

Retinal Disorders

Updated: May 21, 2010

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- **retina-related visual loss** is **painless** and almost always associated with **abnormality on funduscopic examination** (esp. in acute setting).
- **macular lesions** cause afferent pupillary defect only very late in course (vs. optic nerve lesions - afferent pupillary defect even with apparently normal vision).
- **retinal ischemia / hemorrhages** provoke **NEOVASCULARIZATION** (proliferation of new vessels lacking proper support → rupture, etc).

CENTRAL RETINAL ARTERY OCCLUSION (CRAO)

PATHOPHYSIOLOGY & OPHTHALMOSCOPY

- loss of blood supply to **inner layer of retina**.

- **ophthalmic artery** (first branch of internal carotid artery) enters orbit through optic canal (underneath optic nerve).
- **central retinal artery** (first intraorbital branch of ophthalmic artery) enters optic nerve 8-15 mm behind globe – direct supply to retina.
- **short posterior ciliary arteries** (branch more distally from ophthalmic artery) supply choroid; anatomical variant (≈ 14%) - **cilioretinal artery** (branch from short posterior ciliary artery) - additional supply to macula from choroidal circulation.
 - 25% eyes with CRAO have cilioretinal artery!
 - if cilioretinal artery supplies fovea, visual acuity (central vision) in 80% returns to 20/50 (or better) over 2-week period.

fovea is the only part with 20/20 vision!

Acute stage - inner retinal layer **edema**, ganglion cell nuclei **pyknosis**.

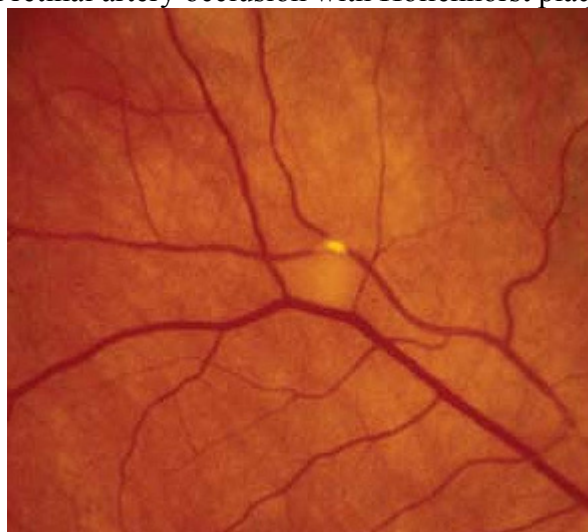
pale, opaque fundus with red fovea

- **ischemic necrosis** - **retina becomes opacified** (yellow-white “ground glass” retina); opacity most dense in posterior pole (more thick nerve fiber layer and ganglion cells); opacification takes 15 minutes ÷ several hours to become evident.
 - **irreversible cell injury** occurs after 90-100 minutes of total CRAO
- **foveola assumes CHERRY-RED SPOT** (pigment of intact retinal epithelium & choroid seen through thin macula ± foveolar retina may also be nourished by choriocapillaris).
- **arteries** are attenuated and may even appear bloodless.
- **boxcar appearance of blood column** (blood column segmentation) can be seen in both arteries and veins (sign of severe obstruction).



- **emboli** at retinal vascular bifurcations (can be seen in ≈ 20%):
 - yellow (HOLLENHORST plaque)** – cholesterol plaque – most common emboli!
 - white** – calcium, talc (from intravenous drug abuse).
 - fluffy** – platelet fibrin
 - red** – sickle cells, thromboembolism

Branch retinal artery occlusion with Hollenhorst plaque:



Chronic stage - **homogenous scar** replacing inner retinal layer (i.e. retinal opacification resolves in 4-6 weeks), **optic nerve pallor** may be the only sign left.

- retinal **pigment epithelium** is unaffected (pigmentary changes are absent).

ETIOLOGY

Comorbid diseases:

- 1) systemic **hypertension** (≈ 67%)
- 2) **diabetes mellitus**
- 3) **cardiac valvular disease** (≈ 25%), cardiac anomalies (such as patent foramen ovale)
- 4) **atrial fibrillation, endocarditis**
- 5) **hypercoagulable states** (sickle cell anemia, antiphospholipid antibodies, polycythemia) - more common in patients < 30 years.
- 6) **atherosclerotic disease** is leading cause in patients 40-60 years.

1. EMBOLISM

- associated with *poorer visual acuity*, correlates with higher morbidity and mortality (56% mortality rate over 9 years, vs. 27% in patients without arterial emboli).
- **emboli from heart** - most common cause in patients < 40 years.

2. THROMBOSIS

- **temporal arteritis** (patients > 65 years)!!!
- rare causes:
 - 1) Behçet disease
 - 2) syphilis
 - 3) increased intraocular pressure:
 - a) glaucoma
 - b) prolonged direct pressure to globe in unconscious patients (e.g. drug-induced stupor, improper positioning during surgery).

3. VASOSPASM (e.g. migraine).**CLINICAL FEATURES**

- *sudden, severe, persistent, painless VISION LOSS.*

- vision loss is sudden (in seconds of occlusion), in range of **counting fingers ÷ light perception**; if visual acuity is even worse - consider **ophthalmic artery occlusion**.
- 1-2% bilateral.
- afferent pupillary defect (*Marcus Gunn pupil*) may precede fundoscopic retinal changes by 1 hour.
- mean age - early 60s.
- some patients reveal preceding episodes of **AMAUROSIS FUGAX** (transient ischemic blindness).

DIAGNOSIS

- perform systemic examination for temporal arteritis (ESR is absolutely necessary test!!!)
- in case of emboli, listen for carotid bruits & cardiac arrhythmias.
- **laboratory studies** are helpful in determining etiology: CBC, ESR, coagulation studies, etc.

Fluorescein angiogram

- *delay in retinal arterial filling.*
- *normal choroidal filling* (normally begins 1-2 seconds before retinal filling and completely filled within 5 seconds); significant delay (> 5 sec) in choroidal filling - consider ophthalmic artery occlusion / carotid artery obstruction.
- *arteriovenous transit time* ↑ (< 11 seconds is normal).
- arterial narrowing with normal fluorescein transit after recanalization.

Electroretinogram - diminished b-wave (Muller and/or bipolar cell ischemia).

TREATMENT

- must be very urgent!!!

Mainstay of therapy – **REDUCING INTRAOCULAR PRESSURE** - *allows greater perfusion* (pushing emboli further down).

- controversy exists regarding *optimal window of treatment*, but treatment may help up to 24 hours.

PROCEDURES**1. Intermittent digital massage over closed eyelids**

- forces humor into canals of Schlemm, can *dislodge embolus* further down arterial circulation.
 - direct eye pressure for 5-30 seconds, then release; repeat several times.

2. Anterior chamber paracentesis

- local anesthesia; 30-gauge needle on tuberculin syringe.
- enter at limbus with bevel up (do not damage lens!).
- withdraw fluid until the anterior chamber shallows slightly (0.1-0.2 cc).
- postprocedure topical antibiotic.

