Advanced Anterior Segment Cases: timely Diagnosis and Treatment

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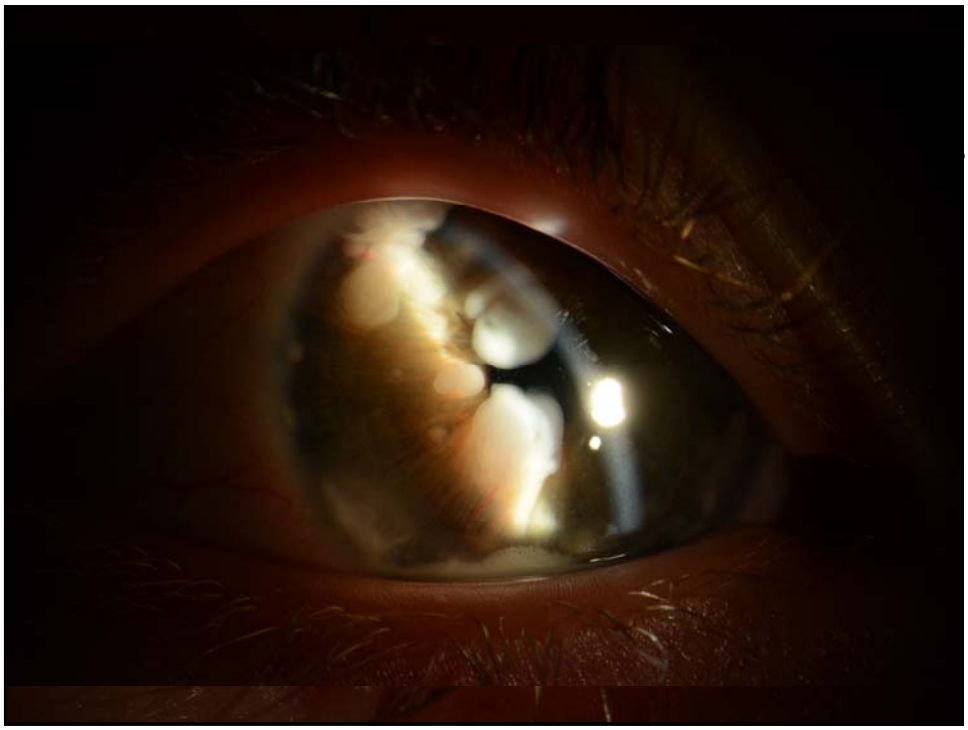
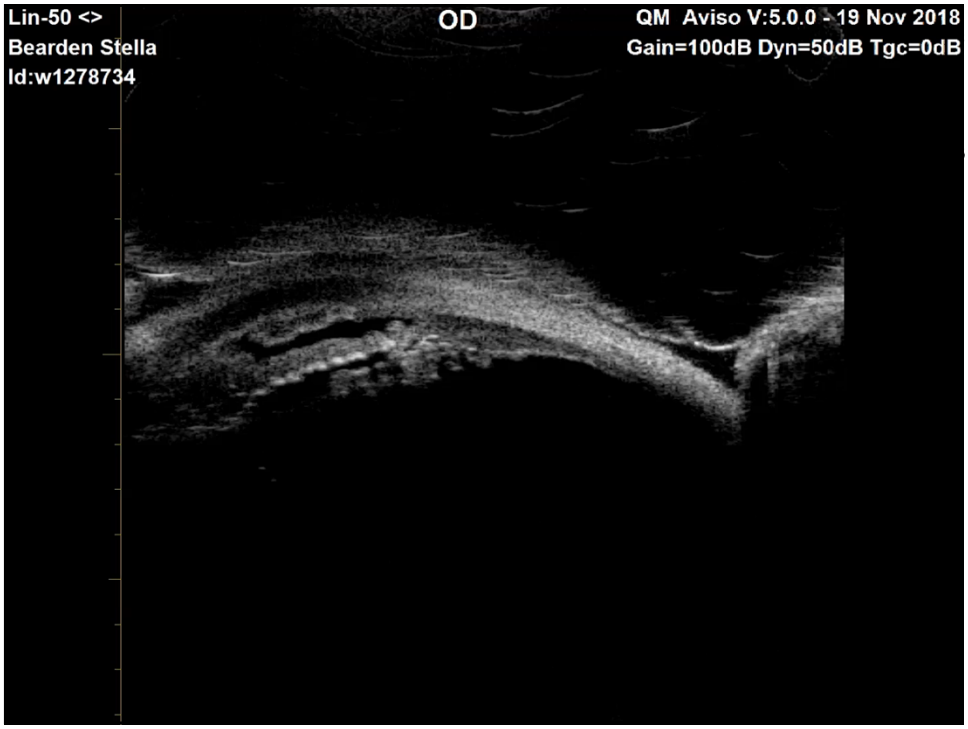
7yo F with a white OD

- History:
  - Mom noted OD whiter than OS a week ago and now sees a white spot on the pupil
  - Vision seems fine
  - No know medical problems or med or allergies
  - Normal birth hx and no trauma
  - Fam HX negative for eye disease

7yo F with a white OD

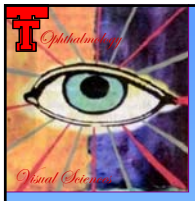
- Exam :
- Vasc OD = 20/25
- IOP = 30 mmHg
- SLE: white and quiet with 3-4+ cells and clumps circ without fibrin; no Cataract.
- Iris – SLE photos**>>





7yo F with a white OD

- Findings: muticentric creamy white mass lesions of iris without inflammation and with secondary obstructive hypertension
- Differential Diagnosis:
  - Hematopoietic cancer (leukemic or lymphomatous)
  - Medulloblastoma (diktyoma)
  - Retinoblastoma (rare diffuse multicentric)
  - Neuroblastoma (metastatic)
  - Juvenile xanthogranuloma (JXG)
  - Uveitis?



