

Kalıtsal Metabolik Hastalıklar ve



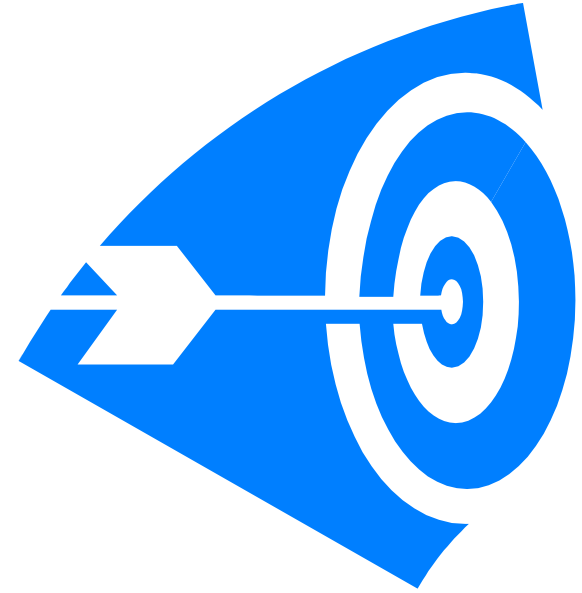
Dr. Şengül Özdek



GAZİ ÜNİVERSİTESİ TIP FAKÜLTESİ GÖZ HASTALIKLARI AD,
ANKARA

Göz Tutulumu

- En az %25'inde
- En sık etkilenen 4. sistem





Metabolik hast-Oftalmoloji

- Bilinen metabolik hastalık Göz tutulumu?
- Primer göz patolojisi Metabolik hastalık?



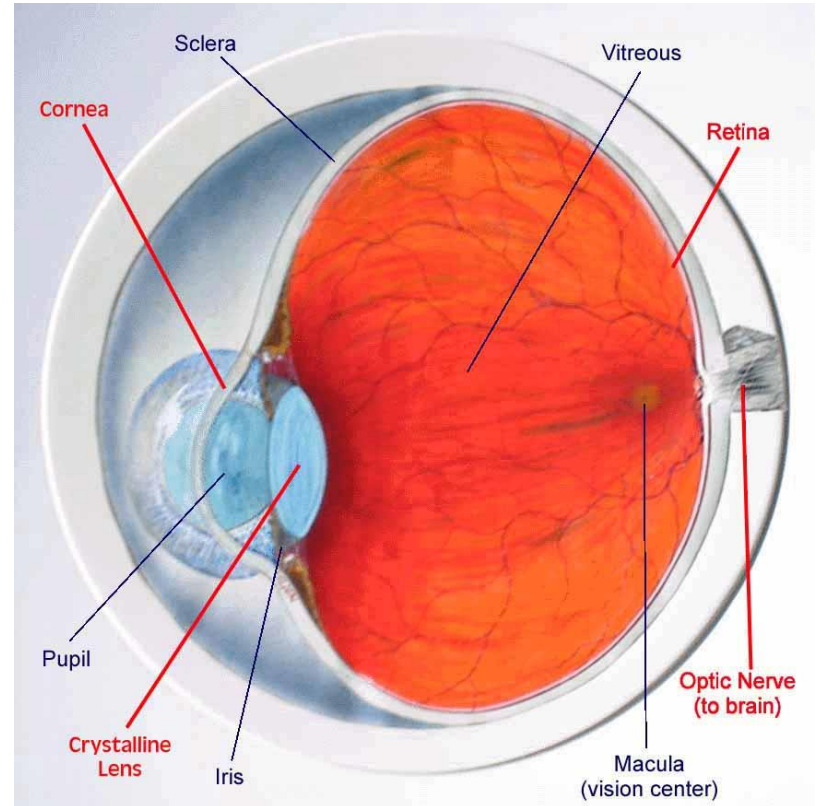
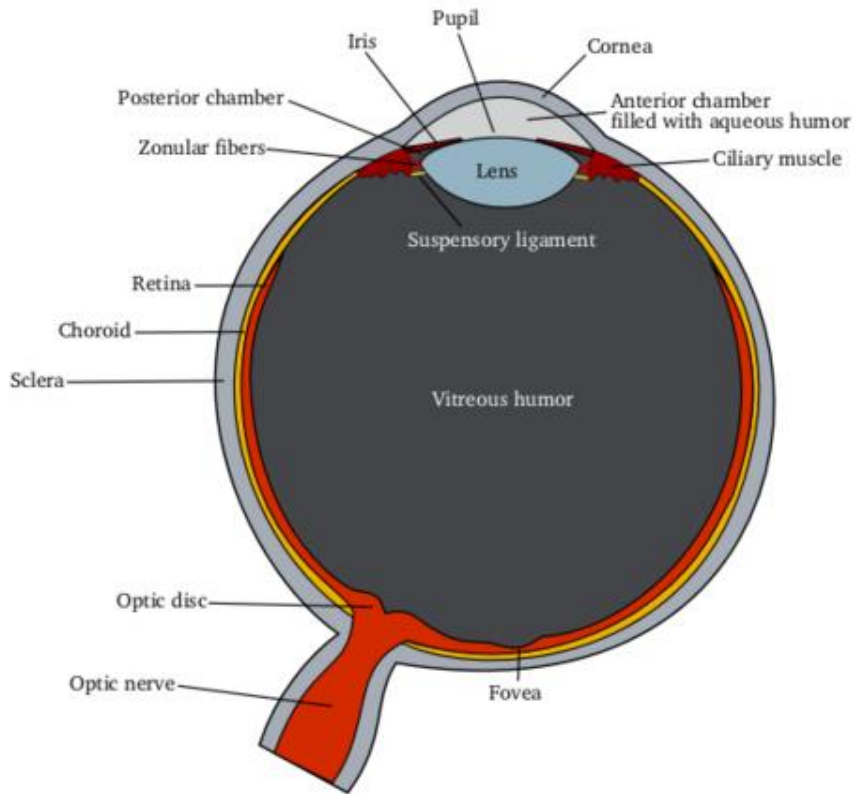
Oküler Tutulum

- İzole oküler / Sistemik multiorgan tutulumu
- Bilateral/simetrik

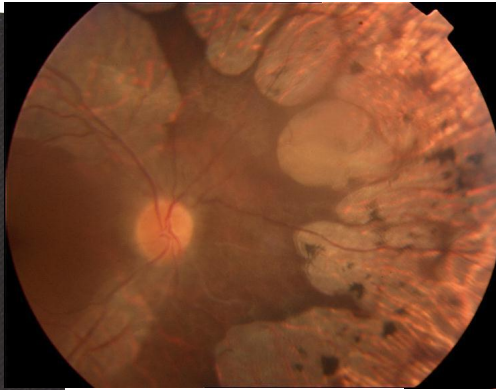
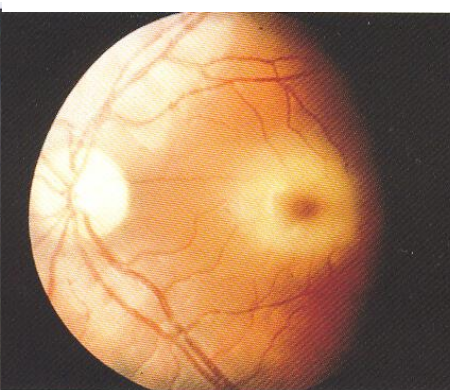
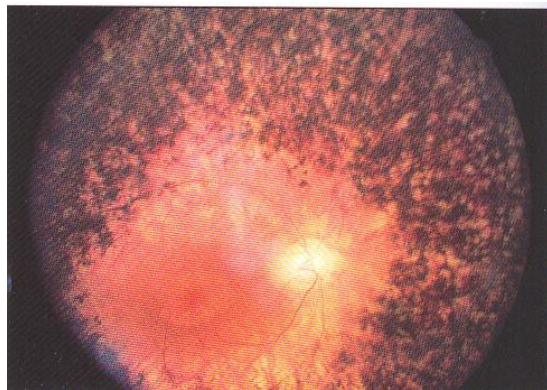
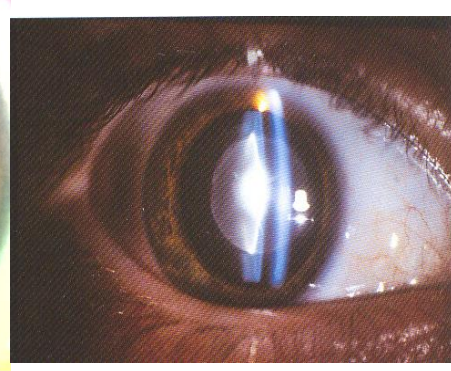
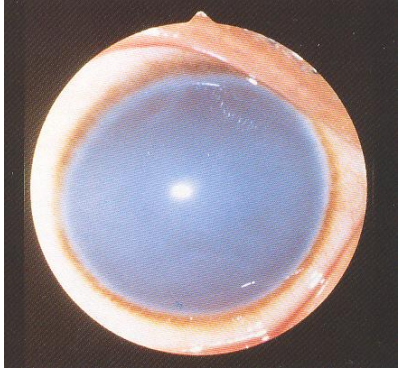
Patogenez