3. Intra-arterial fibrinolysis (controversial)**CONSERVATIVE MEASURES****1. Immediate lowering of intraocular pressure** (as in glaucoma)

- 1) **ACETAZOLAMIDE** 500 mg (IV or PO) once.
- 2) topical medications (e.g. **DORZOLAMIDE**, **APRACLONIDINE**, **DIPIVEFRIN**, **TIMOLOL**).
- 3) if no drug lowers IOP → **MANNITOL** rapidly IV after test dose.

2. Increasing oxygenation

- 1) **100% O₂ inhalation at 2 atm.** (some studies show 40% improvement of visual acuity).
- 2) **HYPERBARIC OXYGEN therapy** (beneficial if begun within 2-12 hours → increased visual recovery).
- 3) **CARBOGEN therapy** (5% CO₂, 95% O₂): CO₂ *dilates retinal arterioles*, O₂ *increases oxygen delivery* to ischemic tissues - perform for 10 min every 2 hours for 48 hours.

- some also advocate **ASPIRIN** in acute phase.
- if temporal arteritis is suspected / confirmed → **corticosteroids**.

FURTHER CARE

- ischemic damage produces angiogenesis factors → abnormal vascularization - repeat examination in 1-4 weeks - checking for **neovascularization of iris** (20%; detected best on undilated iris) or **optic disc** (2-3%) – if it occurs → **PANRETINAL PHOTOCOAGULATION**.
- patients must understand that prognosis for *visual recovery is poor* and that visual changes are result of *systemic process that needs treatment*.

BRANCH RETINAL ARTERY OCCLUSION

- often caused by **embolus** (original or dislodged during CRAO treatment).
- fundus abnormalities are limited to that *sector of retina* → permanent subtotal visual field loss (unless occlusion is relieved).
- treatment is the same as for CRAO.

ROTH spots – hemorrhagic retinal infarcts (emboli from *infective endocarditis*) – white spots surrounded by hemorrhage.

CENTRAL RETINAL VEIN OCCLUSION (CRVO)

PATHOPHYSIOLOGY & ETIOLOGY

- blockage of **central retinal vein** → blood stagnation and ischemia of inner retinal layers.

- central retinal artery and vein share common adventitial sheath (as they pass through narrow opening in lamina cribrosa) - vessels are in **tight compartment** with limited space for displacement
- predisposes thrombus formation in central retinal vein.

A. **Vein compression:**

- 1) **most common CRVO cause - central retinal artery atherosclerosis** (in diabetes mellitus, hypertension) transforms artery into rigid structure that impinges upon pliable central retinal vein → thrombus formation.
- 2) structural changes in **lamina cribrosa** (e.g. glaucomatous cupping).
- 3) inflammatory **optic nerve** swelling
- 4) **orbital** disorders.

B. **Hemodynamic disturbances** (hyperdynamic or sluggish circulation).

C. **Vessel wall changes** (e.g. vasculitis).

D. **Changes in blood** (hyperviscosity, ↓thrombolytic factors, ↑clotting factors).

E. **Idiopathic** (resembling retinal phlebitis) - in young persons.

- clot dissolution, formation of optociliary shunt vessels may restore circulation.

CLINICAL FEATURES

- **monocular painless subacute variable VISUAL LOSS.**

- **less abrupt than in arterial obstruction** (evolves over hours); patients can present with transient vision obscurations initially, later progressing to constant visual loss.
- vision is more preserved (than in CRAO) and pupillary light reflex is ≈ normal.
- usually in elderly patients (> 90% are > 50 yrs).

DIAGNOSIS

- no laboratory studies are indicated routinely.
- **OPHTHALMOSCOPY:**
 - 1) **dilated tortuous retinal veins**
 - 2) **congested edematous fundus** (incl. macular edema and optic disc edema).
 - 3) numerous **retinal hemorrhages** (superficial, dot and blot, and/or deep) along veins, extending all over fundus ("**blood and thunder**" or "**stormy sunset**" appearance)
 - 4) **cotton wool spots** (concentrated around posterior pole)

Central retinal vein occlusion:



Branch retinal vein occlusion:



- **FLUORESCIN ANGIOGRAPHY** - most useful test for CRVO classification – detects *areas of retinal capillary nonperfusion* (hypofluorescence), *posterior segment neovascularization*, and *macular edema* (as leakage from perifoveal capillaries).
N.B. in acute stages, hemorrhages can block fluorescence (false-positive hypofluorescence) - fluorescein angiography is not useful in acute stages!
- **ELECTRORETINOGRAPHY** - amplitude of **b wave** ↓ (b-to-a ratio < 1).

TREATMENT

- **no generally accepted medical therapy!!!**
- different authors advocate – aspirin, systemic anticoagulation, local anticoagulation (intravitreal alteplase), fibrinolytic agents, systemic corticosteroids, NSAIDs, isovolumic hemodilution, plasmapheresis, intravitreal injection of **TRIAMCINOLONE**, intravitreal injection of **BEVACIZUMAB** (effective not only in resolving the edema but also in corresponding improvement in vision!).

COMPLICATIONS

- **neovascularization** can occur weeks to months after occlusion:
 - a) **iris** (rubeosis iridis) → **secondary (neovascular) glaucoma**.
 - b) **retina, optic disc*** → **preretinal, vitreous hemorrhages**.
*differentiate from **optociliary shunt vessels** (compensatory blood vessels on disc, directing blood from retinal circulation to choroidal circulation).
 - neovascularization is treated with **PANRETINAL PHOTOCOAGULATION**; prophylactic panretinal photocoagulation is not recommended.
 - if ocular media is hazy for laser to be applied, **TRANSCLERAL CRYOABLATION** of peripheral fundus is performed.
- **macular edema** (common cause of decreased vision after CRVO);
 - **NO EFFECTIVE TREATMENT** (**grid pattern argon laser macular photocoagulation** is not effective!)
 - may resolve or develop permanent degenerative changes.

CLASSIFICATION

- it may be difficult to classify on initial presentation (since CRVO may change with time).

Nonischemic CRVO - milder form.

- presents with good vision, few retinal hemorrhages and cotton-wool spots, no relative afferent pupillary defect, good retina perfusion.
- macular edema is more common!
- 10% resolve fully (with good visual outcome); 30% progress to ischemic type.

Ischemic CRVO - severe form.

- presents with severe visual loss, extensive retinal hemorrhages and cotton-wool spots, relative afferent pupillary defect, poor perfusion to retina, severe electroretinographic changes.
- in > 90% patients, final visual acuity is 20/200 or worse.
- may end up with **neovascular glaucoma** (> 60% patients) → **painful blind eye**.

RETINAL DETACHMENT

- **neural retina** separation from **retinal pigment epithelium**.

ETIOLOGY & PATHOPHYSIOLOGY

N.B. in every case, eventual fluid accumulation leads to neurosensory retina separation.

Myopic eyes, in general, are more prone to retinal detachments!

Rhegmatogenous detachment [G. *rhegma*, breakage] - produced by **retinal tear** - most common type of retinal detachment!