7yo F with a white OD

- Plan:
  - Urgent EUA for thorough Retinal exam for RB and poss AC washout and biopsy with vitrectomy probe IF no RB seen.
  - Pathology consultation> Lymphoma specialist on call for specimen handling
  - Rescheduled elective cases and took to surgery the next working day.
  - Procedure **

7yo F with a white OD

- Pathology results:
  - TTUHSC – small blue cells not cw lymphoma/leuk with epithelioid characteristics > consult
  - Mayo eye path > small blue cell tumor cw RB, MB, LL, NB
  - Houston Dr. Barrios > RB: cytology, (+)synaptophysin, though (-)RB protein; fam req add opin
  - Will's Path Dr. Eagle confirmed RB
- Meanwhile seen at MDA then two more local opinions from uveitis and retina specialists

Will's Eye Institute
Dr. Ralph Eagle

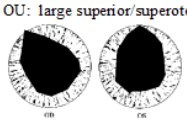
- "Both show clumps and cohesive aggregates of small basophilic cells with scant cytoplasm that have a high NC ratio and irregular nuclear contours. .... Characteristic background of necrotic and apoptotic cells and cellular debris as well as scattered macrophages. A few small aggregates of cells have an arrangement reminiscent of rosettes. The tumor cells show positive cytoplasmic immunoreactivity for synaptophysin consistent with retinoblastoma. The tumor cells are not immunoreactive for RB protein with appropriate positive and negative controls. This pattern of immunoreactivity is also consistent with retinoblastoma.
- Diagnosis: anterior chamber fluid, right eye, fine needle aspiration biopsy adequate cytologic preparation positive for malignancy. Cytologic features consistent with retinoblastoma. Iris nodule, right, fine needle aspiration biopsy adequate cytologic prep in preparation positive for malignancy. Cytologic features consistent with retinoblastoma.
- Comment: a small blue cell tumor in the anterior chamber and iris of a child is a retinoblastoma until proven otherwise. The clumps of cells seen in the cytologic preparations resemble the tumor seeds that commonly involve the vitreous in retinoblastoma. Retinoblastoma cells show positive immunoreactivity for synaptophysin, as this case does. This observation excludes leukemia or lymphoma. Neuroblastoma metastatic to the eye is quite rare, involves infants and usually occurs in patients who are known to have metastatic neuroblastoma.

- The diffuse infiltrative variant of retinoblastoma's typically occurs in older children with an average age of 6 to 7 years who often present with anterior chamber involvement as a pseudohypopyon and or clumps of tumor. Malignant Medulloepithelioma of the ciliary body may contain foci of poorly differentiated tumor that resemble retinoblastoma, but such tumors are exceedingly rare.

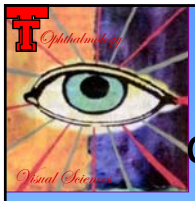
Bilateral corneal opacification and glaucoma

- 59yo MAF referred for corneal edema 10/2013
- Mult LPIs OU for CACG; TRAB OU 2008; IOP 14/17

OD: 1+ DM folds, 3+ microcystic edema, no subepi bullae
OS: 2+ DM folds especially temporally, 3+ microcystic edema, no subepi bullae
Anterior Chamber:
OU: 3+ deep
Iris:
OD: temporal atrophy with history of LPIs
OU: 1arge superior/superotemporal iridectomies s/p trab



Lens:
OD: 2+ NSC
OS: PC IOL with at least 1+ PCO
Optic Disc:
OD: <20/800 view, appears pink
OS: 20/800 view; appears ~0.8 and no clear pallor with 20D on



Bilateral corneal opacification and glaucoma

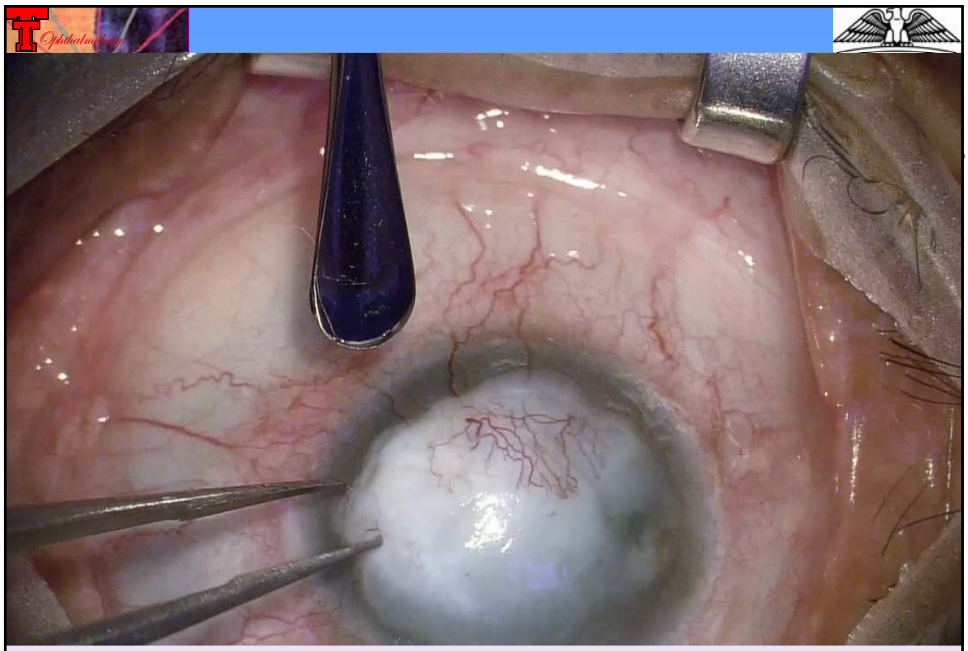
- 59yo MAF referred for corneal edema 10/2013
- PKP 2/2014 OS 6mm
- Lost to FU/ ran out of meds mult times> rejected, treated 20/100 persist edema; OD > HM
- PKP 8/2015 initially cleared but more compliance issues and edema w IOP 40 on MMT 20/400 >>
- JY for Ahmed
- DLM 9/16 VA HM/400 IOP27/26 OS AC fibrosis and forward contraction of iris