- Anormal metabolitlerin direkt toksik etkisi
- Normal metabolitlerin birikimi

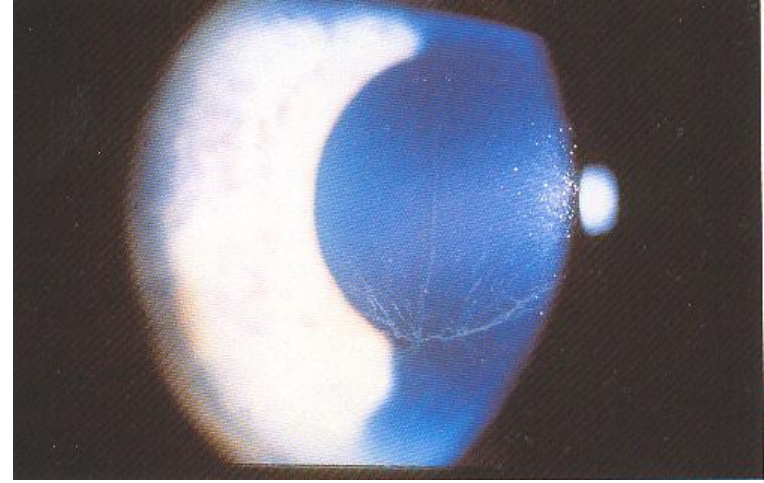
Göz Anatomisi



Göz Tutulumu



Kornea Tutulumu





Kornea Tutulumu

Lizozomal Depo Hastalıkları

- *Mukopolisakkaridoz* tip 1, 4, 6, 7
- Sfingolipidozis: Fabry, Multiple Sulfataz Eksikliği
- Mukolipidozis tip 2, 4 (Oligosakkaridoz), Galaktosialidozis, Gangliosidozis

Lipid ve Lipoprotein Metabolizma Bozuklukları

- Hiperlipoproteinemiler
- Hipolipoproteinemiler:
 - Lesitin-kolesterol açıltransferaz eksikliği, Tangier Hast, *Balık gözü hast.*

Aminoasit Metabolizma Bozuklukları

- Tirozinemi tip 2
- *Sistinozis*
- Alkaptonüri

Nükleik Asit Metabolizma Bozuklukları

- Gut Hastalığı, Xeroderma pigmentozum

Mineral Metabolizma Bozuklukları

- Wilson hastalığı (Cu), Hemakromatozis (Fe)



Mukopolisakkaridozlar

Hurler Send (MPS I-H): En sık

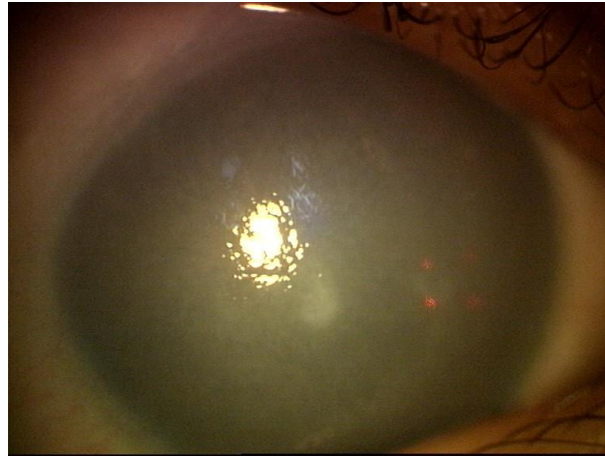
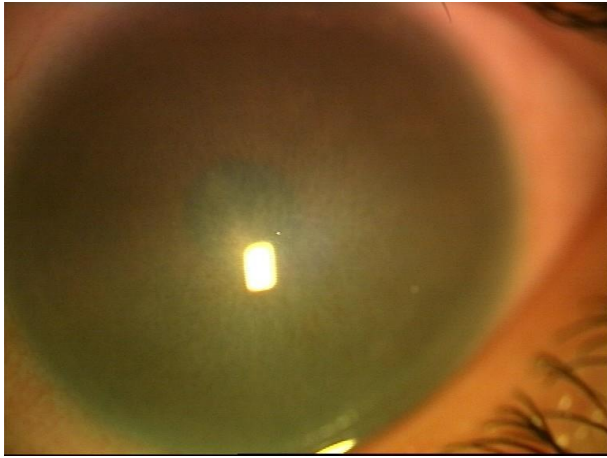
- Korneal depositler: Heparan ve Dermatan Sülfat
- 2. dekatta ölüm
- *Korneal bulanıklık ve fotofobi: 1-3 yaş*
- Optik atrofi ve retinal hastalıklar

■ Scheie's Send (MPS I-S): En hafif MPS

- *Korneal bulanıklık ve fotofobi: >4 yaş*
- Optik atrofi ve retinal hastalıklar

Mukopolisakkaridozlar

- Hurler ve Scheie (+++)
- Hunter ve Sanfilippo (-)
- Ted: PPK



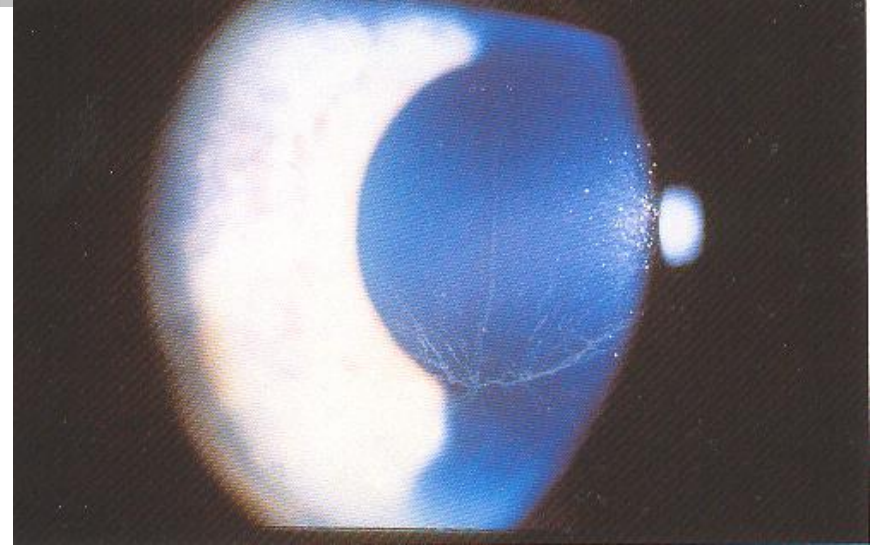
Sfingolipidozis

Fabry hastalığı

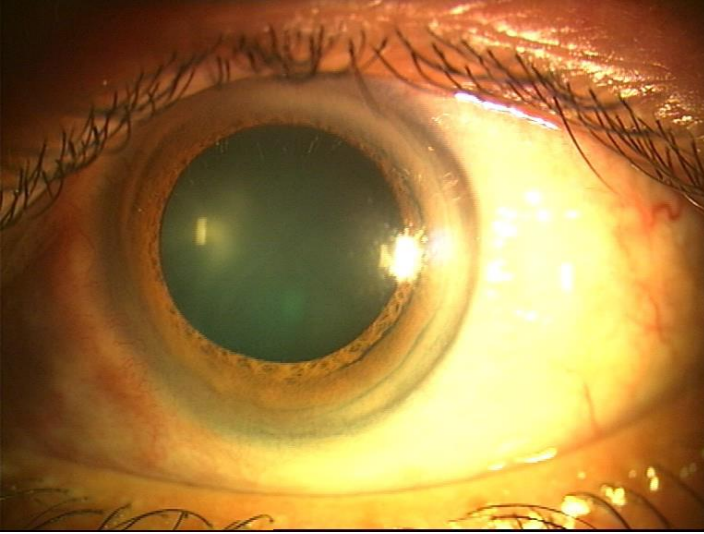
- α -galaktosidaz A eksikliği
- X'e bağılı resesif
- Bazal epitel tabakasında birikim: asemptomatik

Kornea verticillata-vorteks keratopati: Tipik (ilk dekad)

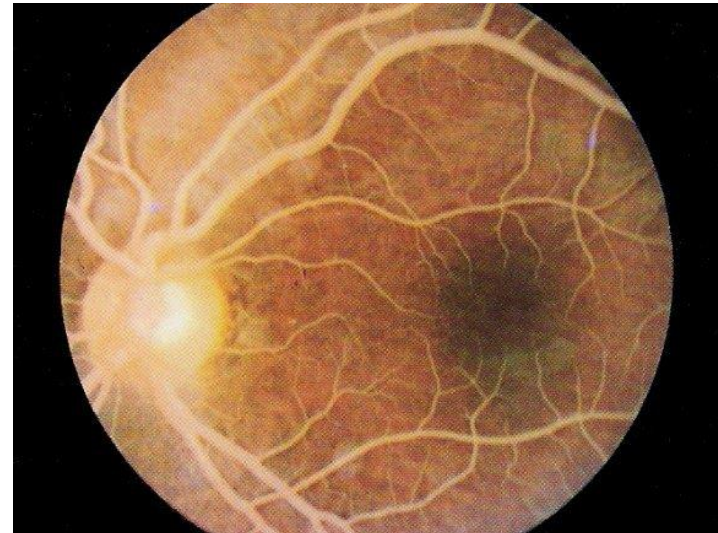
- Taşıyıcı K (+)
- Katarakt (%37), optik atrofi,
- Konjonktiva ve retina damarlarında telanjiektazi ve tortuosite artışı: %70



Lipid ve Lipoprotein Metabolizma Bozuklukları

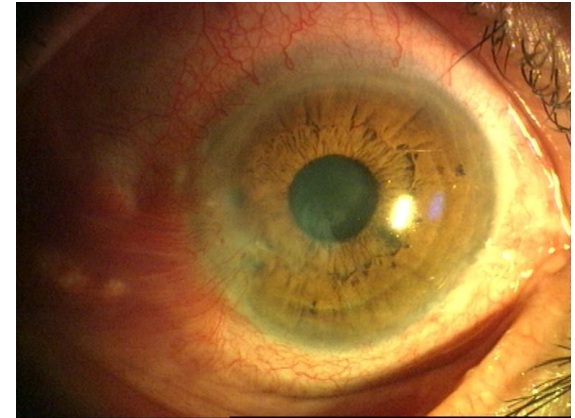
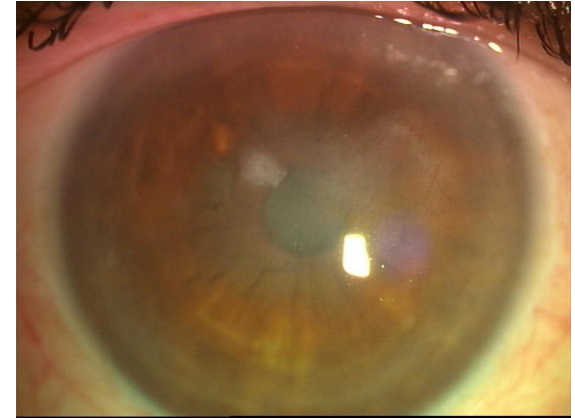


