non-nephropathic cystinosis, ocular non-nephropathic cystinosis. (*Refer to Supplementary Text for descriptions of listed conditions*).

The diagnosis requires; **a)** measurement of cystine in polymorphonuclear leucocytes (Tandem Mass spectrometry), **b)** Biopsy - crystals on tissue biopsy of bone marrow, conjunctiva, kidney, liver, intestine. Cystine crystals appear hexagonal or rectangular in shape and are birefringent under polarising light, [1], **c)** Molecular genetic testing.

Treatment for cystinosis can be categorised into; **a)** Specific, **b)** Systemic and **c)** Supportive. (*Refer to Supplementary Text for details of treatment*)

REFERENCES

1: Nesterova G, Gahl WA. Cystinosis. 2001 Mar 22 [Updated 2012 May 17]. In: Pagon RA, Bird TD, Dolan CR, et al, editors. GeneReviews™ [Internet]. Seattle (WA): University of Washington, Seattle; 1993. (Available from http://www.ncbi.nlm.nih.gov/books/NBK1400/). (Accessed date 3rd May 2013).

2: Wilmer MJ, Schoeber JP, van den Heuvel LP, et al. Cystinosis: practical tools for diagnosis and treatment. Pediatr Nephrol. 2011; 26:205-15.