Bilateral corneal opacification and glaucoma

- 59yo MAF referred for corneal edema 10/2013
- 4/17 VA HM/HM, IOP 29/36 (ran out meds) 4+ edema OS and fibrous changes OD: compliance discussion > kept 4 monthly visits >
- 8/17 PKP OS and tube trim> cleared to 20/150 but cyclitic membrane pushing AC shallower w tube touch > edema
- 7/18 down to LP/CF > disc options

Bilateral corneal opacification and glaucoma

- 59yo MAF referred for corneal edema 10/2013
- Options:
  - 4th PKP OS
    - Immune suppression syst
    - Other surgery for cyclitic membrane
  - Boston Kpro 1 OS w Pedi size 8.0mm back plate?
  - What about OD?
    - SK, PKP, CE, IOL + ?
    - Vispot?



Ectopia Lentis Case 1812

- 59yo WF referred for CE w bilat. Zon laxity
  - No FHx eye, No known syst Dz.

Visual Acuity:	cc				cc ph
OD Distance:	20/40-2				NI
OS Distance:	20/50				20/40
Refractions:	**Eye**	**Sphere**	**Cylinder**	**Axis**	**Dist**
Present GL1	OD	-7.75	+0.25	175	20/70-2
	OS	-8.50	+1.00	128	
MR 1	OD	-12.00	+5.50	92	20/40-1
	OS	-14.75	+5.75	050	20/50+2

Ectopia Lentis Case 1812

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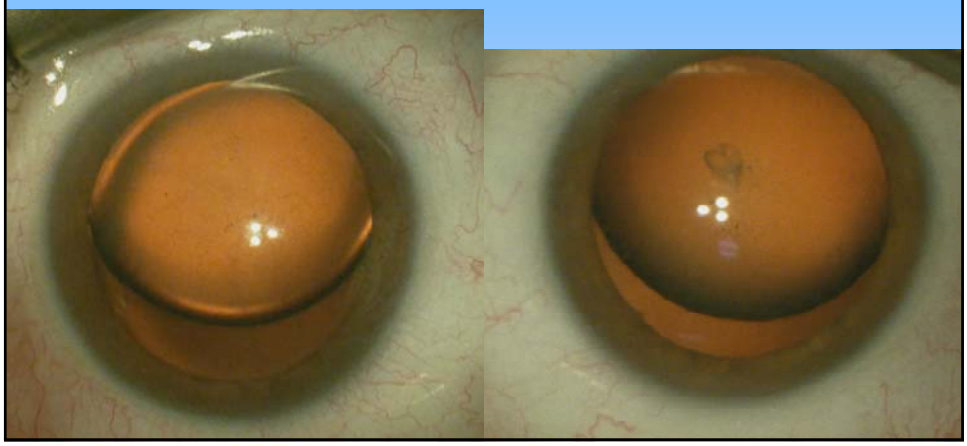
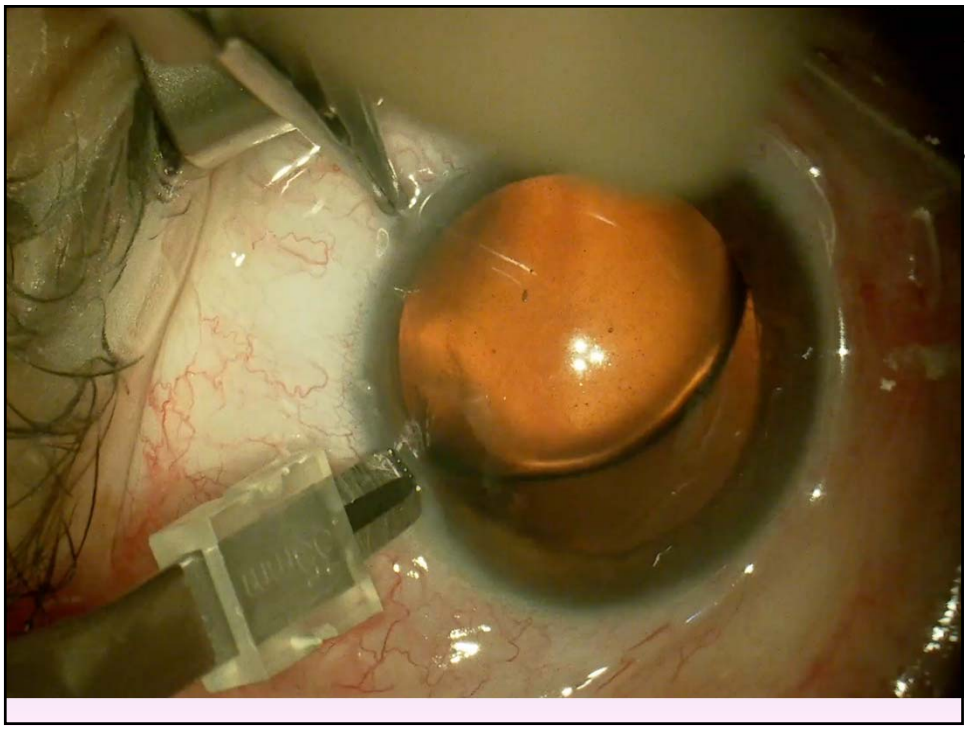
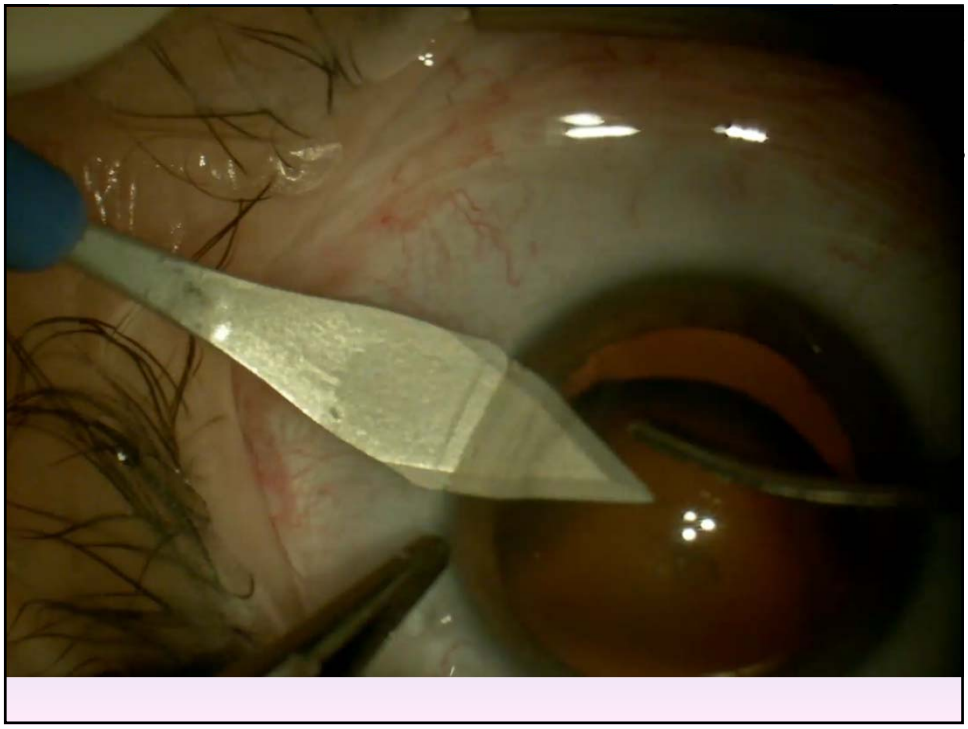