- Hiperlipoproteinemiler
 - Korneal arkus
 - Ksantelazma
 - Lipemia retinalis



Hipolipoproteinemiler

- Lesitin-kolesterol açiltransferaz (LCAT) eksikliği,
- Tangier Hast.
- Balık gözü hast.
- *Arkus ve diffüz stromal haze*



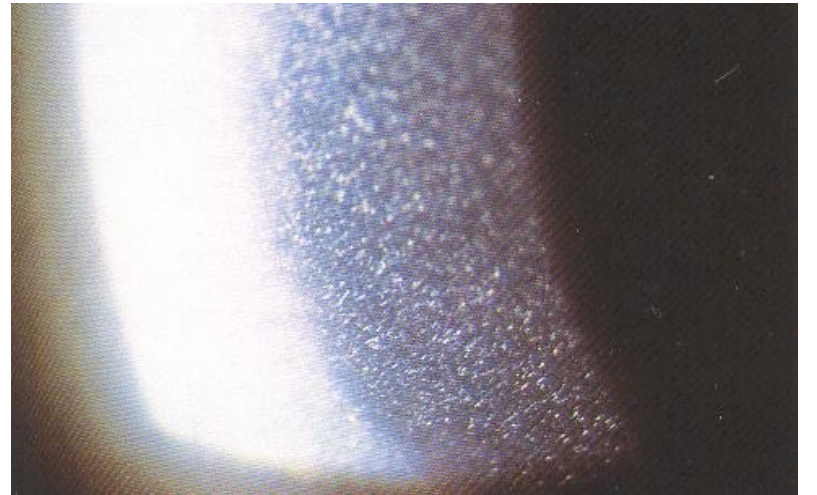
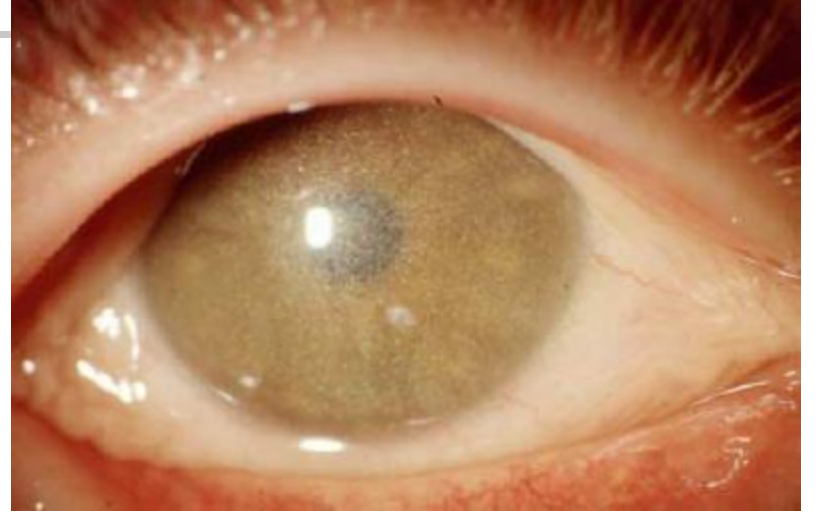


Aminoasit metabolizma bozukluğu

- Sistinozis:
 - Fotofobi, Korneal kristaller
- Tirozinemi tip 2:
 - Fotofobi, Kristaller
- Alkaptonüri:
 - Kornea ve sklerada pigmentasyon

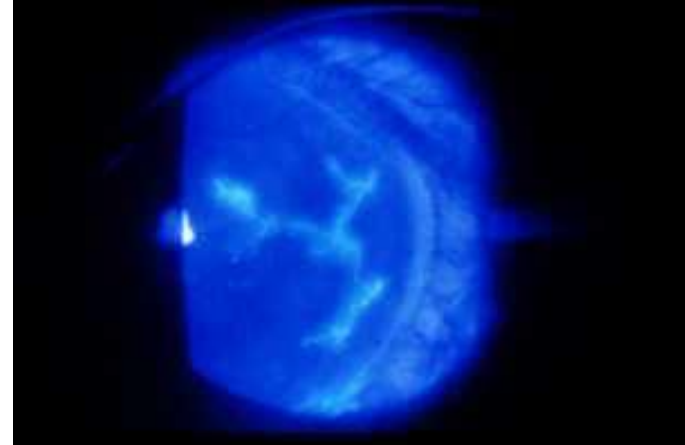
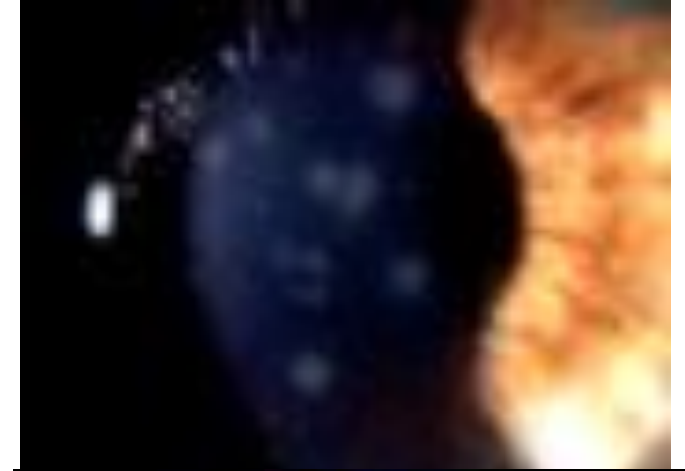
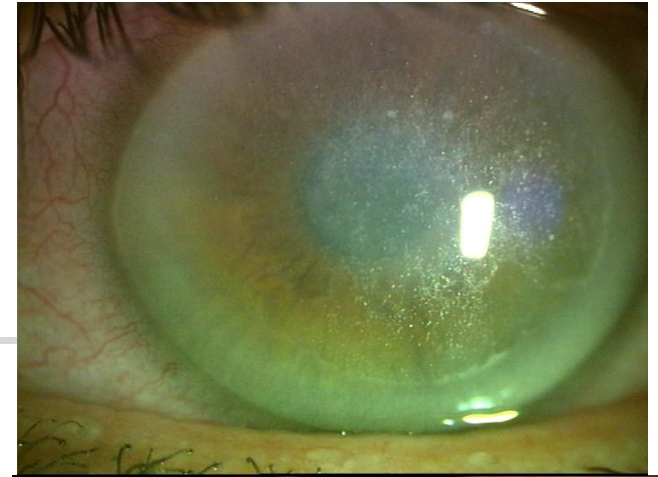
Sistinozis

- *İnfantil (nefropatik)*, adolesan, erişkin tip
- Korneada kristal benzeri sistein birikimi: **ilk bulgu!..**
- **Fotofobi**, korneal duyu↓
- Tekrarlayan korneal erozyonlar
- Lens ve retinada birikim olabilir
- Topikal sisteamin damlası
- Keratoplasti



Tirozinemi - Tip 2

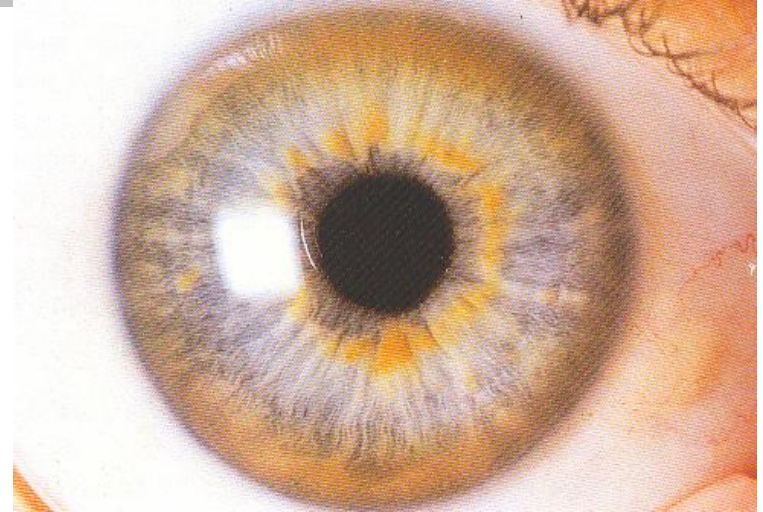
- Keratokonjonktivit
- **Fotofobi**: Erken dönemde (ilk 2 hafta içinde): **ilk bulgu!**..
- Korneada yüzeyel kristalin depozitler-dentritiform opasiteler
- Ted: Plazma tirozin düzeylerinin normalizasyonu ile 5 günde kristaller kaybolur.