Causes of retinal tears:

- VITREORETINAL TRACTION** (most common cause) - as vitreous becomes more synergetic with age, posterior vitreous detachment occurs; only if strong *vitreoretinal adhesions* are present → retinal tear.
- RETINAL NECROSIS** (e.g. CMV retinitis in AIDS) → retinal tear.
- CATARACT SURGERY** (intact posterior capsule delays posterior vitreous detachment)
N.B. it is imperative that general ophthalmologist examines peripheral retina prior to referral to cataract surgeon!
- OCULAR TRAUMA**

Traction detachment - produced by **vitreoretinal traction** - second most common type of retinal detachment!

- proliferative vitreoretinopathy** after *penetrating ocular trauma*, *retinal reattachment surgery* (see below).
- progressive retinal ischemia** (e.g. *proliferative diabetic retinopathy!!!*, *retinopathy of prematurity!!!*, sickling hemoglobinopathies, retinal venous obstructions) → neovascularization (vitreous serves as scaffold where strong vitreoretinal adhesions develop; with time, vitreous starts pulling away).

Exudative detachment - produced by **fluid transudation** into subretinal space.

- under normal conditions, water flows from vitreous cavity to choroid (relative hyperosmolarity of choroid with respect to vitreous + retinal pigment epithelium pumps); pathophysiology:
 - fluid inflow**↑ (e.g. abnormal leaky blood vessels, broken blood-retinal barrier).
 - fluid outflow**↓ (e.g. abnormally thick sclera in nanophthalmos, damage to retinal pigment epithelium).

Etiological causes:

uveitis [esp. Vogt-Koyanagi-Harada syndrome], scleritis, choroidal tumors, chronic renal failure, preeclampsia-eclampsia, Coats disease, central serous chorioretinopathy, sympathetic ophthalmia, rheumatoid arthritis, Wegener granulomatosis, exudative age-related macular degeneration, etc.

CLINICAL FEATURES

- *subacute monocular VISUAL LOSS evolving over hours.*

- **painless**.
- may be preceded by **shower of "sparks" (photopsia)** (due to mechanical vitreoretinal traction on retina) / **shower of floaters** (vitreous opacities).
- only after retina actually separates from pigment epithelium does **"black curtain" of visual loss** move across visual field.
- if macula is involved, central visual acuity fails drastically.

DIAGNOSIS

OPHTHALMOSCOPY:

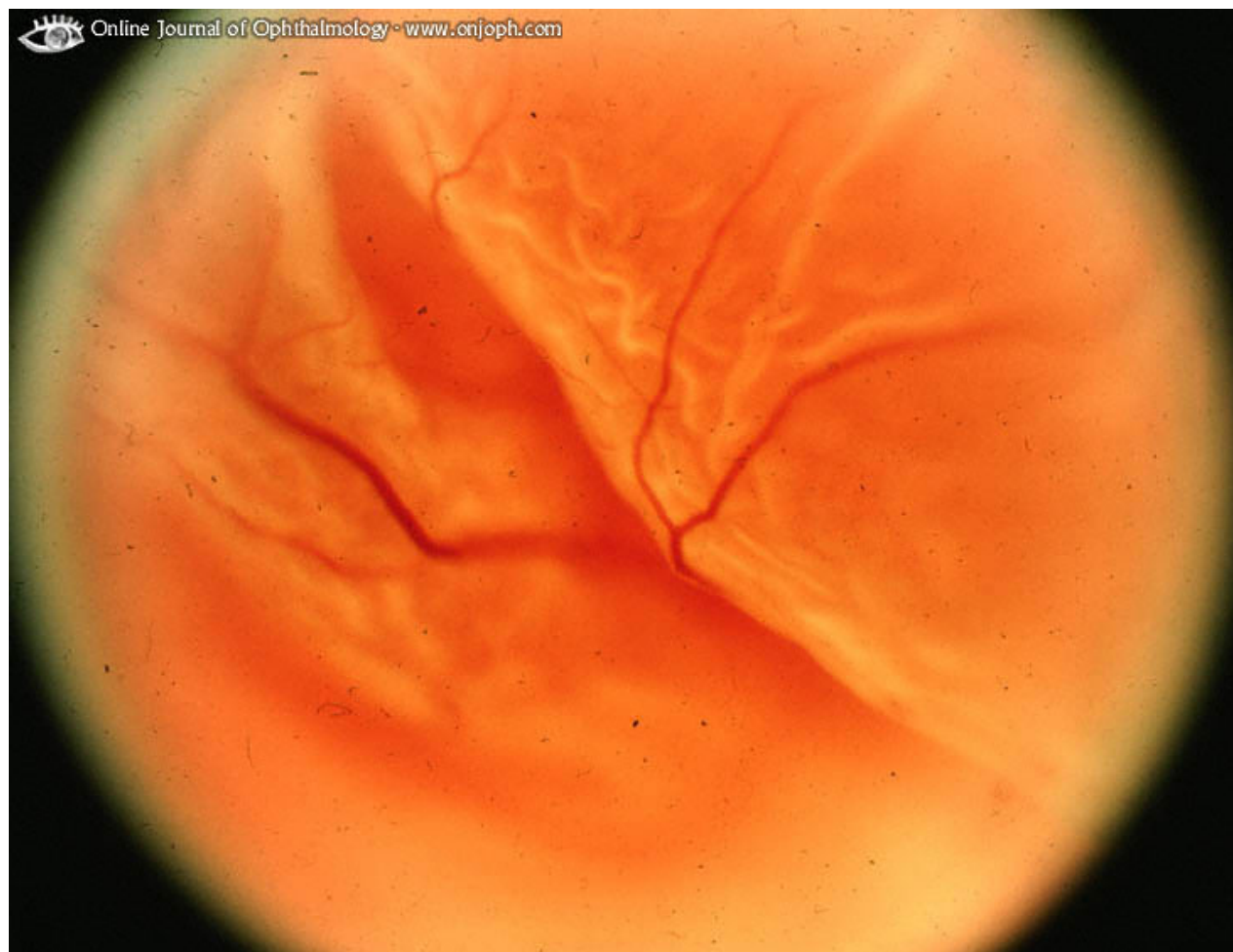
retina is slightly opaque (secondary to intraretinal edema);

in **TEARS** - retinal irregularities (*corrugated retina*);