Ectopia Lentis

- Non Surgical Treatments if lens clear
  - Refractive correction if good BCVA
  - Aphakic CL for luxation or if subluxed sufficient to make vis axis aphakic
  - Pupillary constriction for dysphotopsias from aphakic crescent





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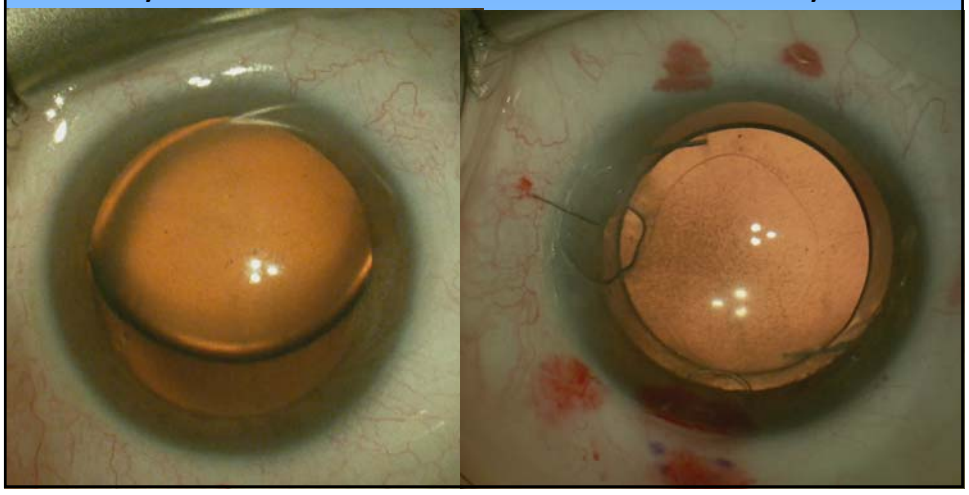

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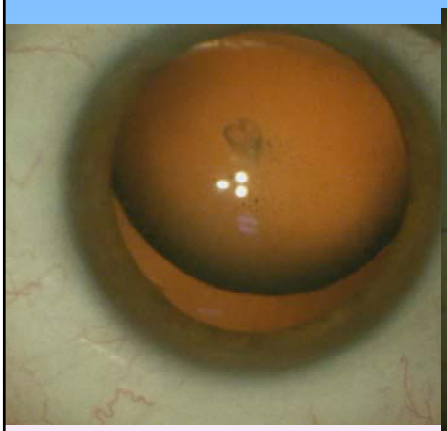
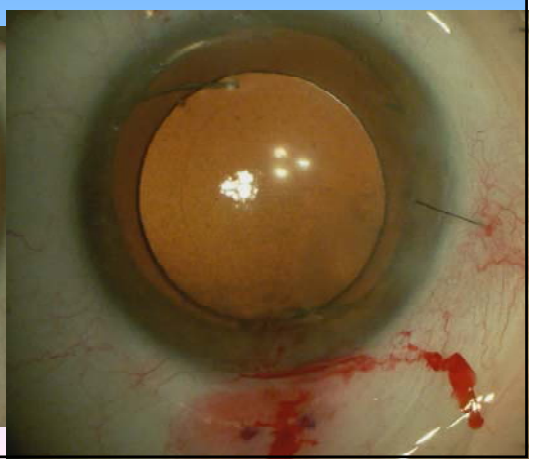
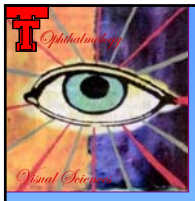