Mineral Metabolizma Bozukluđu

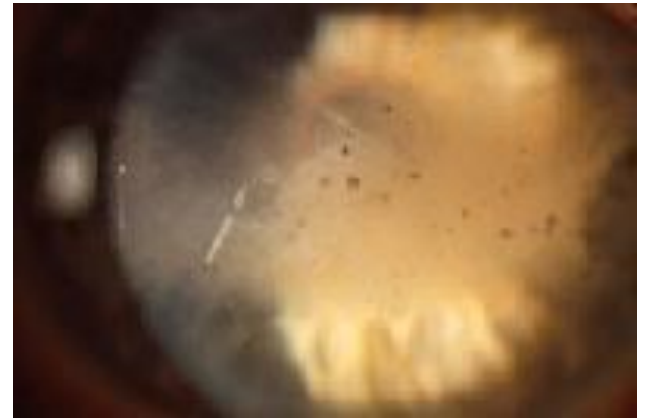
Wilson Hastalığı (Cu)

- Descemet tabakasında bakır birikimi
(Kayser-Fleischer halkası)
- “Günebakan kataraktı”
- Reversible
(D-penicillamine)
- Tedaviye cevabın monitörizasyonu

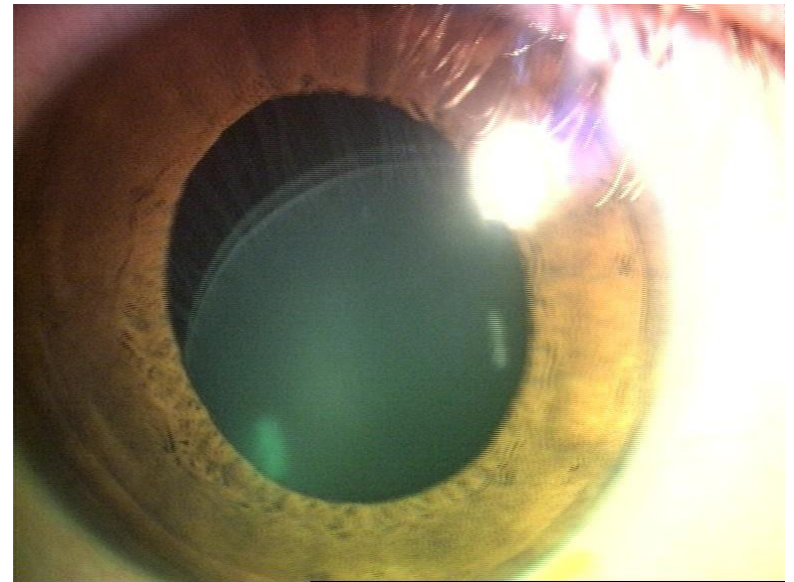
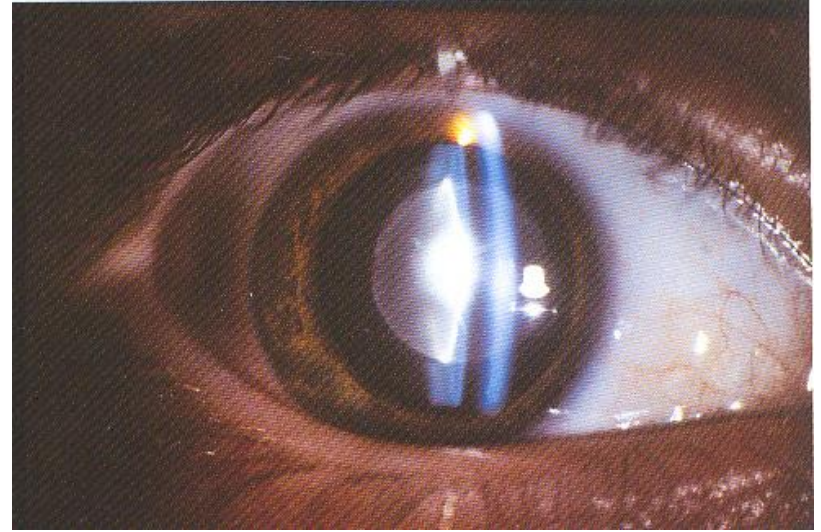


Nükleik Asit Metabolizma Bozuklukları

- Gut Hastalığı:
 - Sıcak gözler:
konjonktival hiperemi
ve iridosiklit atakları
 - Band keratopati



Lens tutulumu

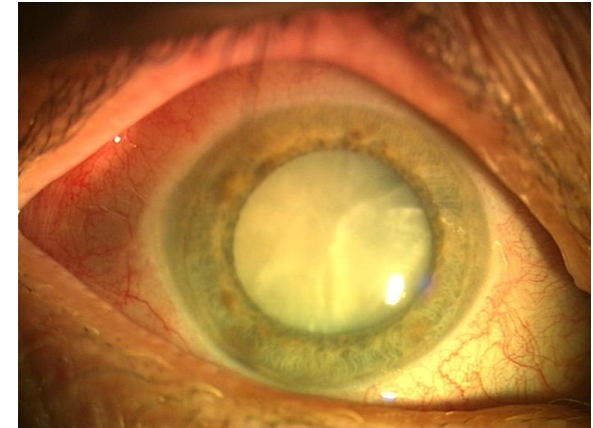
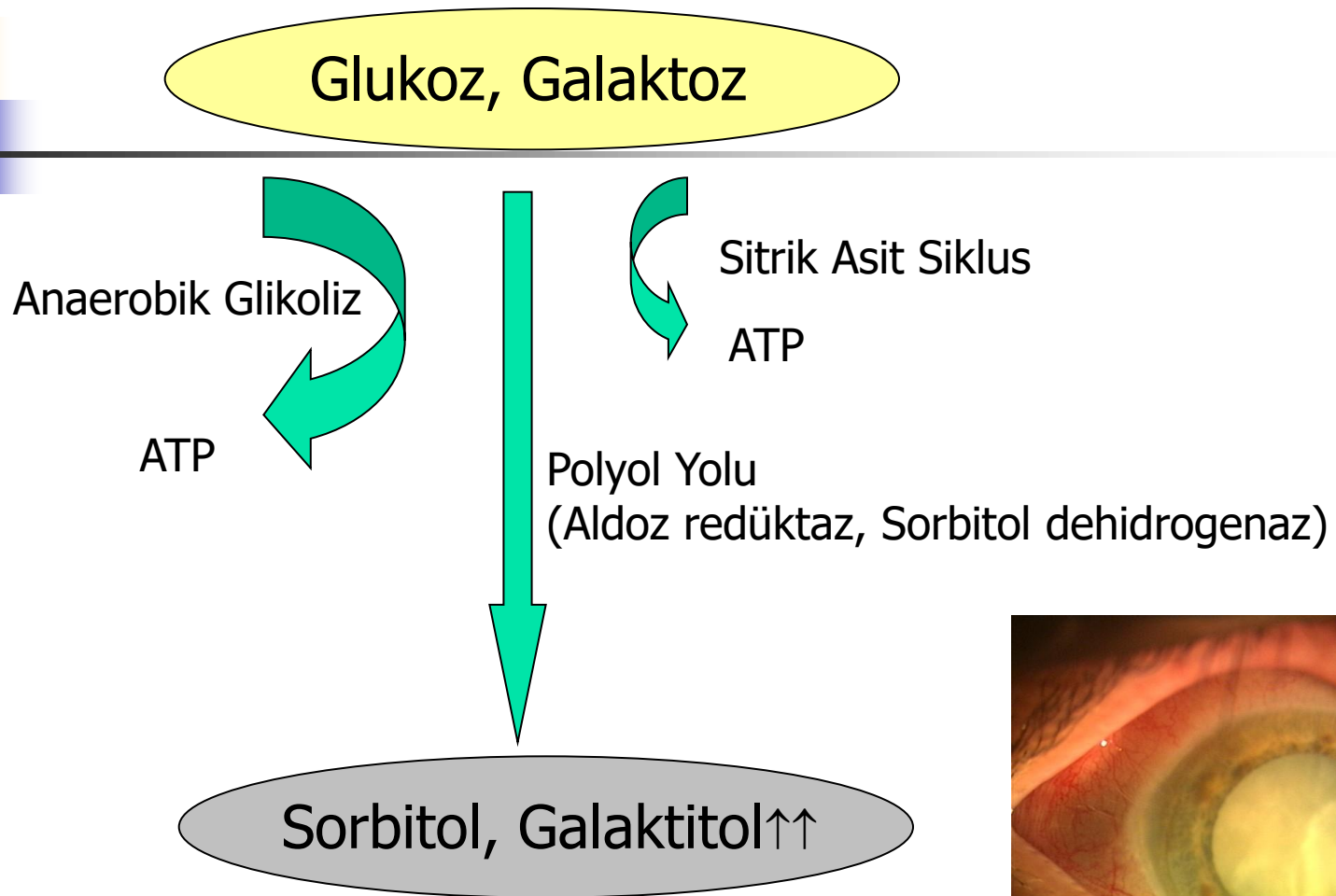




Katarakt

- **Şeker metabolizma bozuklukları**
 - **Galaktozemiler**
 - Sorbitol dehidrogenaz eksikliği
- **Kolesterol metabolizma bozukluğu**
 - Mevalonat kinaz eksikliği (klasik form)
 - Kolestanol lipidozis
 - Konradi-Hünemann Send, Smith-Lemli-Opitz Send
- **Lizozomal hastalıklar**
 - Oligosakkaridoz : α -mannosidoz, sialisidoz, galaktosialisidoz
 - Fabry hastalığı
- **Peroksizomal hastalıklar**
 - Peroksizom biogenez defektleri
 - Rizomelik kondrodisplazia punktata
- **Wilson hastalığı**
- **Lowe Sendromu**