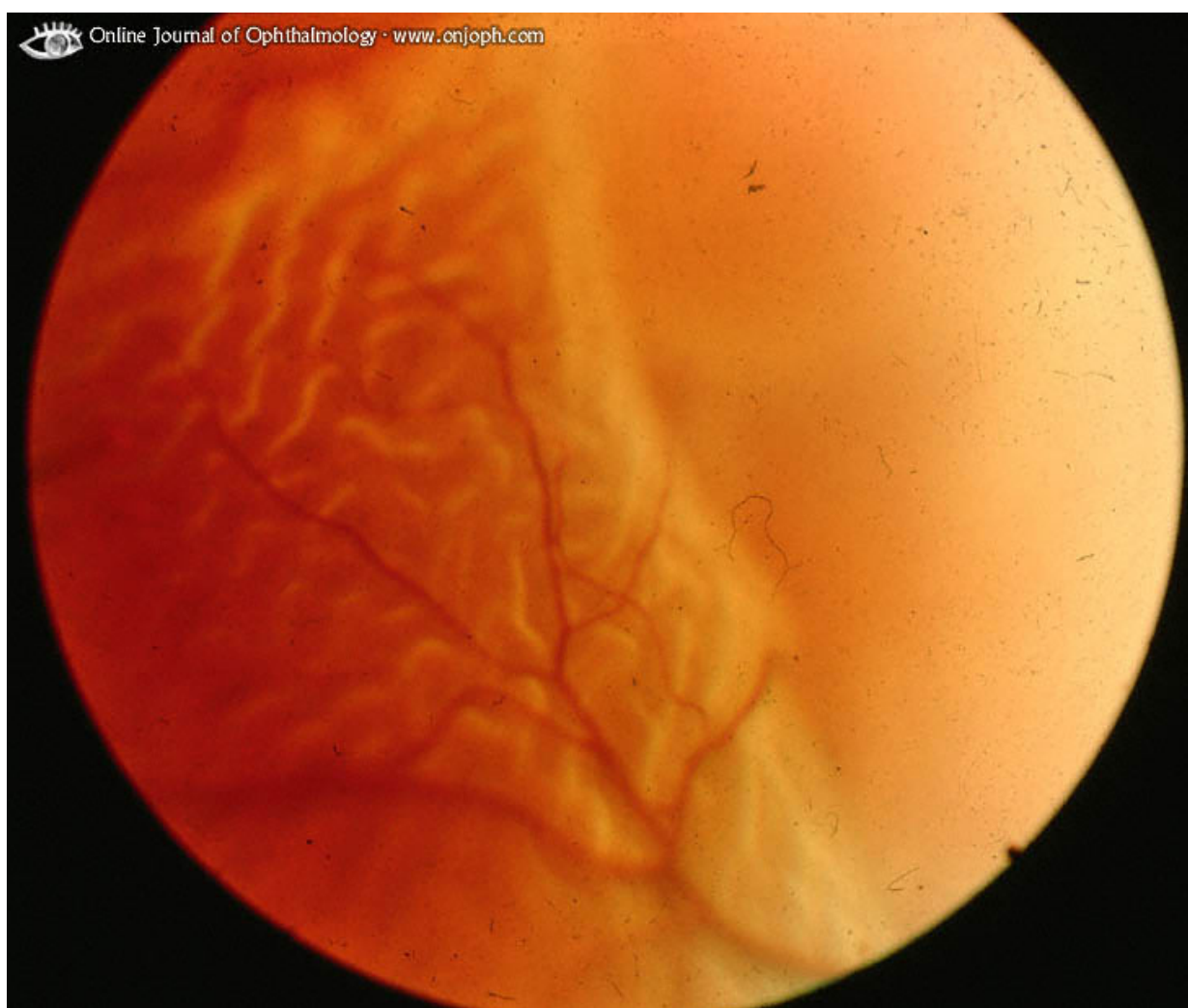
- **indirect ophthalmoscopy** (incl. scleral depression) is necessary for detecting *peripheral* breaks and detachment.
- 60% tears are in **upper temporal quadrant**.
- cell and flare in anterior chamber.
- pigment in anterior vitreous (tobacco dusting or SHAFER sign).

in **EXUDATIVE** forms - *bullous (convex) retinal elevation* with **shifting subretinal fluid** (fluid accumulates in its most dependent position) that undulates freely with eye movements.

in **TRACTION** forms - *retina has concave configuration*, retinal mobility is severely reduced (shifting fluid is absent).

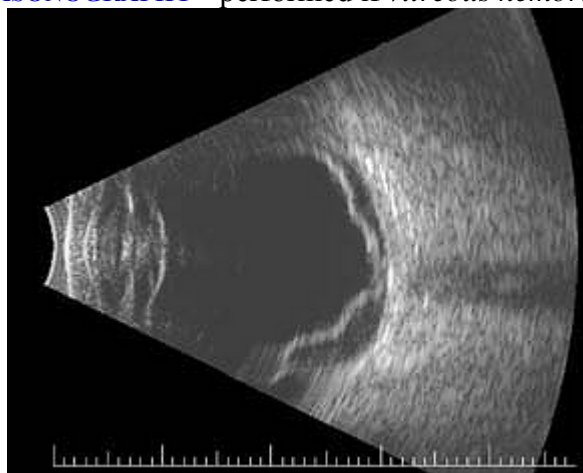


Source of picture: "Online Journal of Ophthalmology" >>



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B-SCAN ULTRASONOGRAPHY - performed if *vitreous hemorrhage* obscures retina.



ELECTRORETINOGRAM is indicated if ultrasound cannot differentiate *retinal detachment* from *partially detached thickened posterior hyaloid* (if good response from ERG is obtained, retina probably is attached).

TREATMENT

N.B. if not treated promptly detachments can expand to involve entire retina.

Rhegmatogenous detachment → sealing all retinal breaks:

- Closure of breaks occurs when break edges are **brought into contact** with underlying pigment epithelium:
 - by bringing eye wall closer to detached retina (**scleral buckle**, ± fluid drainage from subretinal space).
 - by pushing detached retina toward eye wall (**pneumatic retinopexy** - intraocular tamponade with gas bubble).
 - by pars plana **vitrectomy** (used by number of surgeons for primary uncomplicated retinal detachments); ideal candidates are those with pseudophakia, aphakia, or phakic eyes with posterior breaks.
 - Sealing of breaks is accomplished by creating strong **chorioretinal adhesion** around breaks - by **laser / diathermy / cryotherapy**.
- > 90% detachments can be reattached surgically.
 - retinal breaks without detachment:
 - anterior → transconjunctival cryopexy;
 - posterior → photocoagulation.
 - of eyes that are successfully reattached after macula detachment, 50% obtain final visual acuity of 20/50 or better (outer segments of photoreceptors regenerate).

Traction detachments → surgery to relieve vitreoretinal traction:

- scleral buckling** techniques
- vitrectomy**.

Exudative detachments:

inflammatory conditions → systemic **corticosteroids**;

choroidal tumors → **enucleation / radiation / chemotherapy**;

choroidal hemangiomas may respond to photocoagulation / or plaque brachytherapy

- surgical treatment of detachment per se varies according to etiology.

After any vitreoretinal surgery:

- 1) topical **antibiotic**
- 2) topical **corticosteroid** (e.g. prednisolone acetate)
- 3) topical **cycloplegic** (e.g. atropine 1%)
- 4) monitor *intraocular pressure*

Warn patients about potential **detachment risk to fellow eye** - in phakic eyes 10-15%, in aphakic / pseudophakic eyes 25-40%.

Instruct to seek attention immediately if experiencing floaters and/or photopsias!

Most common cause of failure in retinal detachment surgery - **PROLIFERATIVE VITREORETINOPATHY** - it is **reparative process** initiated by retinal breaks (full- or partial-thickness), retinopexy, other types of retinal damage - surrounding glial or retinal pigment epithelial cells to migrate to both surfaces of retina → hypocellular keloid-like process (periretinal proliferation, vitreous contraction) → traction retinal detachment; if not treated successfully → blindness.