Ectopia Lentis

- Definition: Subluxed vs luxated
  - **Onset**
    - **Congenital – may have overlay of Amblyopia**
    - **Developmental**
    - **Acquired**
  - **Diagnosis**
    - **SLE signs**
      - **HOAs by retinoscopic reflex with NL topo,**
      - **iridodonesis,**
      - **equator of crystalline lens visible**



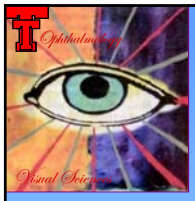
Ectopia Lentis

- Etiology
  - Simple Ectopia Lentis
  - Ectopia lentis et pupillae
  - Syndromic/Heritable/systemic associations
  - Secondary to other ocular disorders
  - Infectious
  - Traumatic
  - Mass mechanical

Ectopia Lentis

Isolated

- Simple Ectopia lentis – congenital or acquired – usually bilateral and up and temporal
- Vit prolapse and RD risk higher
- Inheritance: AD + AR
  - » Mutations in the *FBN1* (AD)(Chromasome 15) or *ADAMTSL4* (AR) (Chromasome 1)gene impair protein function and lead to a decrease in microfibril formation or result in the formation of impaired microfibrils. Fibrillin 1 gene.



Ectopia Lentis

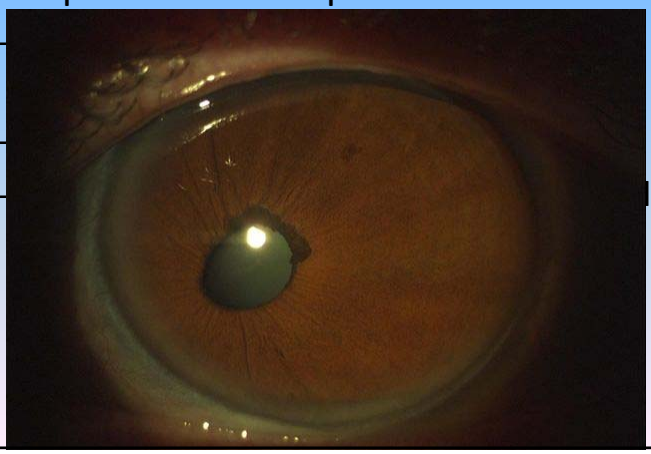
- **Syndromic and heritable**
  1. **Marfan Syndrome – up and out like simple, Aortic Dissection**
  2. **Homocysteinuria -** increased risk of thrombotic episodes. 60% inferior or nasal
  3. **Weill-Marchesani syndrome**

Ectopia Lentis

- **Secondary to other ocular disorders**
  - **Aniridia**
  - **Congenital Glaucoma**
  - **Pseudoexfoliation**
  - **Retinitis Pigmentosa**
- **Infectious - lues**
- **Traumatic**
- **Mass**

Ectopia Lentis

- Ectopia Lentis et Pupillae
  -
  -
  -

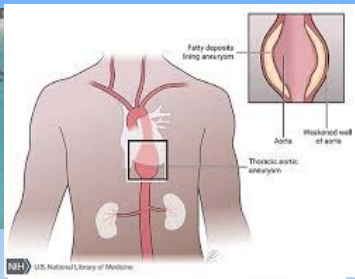


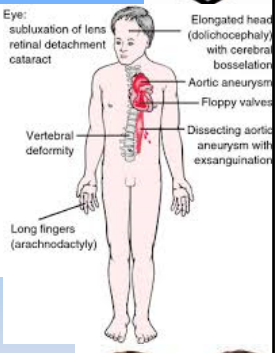
locornea,

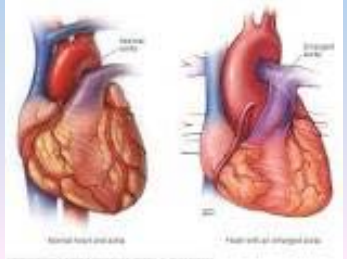
Ectopia Lentis

- Marfan Syndrome
  - Systemic disease of Connective tissue
  - Fibrillin-1 defect DT FBN1 gene **AD** (25% de novo mut)
  - 75% bilat symmetric Ectopia lentis **UP & OUT**
  - Unusually flexible joints, long fingers, Tall and thin, arm span > stature, long narrow face, high arched palate, crowded teeth, scoliosis, pectus excavatum, Mitral valve prolapse or aortic dissection, Axial myopia

Marfan Syndrome



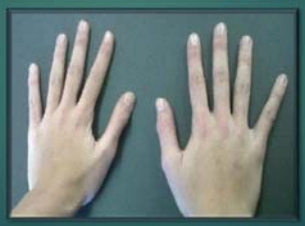




Marfan Syndrome

Marfan Syndrome

- An autosomal **DOMINANT MULTISYSTEM** disorder characterized by abnormal manifestations in the **skeletal**, **cardiovascular**, and **ocular** systems.