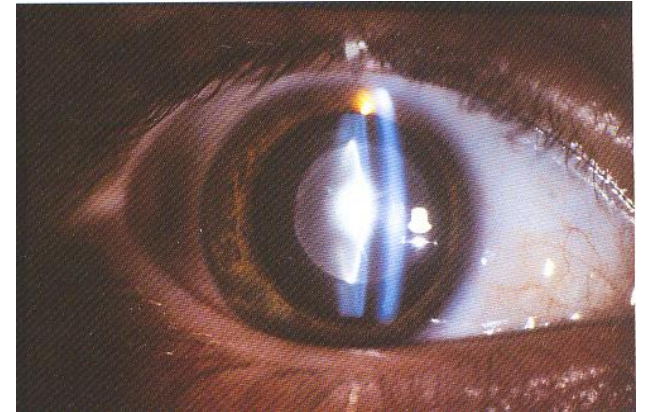
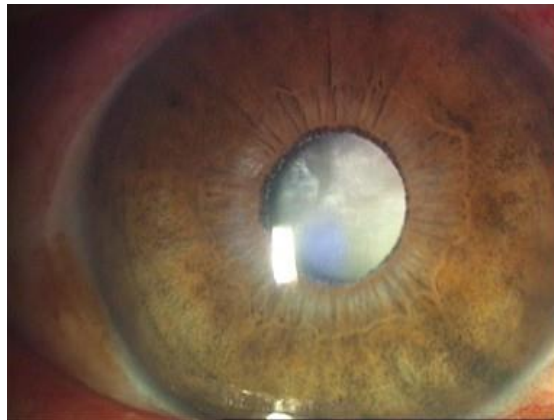
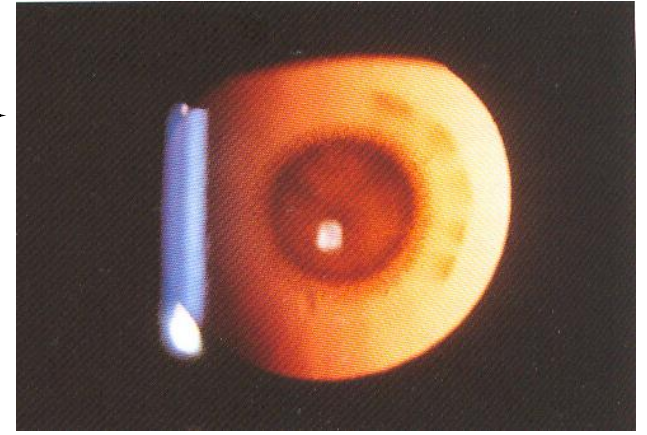
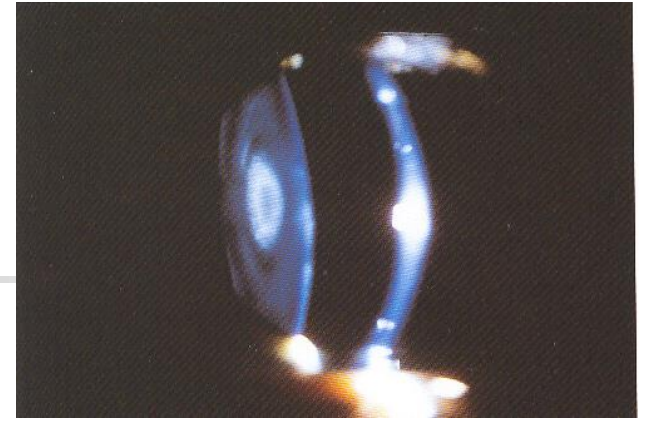
Lens şeker metabolizması



Galaktozemi

Bütün galaktozemi tiplerinde katarakt gelişir.

- Doğumda veya ilk haftalarda
- "Yağ damlacığı" Tipik
- Galaktokinaz eksikliğinde katarakt tek bulgu olabilir
- Diyet yapılmazsa lens tamamen opaklaşır



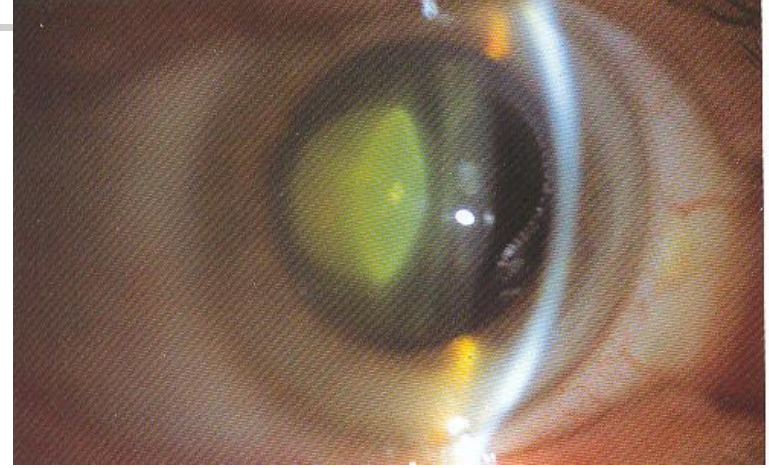
Kolesterol Metabolizma bozuklukları

Lens membranı



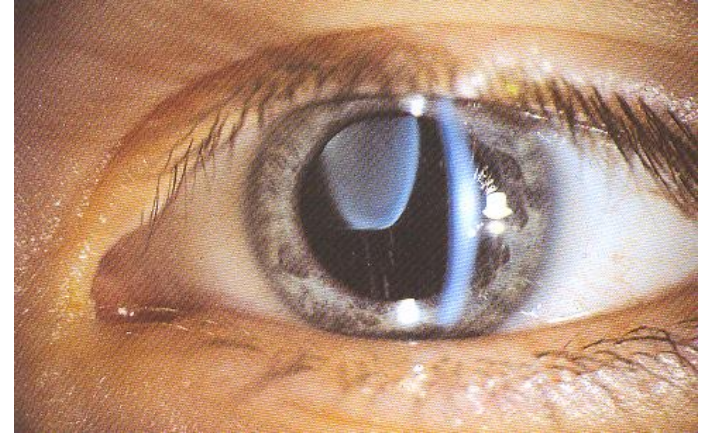
kolesterolden zengin

- Kolesterol sentez bozukluğu
- Mevalonat kinaz eksikliği
- Conradi-Hünemann sendromu
- Smith-Lemli-Opitz sendromu
- Serebrotendinöz xantomatozis



Lens Dislokasyonu

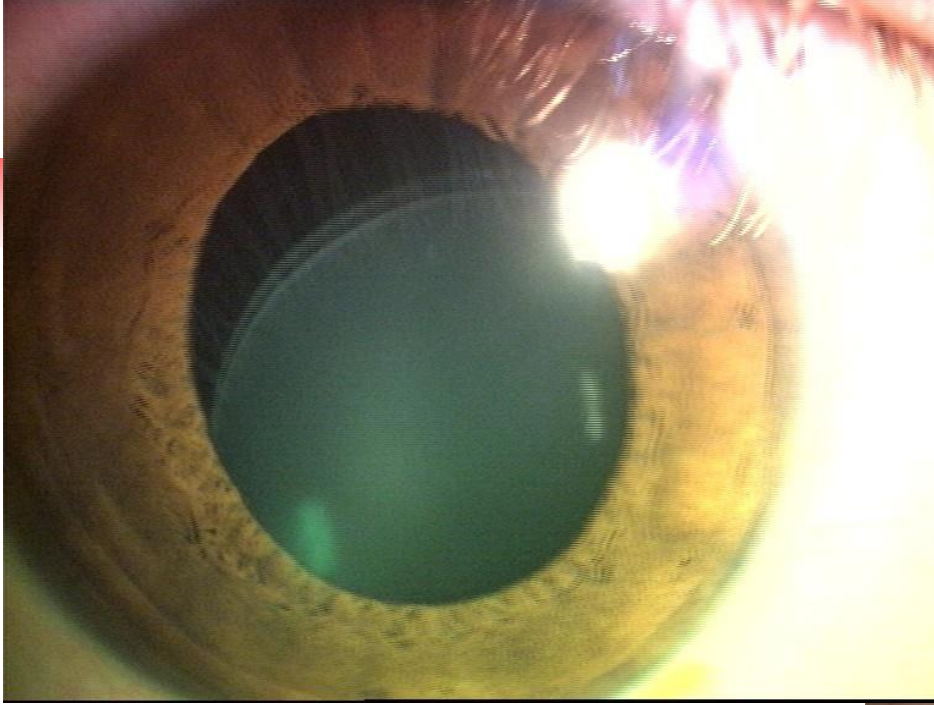
- İlk bulgu oküler
- Marfan Sendromu
(superior, %70)
- Homosistinüri
(sistatyonin β sentetaz eksikliği,
inferior, %90)
- Weill-Marchesanni sendromu
(inferior, %50)
- Sulfid-oksidad eksikliği
- Hiperlizinemi
- Ehlers-Danlos sendromu





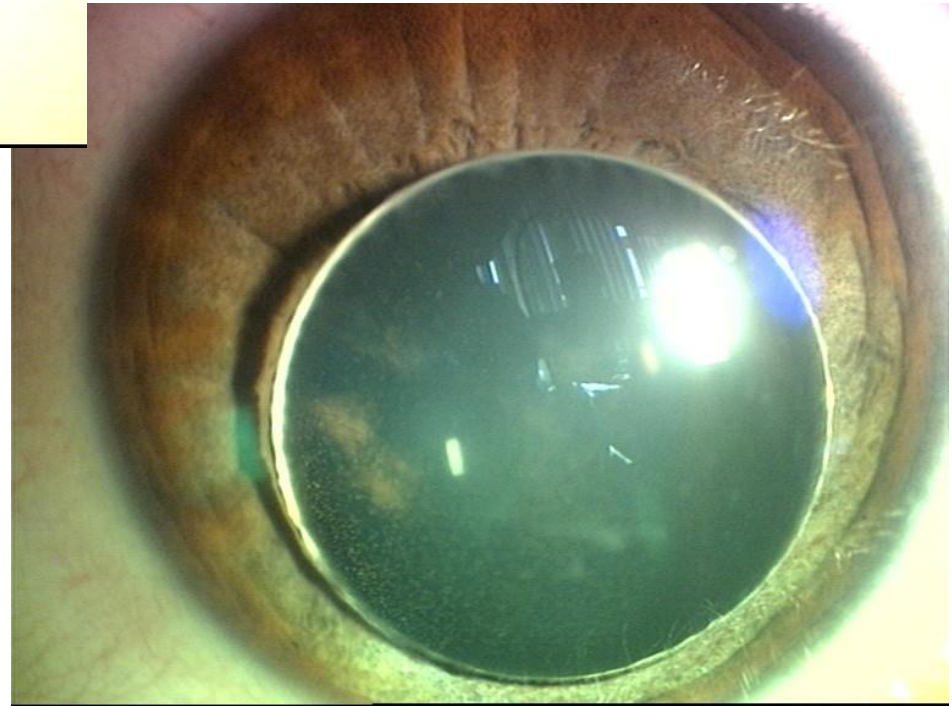
Tedavi

- Erken dönemde diyet: progresyonu↓
- Geç dönemde: Cerrahi: Lensektomi-GİL implantasyonu
- Özdek Ş, et al. Surgical treatment of hereditary lens subluxations. *Ophthalmic Surg and Lasers* 2002, Jul-Aug;33(4):309-13.
- Özdek Ş, ve ark. Homosistinüride lens dislokasyon cerrahisi ve oküler komplikasyonlar. *MN Oftalmoloji* 2005;1:17-21.