RETINITIS PIGMENTOSA

- phenotypic description of several related, yet distinct, **DYSTROPHIES** of **photoreceptors** & **pigment epithelium**,

- i.e. **loss of viable photoreceptors** + **pigmentary changes in retinal pigment epithelium** (primary or secondary to photoreceptor loss).

- **hereditary pattern:** to date, > 70 different genetic defects have been identified (most cases **autosomal recessive**, but may also be autosomal dominant or, infrequently, X-linked).
- may occur as:
 - a) **ISOLATED form** (primary RP).
 - b) **association with SYSTEMIC SYNDROMES** (e.g. Usher, Alport, Alström, Jansky-Bielschowsky, Vogt-Spielmeyer-Batten, Zellweger, Refsum, Kearns-Sayre, Bassen-Kornzweig, Laurence-Moon-Biedl).

CLINICAL FEATURES

- slowly progressive, painless, symmetric bilateral vision loss.

- occurs anywhere from infancy to mid 50s; visual degeneration occurs over 30-40 years.

Depending which photoreceptors predominantly are affected:

- A) **CONE-ROD dystrophies** or **PURE-CONE dystrophies** - **day vision** problems: **visual acuity** loss, **color discrimination** loss.
- B) **ROD-CONE dystrophies:**
 - defective **night vision (nyctalopia)**; may become symptomatic in early childhood.
 - midperipheral **ring scotoma (tunnel vision)**; widens gradually → central vision eventually is reduced.

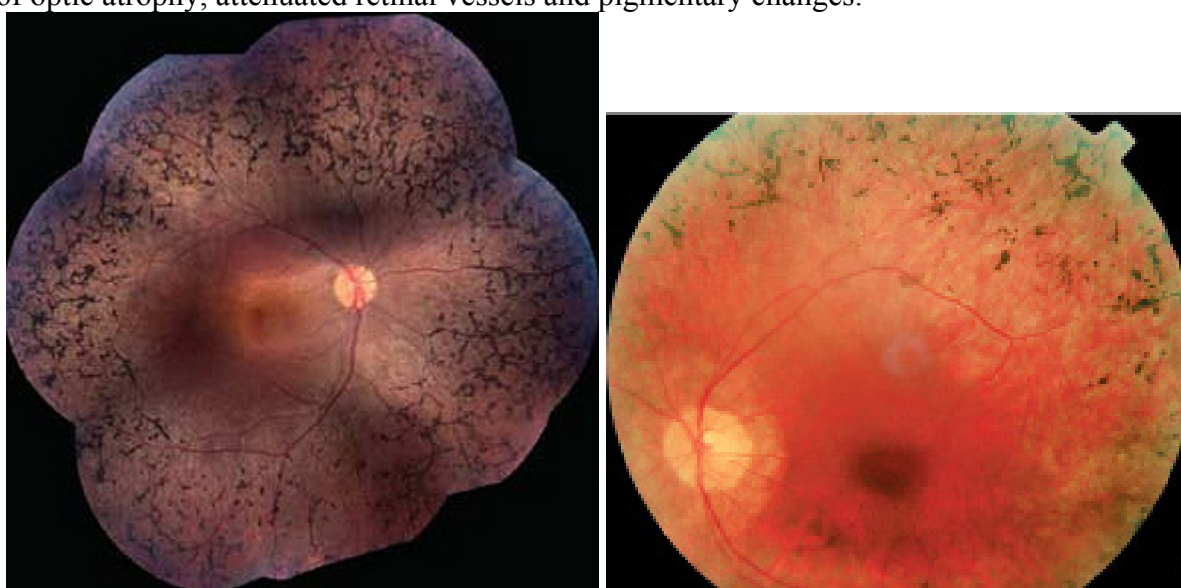
DIAGNOSIS

Depending on stage and type of disorder, VISUAL ACUITY ranges from normal (20/20) to no light perception.

- genetic subtyping + examine family members to establish hereditary mode.

OPHTHALMOSCOPY:

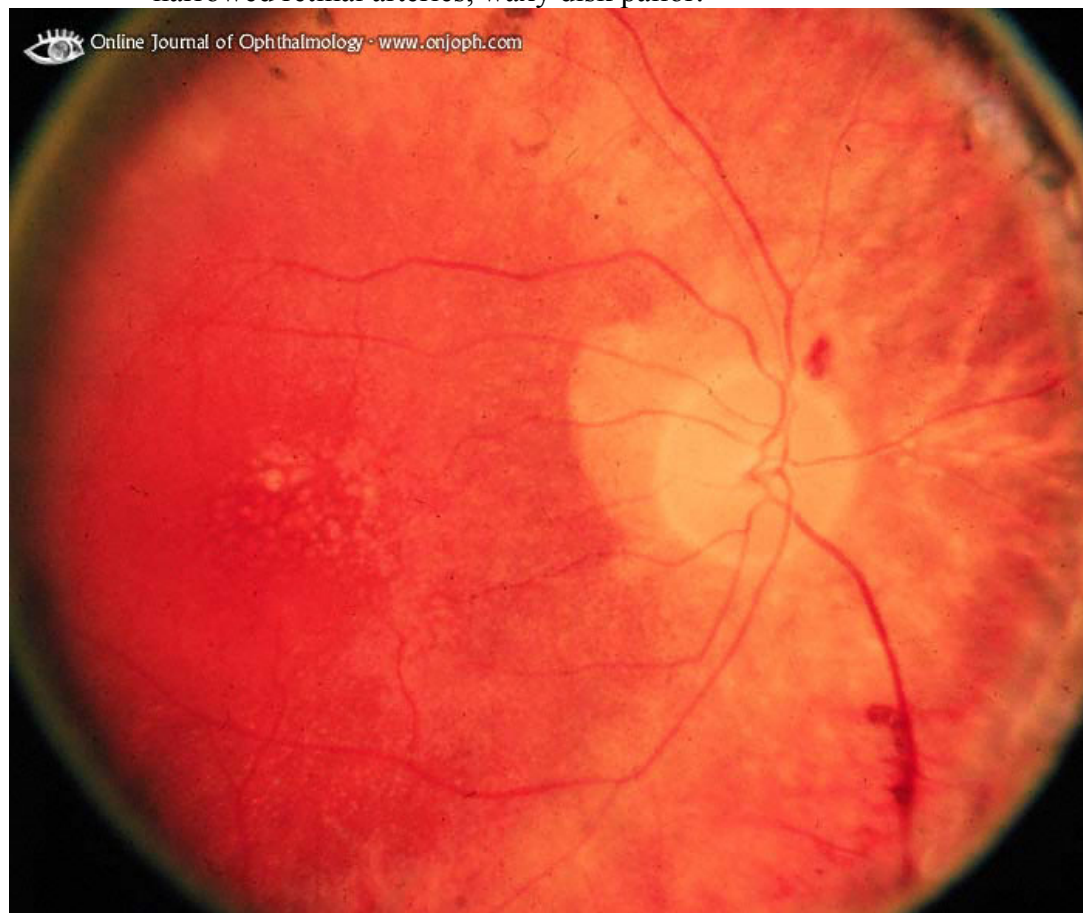
- triad of optic atrophy, attenuated retinal vessels and pigmentary changes.