Wrist Sign	Arachnodactyly	Thumb Sign
		
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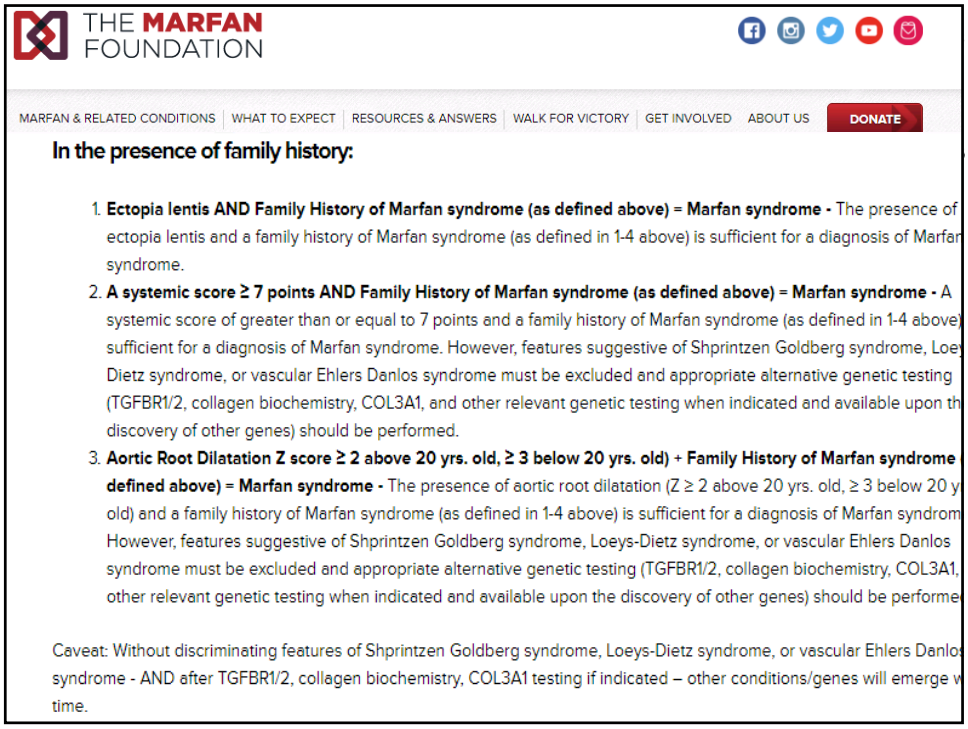


THE MARFAN FOUNDATION

MARFAN & RELATED CONDITIONS | WHAT TO EXPECT | RESOURCES & ANSWERS | WALK FOR VICTORY | GET INVOLVED | ABOUT US | DONATE

In the presence of family history:

1. **Ectopia lentis AND Family History of Marfan syndrome (as defined above) = Marfan syndrome -** The presence of ectopia lentis and a family history of Marfan syndrome (as defined in 1-4 above) is sufficient for a diagnosis of Marfan syndrome.
2. **A systemic score ≥ 7 points AND Family History of Marfan syndrome (as defined above) = Marfan syndrome -** A systemic score of greater than or equal to 7 points and a family history of Marfan syndrome (as defined in 1-4 above) sufficient for a diagnosis of Marfan syndrome. However, features suggestive of Shprintzen Goldberg syndrome, Loey Dietz syndrome, or vascular Ehlers Danlos syndrome must be excluded and appropriate alternative genetic testing (TGFBR1/2, collagen biochemistry, COL3A1, and other relevant genetic testing when indicated and available upon th discovery of other genes) should be performed.
3. **Aortic Root Dilatation Z score ≥ 2 above 20 yrs. old, ≥ 3 below 20 yrs. old) + Family History of Marfan syndrome defined above) = Marfan syndrome -** The presence of aortic root dilatation (Z ≥ 2 above 20 yrs. old, ≥ 3 below 20 y old) and a family history of Marfan syndrome (as defined in 1-4 above) is sufficient for a diagnosis of Marfan syndrom However, features suggestive of Shprintzen Goldberg syndrome, Loeys-Dietz syndrome, or vascular Ehlers Danlos syndrome must be excluded and appropriate alternative genetic testing (TGFBR1/2, collagen biochemistry, COL3A1, other relevant genetic testing when indicated and available upon the discovery of other genes) should be performe

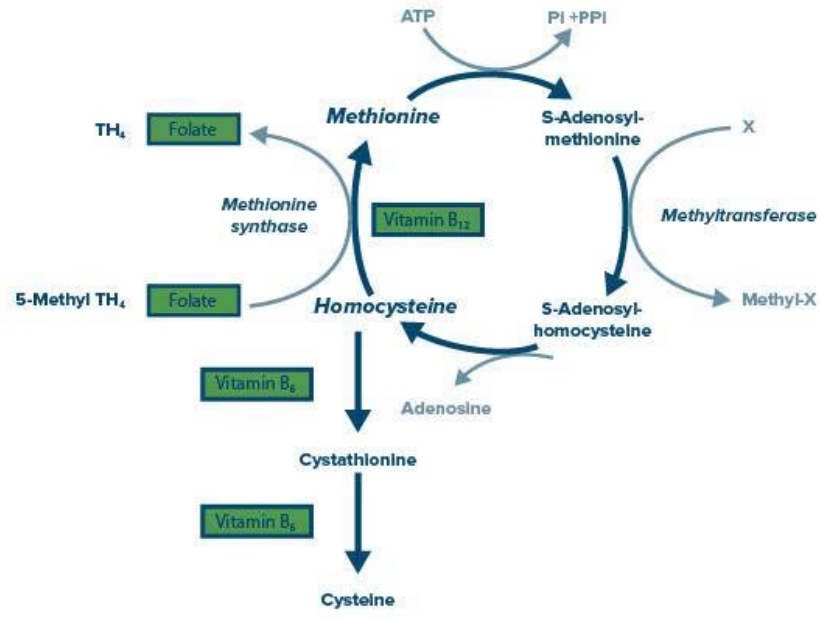
Caveat: Without discriminating features of Shprintzen Goldberg syndrome, Loeys-Dietz syndrome, or vascular Ehlers Danlo syndrome - AND after TGFBR1/2, collagen biochemistry, COL3A1 testing if indicated – other conditions/genes will emerge w time.