11y, K,
ŞİK: her iki gözde görme azlığı
ÖZG: mental-motor retardasyon
G: ?/?

Midriasis ve supin pozisyon
Cerrahi: sağ-sol lensektomi
önerildi
Metabolizma konsultasyonu

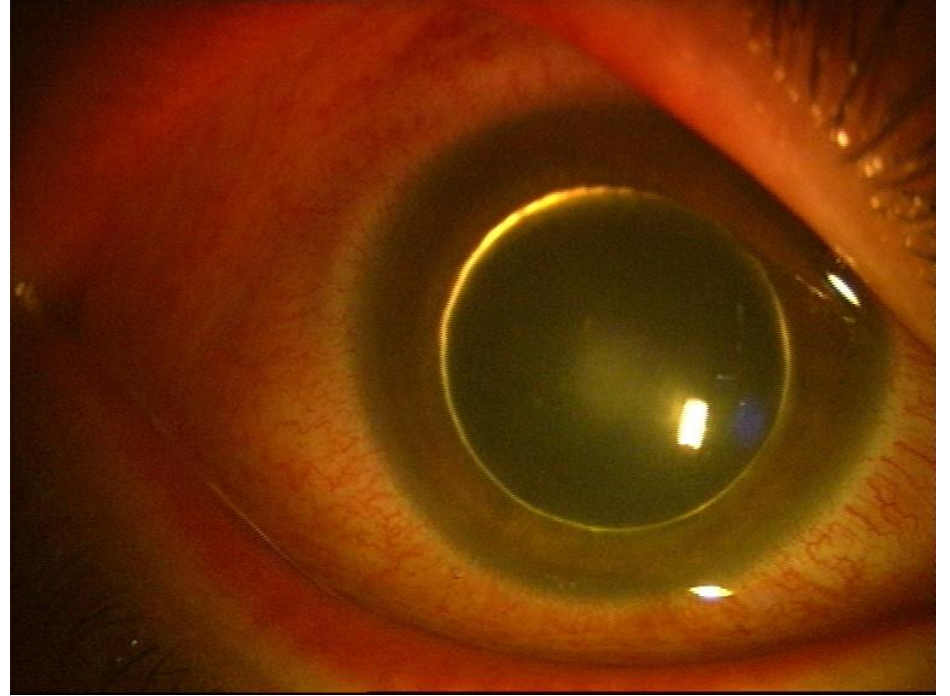


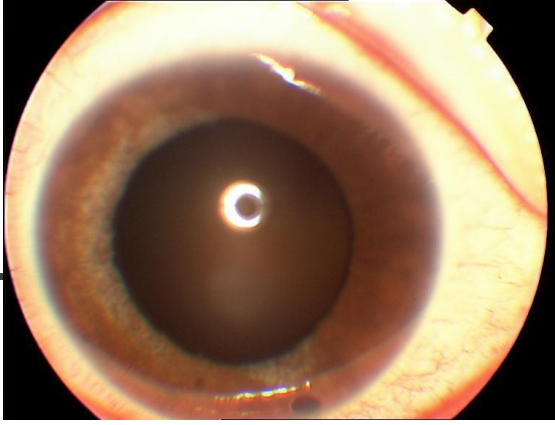
Homosistinüri

Pupiller blok gelişimi

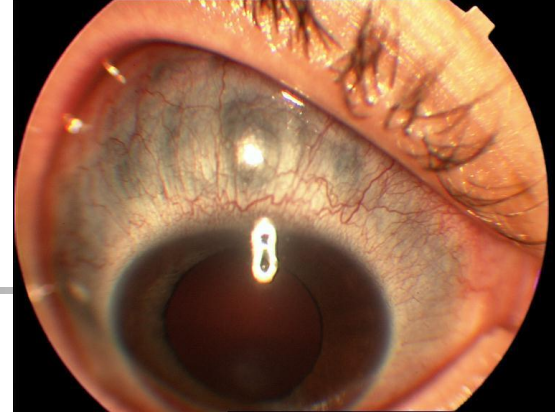


Akut glokom krizi

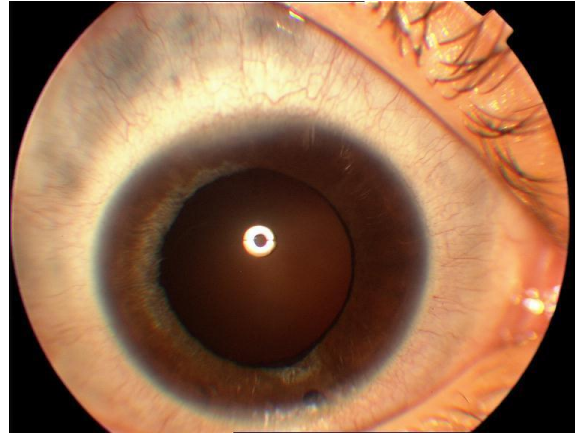




Postop erken dönem



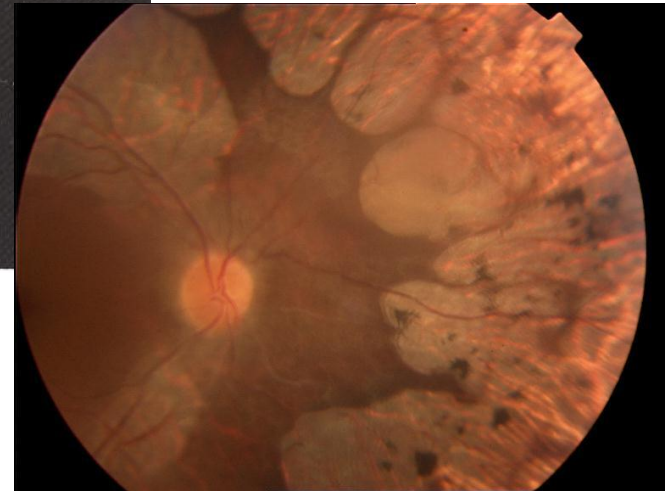
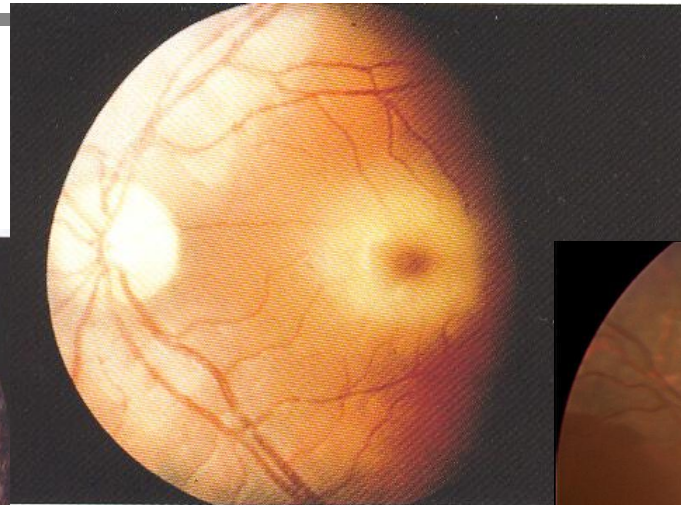
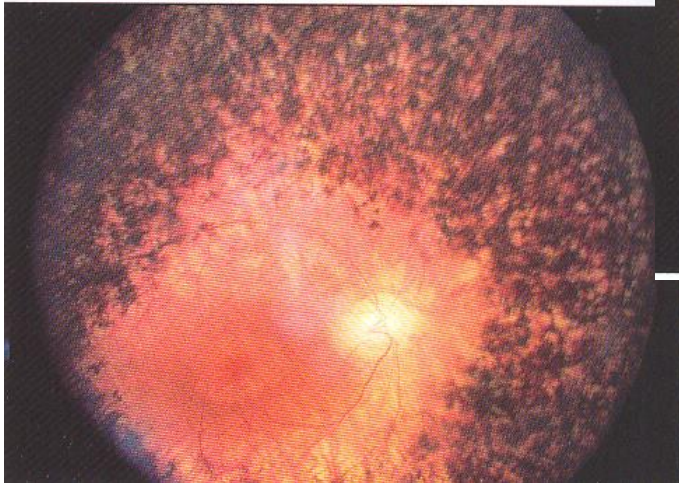
Glokom + Yoğun anterior stafilom (Postop 2. ay)



Gerileyen ant. stafilom

Ozdek S, et al. Postoperative secondary glaucoma and anterior staphyloma in a case with homocystinuria. *Ped Ophthalmol Strabismus*, 2005 (in press)