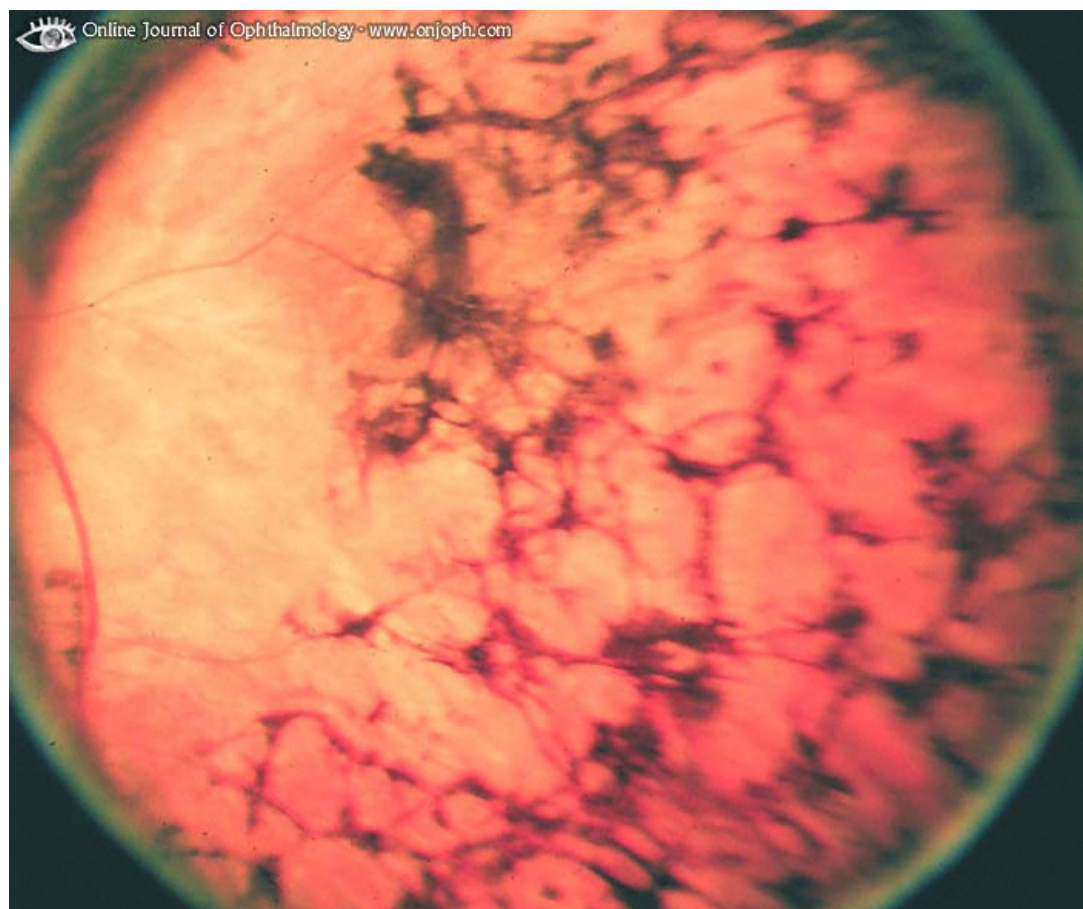
CONE-ROD dystrophies - bull's eye maculopathy.

ROD-CONE dystrophies - dark pigmentation ("bone-spicule" configuration) in equatorial retina.

- narrowed retinal arteries, waxy disk pallor:



Source of picture: "Online Journal of Ophthalmology" >>



Source of picture: "Online Journal of Ophthalmology" >>

ELECTRORETINOGRAPHY (incl. after dark adaptation) - most critical diagnostic test - provides objective measure of rod and cone function.

TREATMENT

No treatment is effective!

Suggested medical therapies:

1. Vitamin A/beta-carotene very high daily doses
2. High doses of vitamin E.
3. 1000 mg/d ascorbic acid.
4. Acetazolamide (for small percentage of patients with cystoid macular edema).
5. Diltiazem
6. Lutein
7. Bilberry.

Experimental methods:

- 1) fetal neural **retina transplantation**.
- 2) **retinal prosthesis** (phototransducing chip)
- 3) intravitreal / subretinal **gene therapy**

AGE-RELATED MACULAR DEGENERATION (ARMD) s. SENILE MACULAR DEGENERATION

- collection of **inherited** diseases (multifactorial) that share common features - age predilection, frequently positive family history.
- no predisposing systemic risk factor is known! (association appears to exist with **smoking**).
- leading cause of visual loss in elderly!
- much more common in *whites*.

PATHOPHYSIOLOGY

RETINAL PIGMENT EPITHELIUM degeneration / atrophy in **macular region**

Macular region: enlarging / coalescing **DRUSEN*** → overlying **retinal pigment epithelium** degeneration / atrophy → loss of overlying **photoreceptors** ("DRY" form).

*yellow-gray extracellular material in Bruch membrane, composed of various substances.

- damaged **retinal pigment epithelium** may also disturb underlying **choroidal perfusion** → choroidal *neovascularization* (conversion to "WET" form).

TRADITIONAL theory - **senescence of retinal pigment epithelium** - accumulates metabolic debris as remnants of incomplete degradation from phagocytosed rod and cone membranes; progressive engorgement of these pigment cells leads to drusen formation.

CLINICAL FEATURES

- slow or sudden, painless **loss of CENTRAL VISUAL ACUITY** (e.g. difficulty with reading and making out faces) + difficulty with night vision and with changing light conditions.

- manifests **after age 50 years** (according to international classification system, ARMD cannot be diagnosed in patients < 50 years).
- variability of vision from day-to-day is common.
- new onset metamorphopsia (self-tested with Amsler grid) may indicate *onset of choroidal neovascularization*.

N.B. biggest treatable risk of visual loss in dry AMD is development of neovascularization – so, new onset metamorphopsia is indication for fluorescein angiography!!!

- although often legally blind (< 20/200 vision), patients have **good peripheral and color vision**.
N.B. patients don't lose all sight!

DIAGNOSIS

FUNDUSCOPY - pathology in MACULAR REGION:

Atrophic (dry) form (more common form) – **ONLY PIGMENTARY DISTURBANCE** (no elevated macular scar, no hemorrhage, no exudation); retinal pigment epithelium atrophic with easier visualization of underlying choroidal plexus.

- peripheral retina often has drusen, as well as retinal pigment epithelium mottling and atrophy.

Dry ARMD with fine drusen:



Dry ARMD with soft drusen:



Exudative (wet) form (more rapidly progressing visual loss) - subretinal **CHOROIDAL NEOVASCULARIZATION** network → subretinal **fluid**, intraretinal **hemorrhage**, pigment epithelial detachment, hyperpigmentation → eventually this complex contracts → distinct elevated **scar** at posterior pole.