Homocystinuria I, II, III

- AR metabolic disorders of Amino Acid metabolism with accumulated homocysteine; prev. 1/250,000 overall but Germany 1/17,800, Norway 1/6,400, Qatar 1/1,800
- Most common form: Ectopia lentis, myopia, osteoporosis, some w developmental delay, Thrombocclusive events
- Mutations in the *CBS*,>>> *MTHFR*, *MTR*, *MTRR*, and *MMADHC* genes

Homocystinuria I, II, III

- Marfanoid habitus; fair skin & course hair
- 90% bil symmetric Ectopia lentis: **Down & IN**
- Mental retardation/seizures in 50%
- Circulation problems with thromboembolic events >>CVA hx or signs



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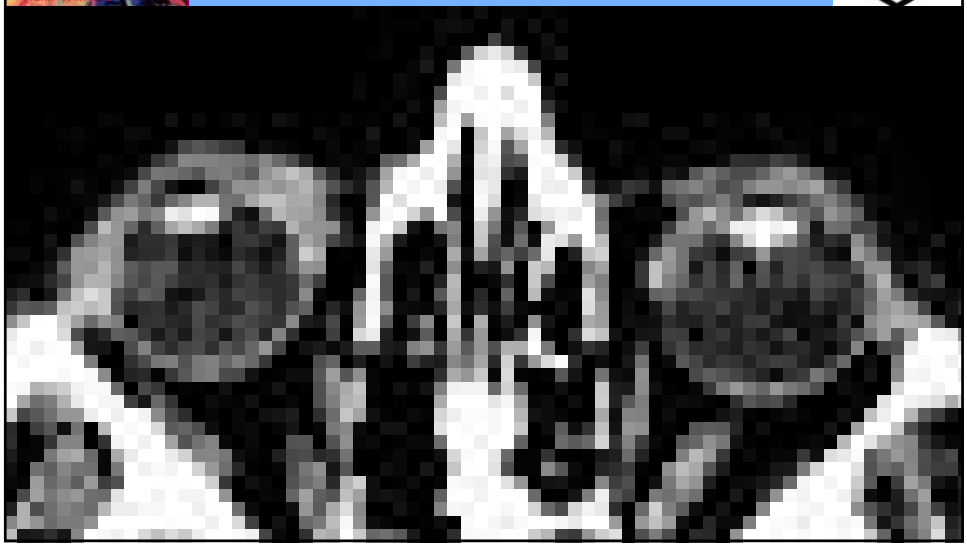

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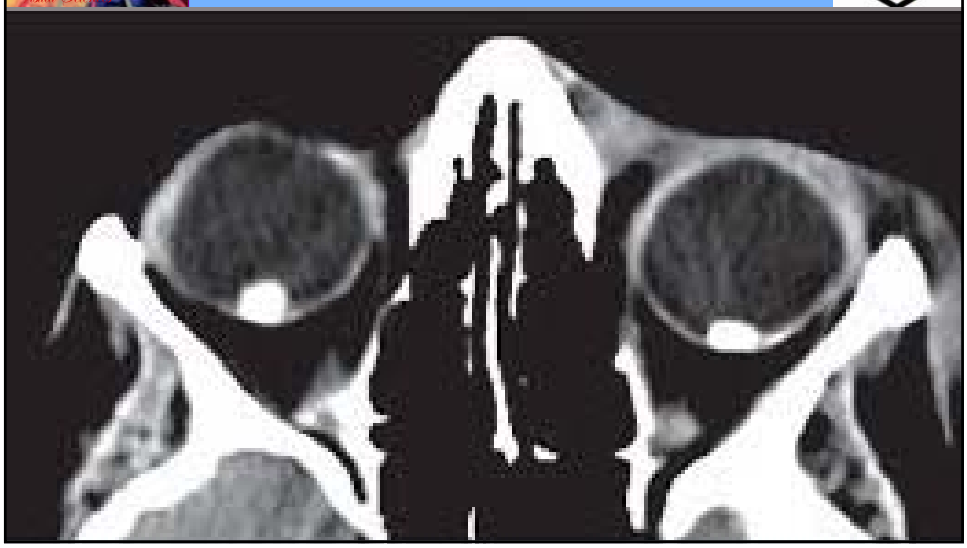
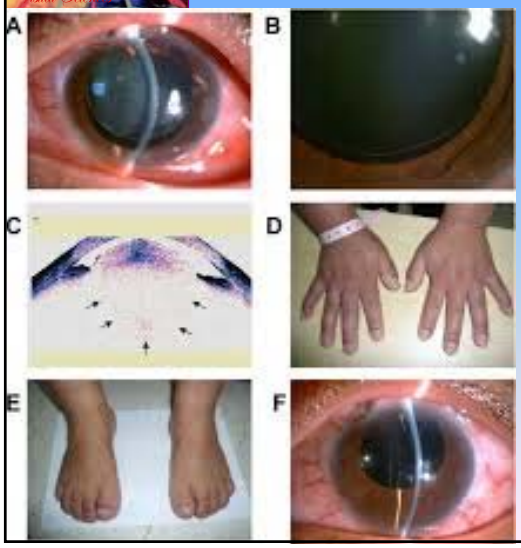
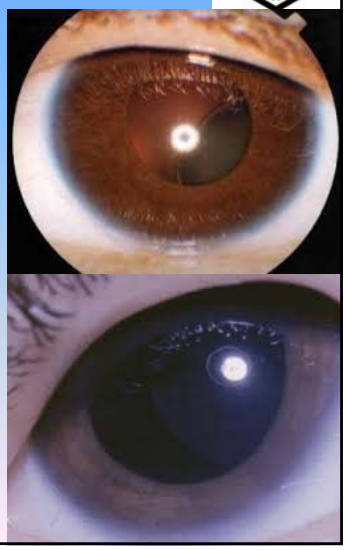