Retina Tutulumu



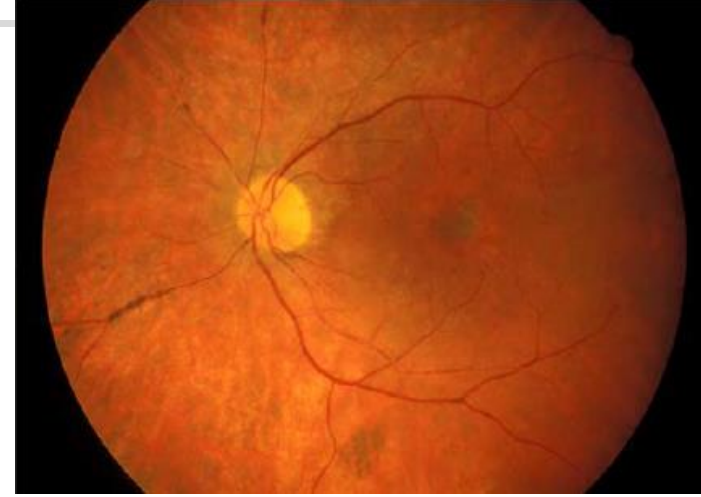
Metabolik hastalıklar ve Retina



- **Lipid metabolizma bozukluğu**
 - Abetalipoproteinemi
 - Refsum hastalığı
- **Lizozomal hastalıklar**
 - Nöronal seroid lipofusinozis
 - Mukopolisakkaridozlar (morquio dışında)
 - Mukolipidozis tip 4, Krabbe hastalığı
- **Kearn-Sayre hastalığı (mitokond. en. Metab.)**
- **Menkes hastalığı (Cu metab.)**
- **Gyrate atrofi (izole)**
- **Kobalamin C bozukluğu**

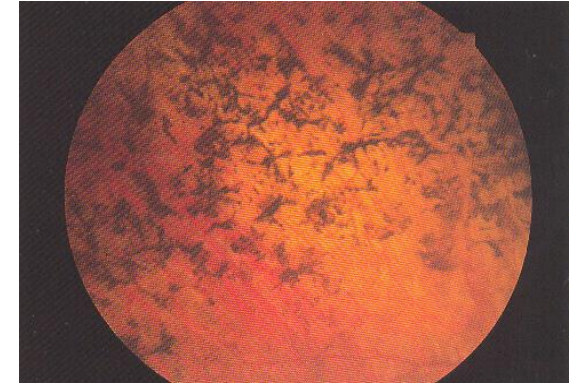
Pigmenter retinopati

- Gece körlüğü, progresif periferik görme alanı kaybı
- Bilateral fotoreseptör ve RPE distrofisi



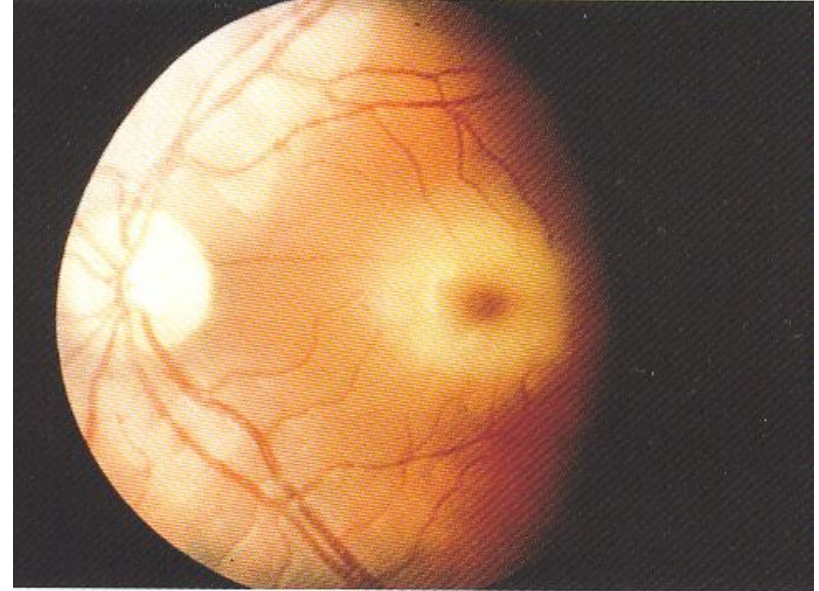
Pigmenter retinopati

- Optik diskte solukluk
(Bal mumu görünümü)
- Arterlerde incelme
- Retinal pigmentasyon
(Kemik spikülleri)
- Korioretinal atrofi
- Ciddi görme kaybı



Japon Bayrağı Görünümü (Cherry-Red Spot)

- Tay-Sachs hastalığı (GM2, Variant B, infantil) %100
- Sandhoff hastalığı (GM2, Variant O, infantil) %100
- Sialidozis tip 1,2: %100
- GM1-gangliosidozis (infantil tip):
Çoğunda
- Niemann-Pick hastalığı tip A:
Çoğunda
- Gaucher hastalığı tip 2
- Farber lipogranülopatisi
- Metakromatik lökoadistrofi
- Galaktosialidozis (infantil tip)



Makülada Japon Bayrağı

- Retinada ganglion hücre tabakasında glikolipid ve fosfolipid birikimi



retinada beyaz görünüm

- Foveolada ganglion hücre tabakası yok
- Geç dönemde kaybolur
- Retinal atrofi ve optik atrofi belirginleşir
- Ciddi görme kaybı

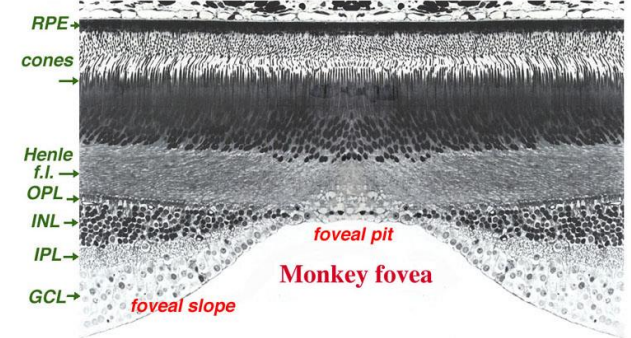
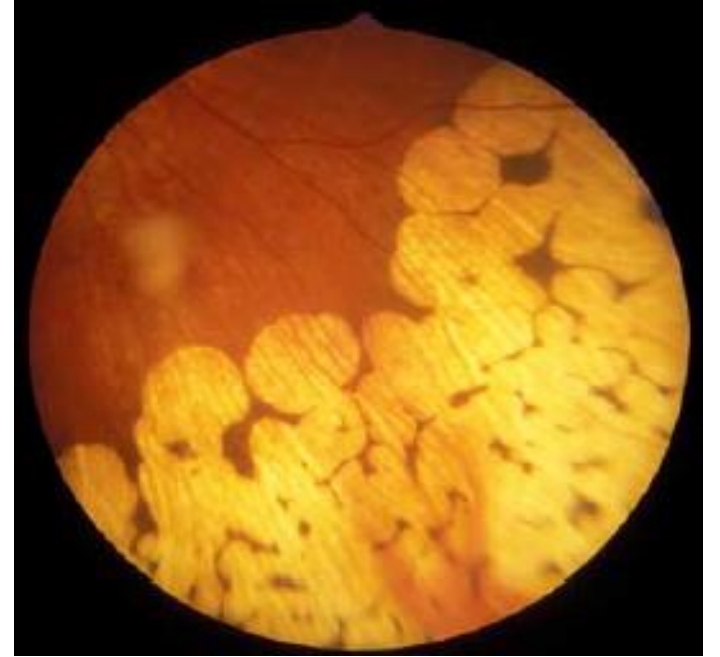