- often bilateral (but not necessarily symmetrical).
- contralateral eye always shows some pigmentary disturbance and **macular DRUSEN**.



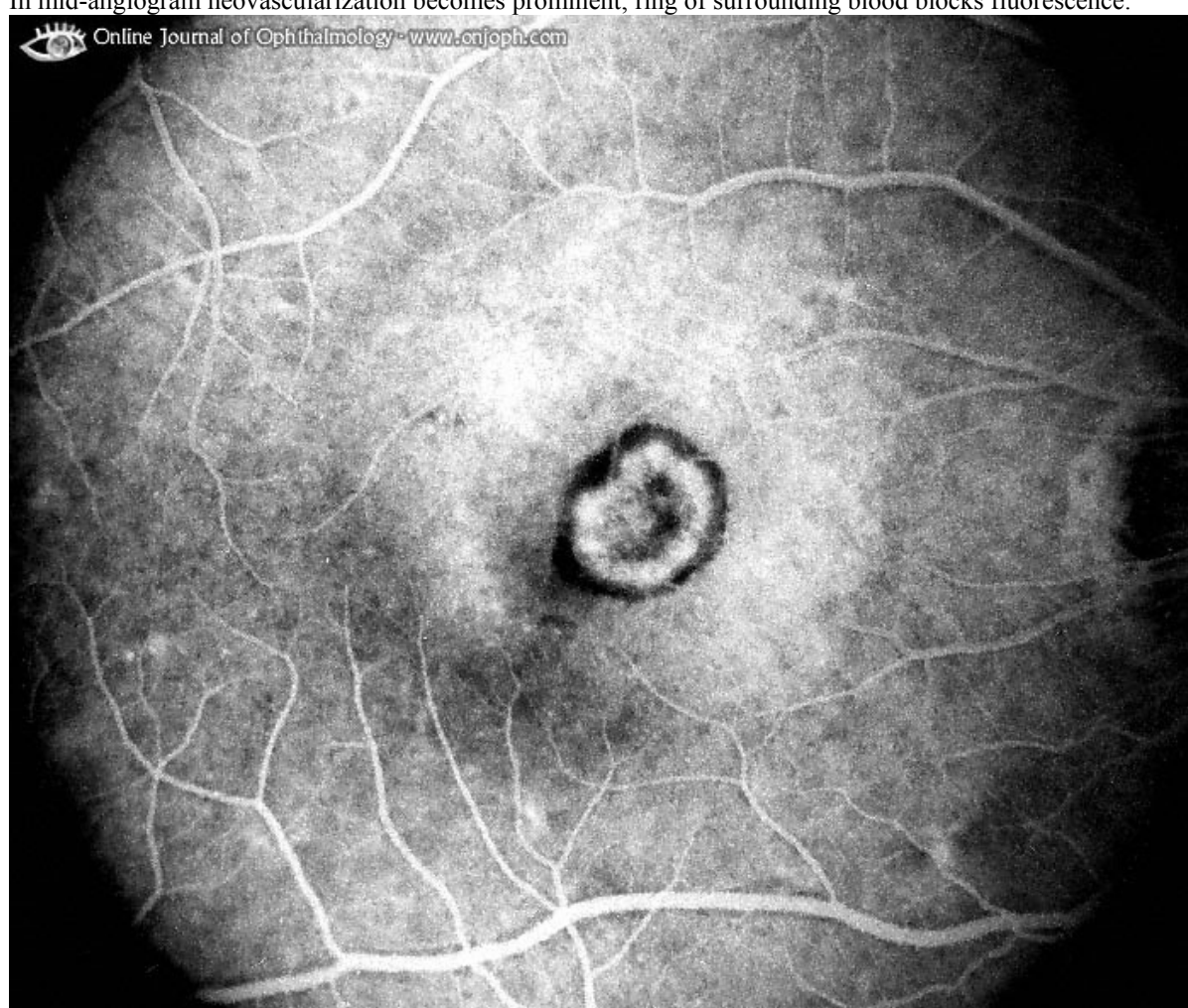
FLUORESCEIN ANGIOGRAPHY - *neovascular membrane* beneath retina (late leakage of fluorescein).

In area of slight depigmentation (previous retinal pigment epithelium detachment) is darkly pigmented spot surrounded by slim ring of subretinal blood:



Source of picture: "Online Journal of Ophthalmology" >>

In mid-angiogram neovascularization becomes prominent; ring of surrounding blood blocks fluorescence:

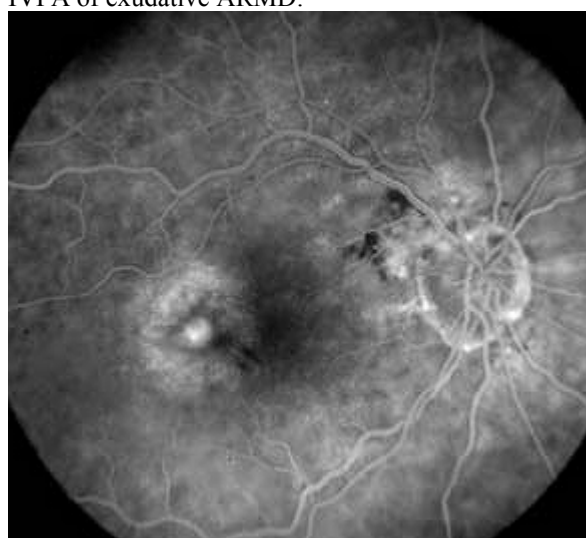


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Exudative ARMD:



IVFA of exudative ARMD:



TREATMENT

- low-vision devices & service counseling.

Dry ARMD - **no proven treatments** available; daily Amsler grid self-evaluation is necessary (to detect conversion to wet ARMD).

- high-dose combination of **vitamin C** (500 mg), **vitamin E** (400 IU), **beta-carotene** (15 mg), **zinc** (80 mg) and **cupric oxide** (5 mg) reduces progression to advanced ARMD by 25% over 5 years, and reduces risk of vision loss by 19% by 5 years.

Wet ARMD:

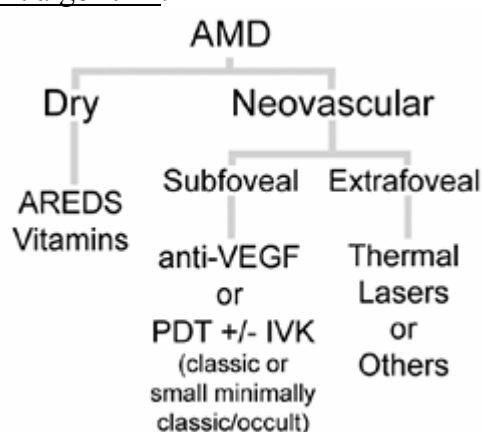
A. Neovascular network **outside fovea*** → **laser photocoagulation** (best-studied and standard treatment!!!);

* if neovascular network is located subfoveally, laser treatment causes blinding central scotoma!