Ectopia Lentis

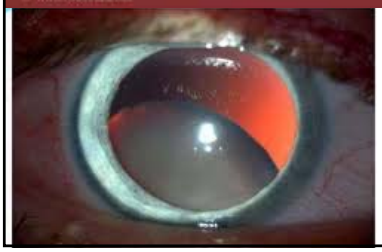
- Weill-Marchesani Syndrome
  - Short stature and fingers
  - IQ reduced in 25% - most Normal
  - Microspherophakia – lenticular myopia
  - Pupillary block or luxation to AC (OAG +NAG)
  - Angle developmental abnormalities and Glaucoma
  - Occ heart defects
  - Inheritance: AR + AD form with same fibrillin gene abnormalities as isolated Ectopia lentis

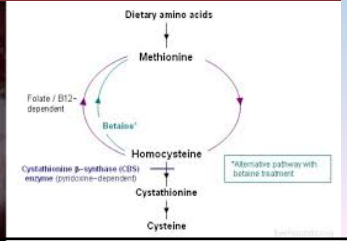
Weill-Marchesani





Homocystinuria I, II, III





Sulfite oxidase deficiency

- Metabolic defect of Sulfur metabolism
  - Ectopia lentis
  - Progressive CNS abnormalities in first yr.

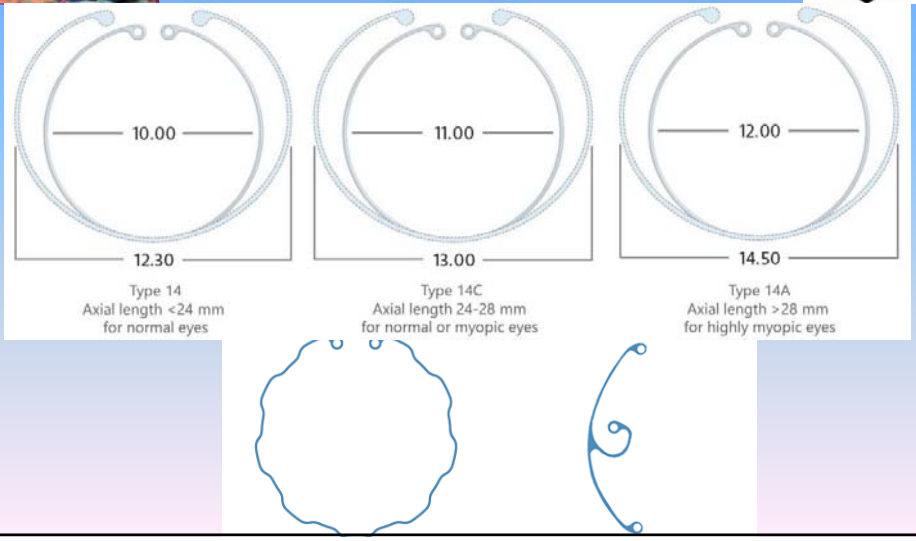
Hyperlysinemia

- AR metabolic defect of lysine
  - Ectopia lentis
  - Mental retardation

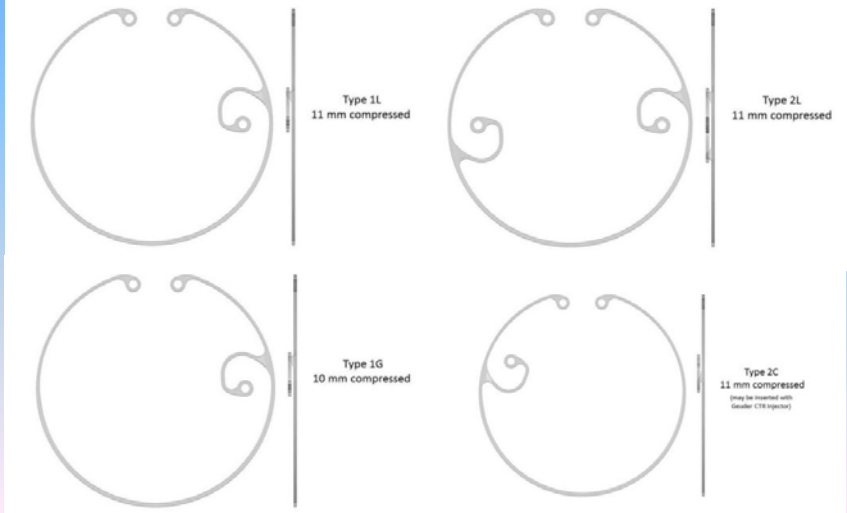
Other syndromes assoc. with Ectopia Lentis

- Ehlers-Danlos Syndrome
- Crouzon Disease
- Refsum syndrome
- Kneist syndrome
- Mandibulofacial dysostosis
- Sturge-Weber syndrome

Capsular fixation options Morcher CTRs



Capsular Fixation Options Cionni CTRs



ACIOL Relocation

- 53 yo LAM w AVM> seizure disorder, depression and peptic ulcers
- RRDs OU
- CE 1998 Galveston > Sil oil and now HM at 4 ft
- OS pneumatic retinopexy then CE uncompl then 3yrs later IOL dislocation>> PPV and ACIOL > 2yrs later dislocation

ACIOL dislocation with corneal edema