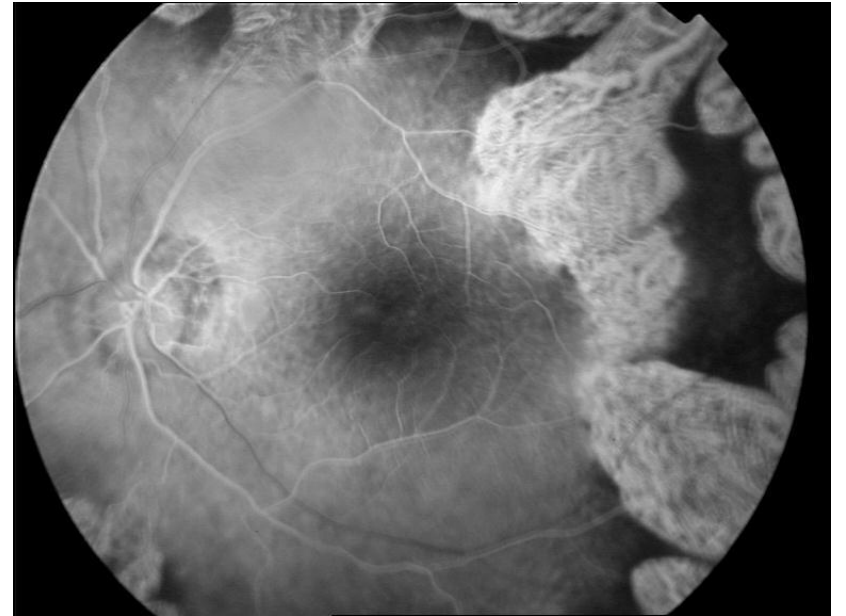
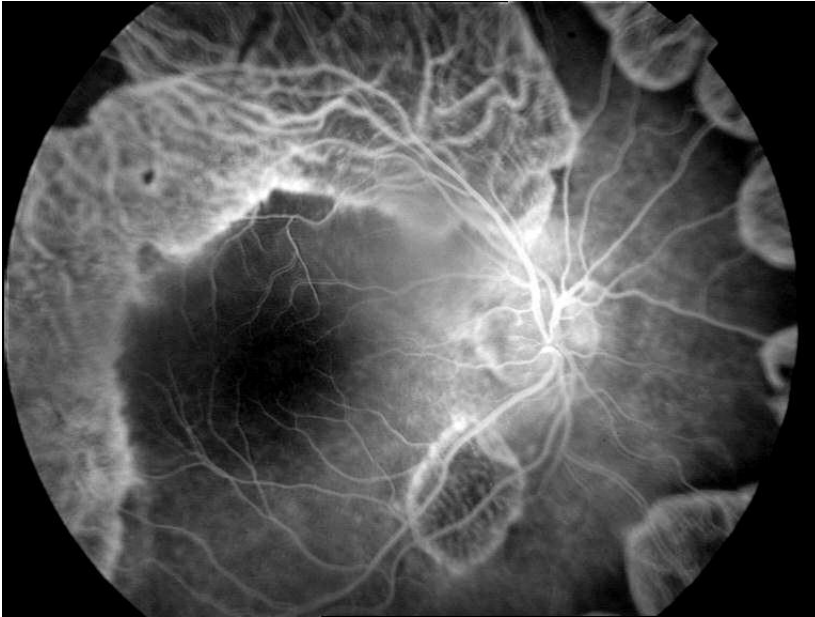
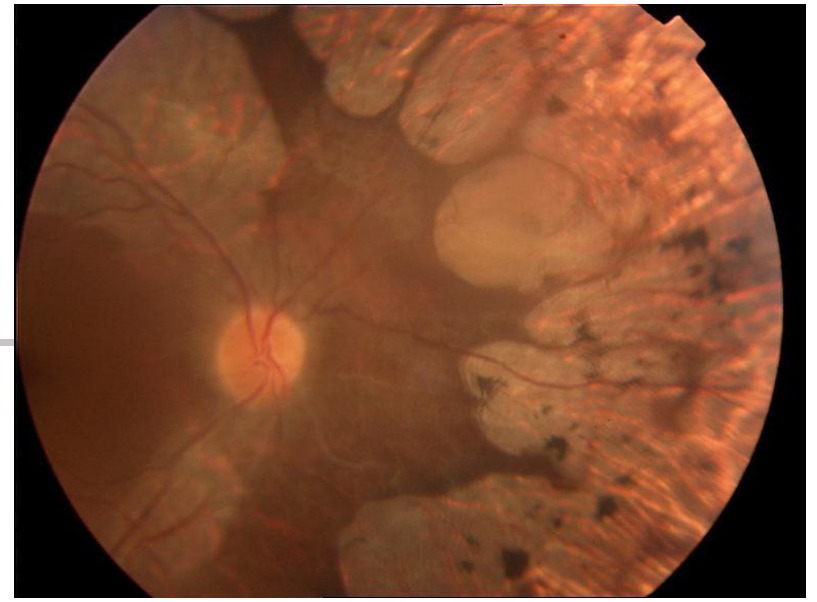
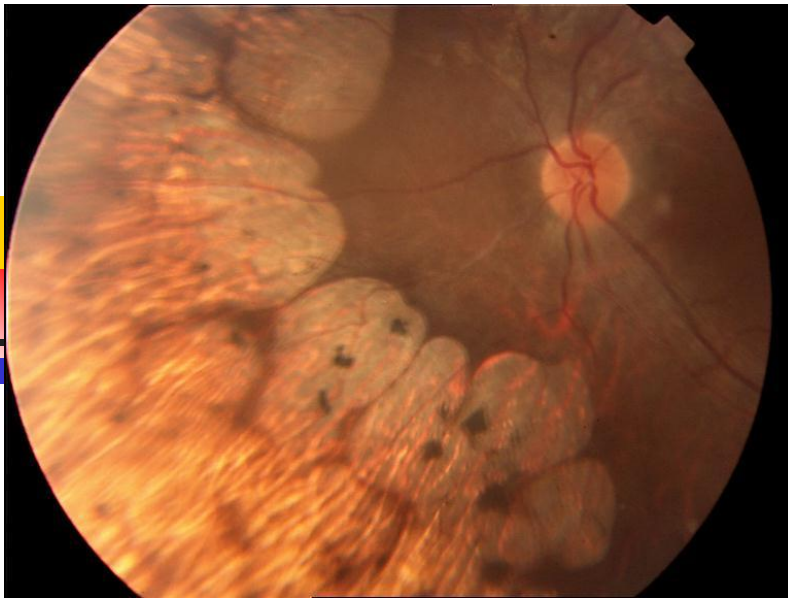
Fig. 12b. Vertical section of the monkey fovea from Hagerman and Johnson (1991).



Gyrate Atrofi

- Ornitin aminotransferaz eksikliđi
- Otozomal resesif
- İzole göz tutulumu
- Gece körlüğü, periferik görme kaybı
- Santral görme genellikle korunur
- Arjininden fakir diet, pridoksin tx

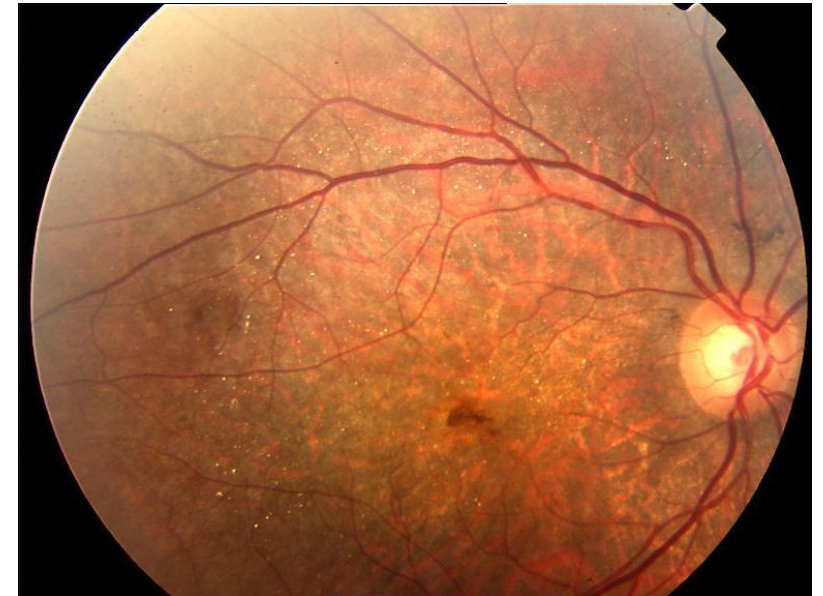




Sarı A, Özdek Ş, Gürel G, Önel M, Hasanreisöğlü B. Hiperornitinemi ile seyreden bir koryoretinal distrofi: Gyrate Atrofi. Retina-Vitreus, 2002;10:293-299.

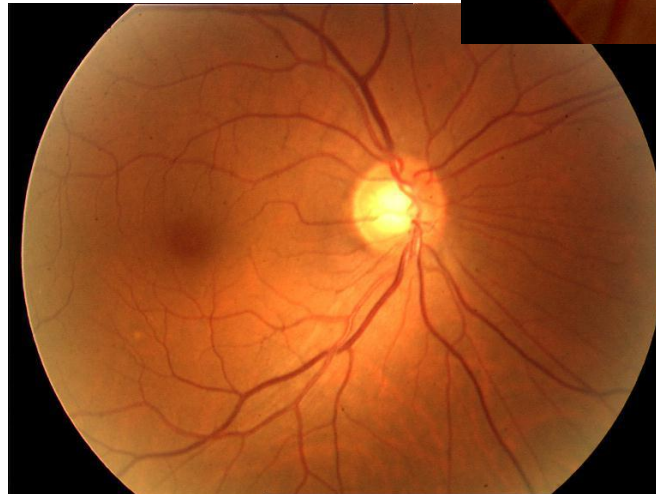
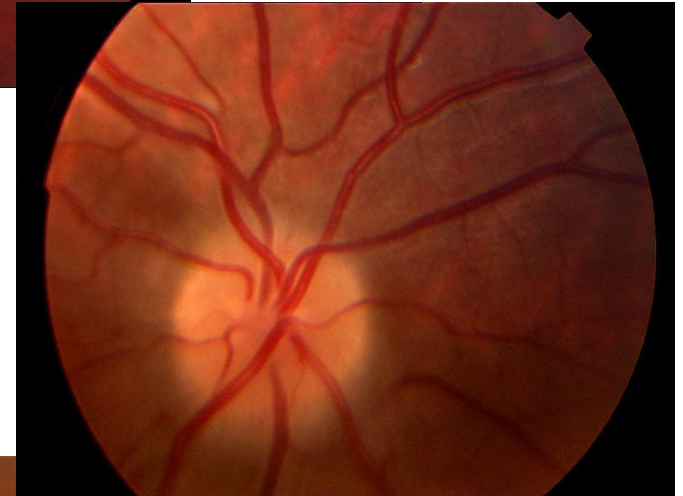
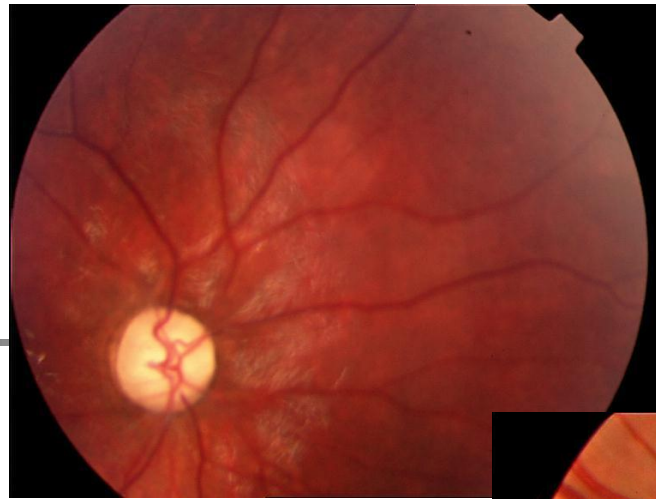
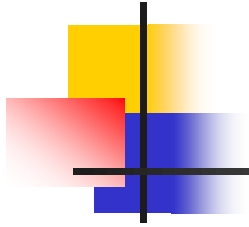
Kristalin Retinopati

- **Bietti'nin kristalin retinopatisi**
 - OR ve OD
 - Progresif korioretinal atrofi ve retinal kristaller
 - İzole oküler tutulum
 - Lipid metabolizma bozukluğu?
- **Sistinozis (infantil)**
 - RPE atrofisi





Optik Sinir Tutulumu



- Optik atrofi
- Papilödem
- Glokomatöz atrofi

Nörodegeneratif hastalıklarda Optik Nöropati



- Lökodistrofiler
- Lizozomal hastalıklar
- Mitokondri enerji metabolizma bozuklukları
- Menkes hastalığı
- Canavan hastalığı
- Friedreich ataksi
- Behr sendromu