B. **Subfoveal** neovascularization:

1. Selective **vascular endothelial growth factor (VEGF) antagonists** (injected intravitreally) – FDA approved:
 - 1) **PEGAPTANIB** (Macugen®) - injected intravitreally q 6 weeks.
 - 2) **RANIBIZUMAB** (Lucentis®) - injected intravitreally q 1-3 month; unlike other treatments can improve visual acuity!
 - 3) **BEVACIZUMAB** (Avastin®); not yet FDA approved.
2. **Photodynamic Therapy (PDT)** (FDA approved): IV photosensitizing dye [**VERTEPORFIN** (Visudyne®)] → nondestructive (cold) laser to activate dye within choroidal neovascularization; performed q 3 months for 1-2 years.

AMD treatment algorithm:



PREVENTION

- 1) daily **multivitamins** (esp. vit. E and zinc) and **LUTEIN**.
- 2) *stop smoking*.

RETINOPATHY OF PREMATURITY (ROP), s. Retrolental Fibroplasia

- bilateral **abnormal retinal vascularization** in **PREMATURE** infants.

PATHOPHYSIOLOGY & ETIOLOGY

- **inner retinal blood vessels** start growing about midpregnancy and have fully vascularized retina by full term; in premature birth their growth is incomplete.
- ROP results if these vessels continue growth in abnormal pattern;
 - abnormal tissue ridge forms between vascularized central retina and nonvascularized peripheral retina;
 - new vessels may invade vitreous →→→ retinal traction detachment;
 - sometimes entire eye vasculature becomes engorged ("plus" disease).
- increased ROP risk correlates with:
 - 1) *proportion of retina that remains avascular at birth* – this correlates with **low birth weight** (> 80% infants weighing < 1 kg at birth develop ROP).
 - 2) **excessive** (esp. prolonged) **O₂ administration**; hyperoxia induces vasospasm → endothelial damage → ischemia → **reactive proliferative neovascularization** → retinal traction → retinal traction detachment.

PROGNOSIS

- abnormal vessel growth often *subsides spontaneously* → NORMAL VISION.
- 4% progress to **retinal detachments** and VISION LOSS within 2-12 mo.
- healed ROP may leave **cicatricial scars** (dragged retina or retinal folds) - risk for **retinal detachments later in life** (should be followed at least annually for life!!!).

PREVENTION after preterm birth (any baby < 31 week or < 1500 g):

- 1) use **O₂** only in amounts sufficient to avoid hypoxia.
N.B. threshold safe level or duration of elevated PaO₂ is not known!
 - 2) **vitamin E** (antioxidant) + restriction of **light exposure** (pro-oxidant).
- retinal vascularization must be closely followed (ophthalmoscopy) at 1-2-wk intervals (started at 4-6 weeks old) until vessels have matured sufficiently (usually 36 postmenopausal weeks).

TREATMENT for severe ROP only:

- CRYOTHERAPY / LASER PHOTOCOAGULATION** to ablate peripheral avascular retina → ↓incidence of retinal fold or detachment.
- if retinal detachments occur, **scleral buckling surgery** or **vitreectomy & lensectomy** may be considered as late rescue with low benefit.

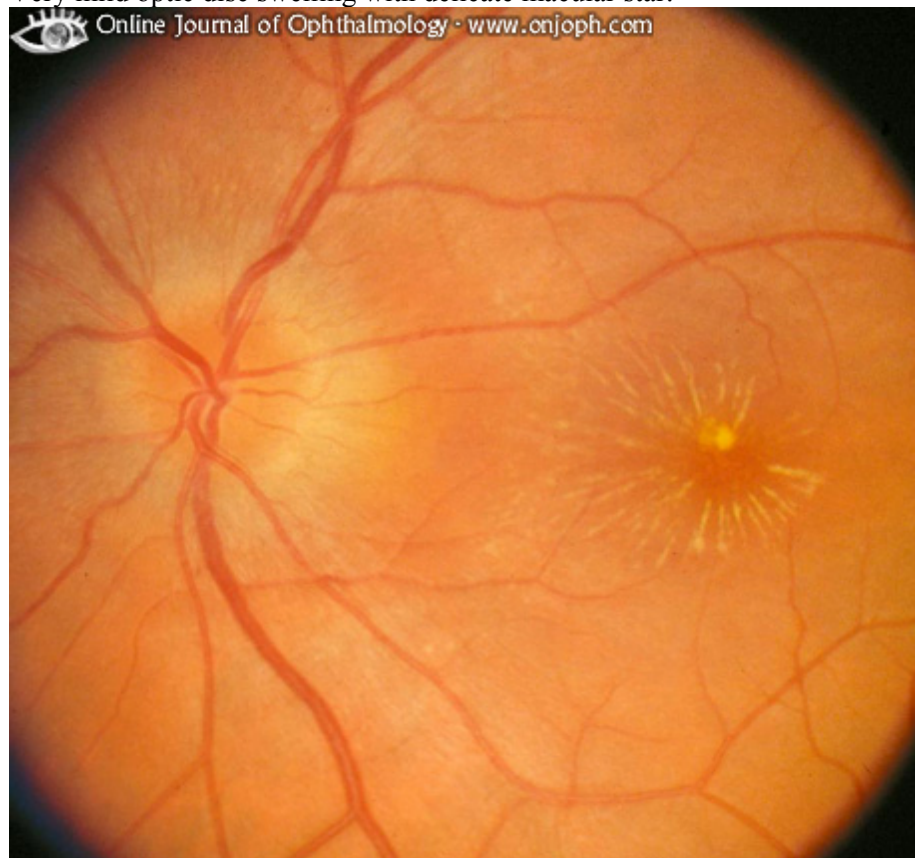
NEURORETINITIS (s. PAPHILORETINITIS)

- inflammation of **OPTIC NERVE HEAD + POSTERIOR POLE OF RETINA** (with cells in nearby vitreous) producing **macular star** (lipid exudate in macula).
- VISUAL LOSS is due to **optic nerve dysfunction** and / or **macular dysfunction**.

Examples:

1. **Leber's idiopathic stellate neuroretinitis** - unilateral neuroretinitis with spontaneous regression in a few months.
2. **Cat-scratch disease** (caused by *Bartonella henselae*).
3. **Syphilis**
4. **Post-viral inflammatory reaction** in optic nerve

Very mild optic disc swelling with delicate macular star:



Source of picture: "Online Journal of Ophthalmology" >>

Disc swelling confined to superior disc pole. Numerous white spots distinct from exudates in deep retina around optic disc:



Source of picture: "Online Journal of Ophthalmology" >>

RETINOBLASTOMA

- **malignant tumor from immature retina.**

- occurs in 1/18,000 to 1/30,000 live births.
- most common primary ocular malignancy of childhood!
- represents 2% of childhood malignancies.
- tumor arises from multipotential precursors of photoreceptor (retinoblasts).

60-70% NONHERITABLE.

30-40% INHERITABLE:

- 5-10% have positive **family history** of retinoblastoma.
- 20-30% have **bilateral** disease (others have **unilateral multicentric** disease); some patients with bilateral retinoblastoma have similar tumor (**pineoblastoma**) of pineal region (**TRILATERAL RETINOBLASTOMA**).
- also increased risk for **OSTEOSARCOMA** from osteoblasts!

"Two hits" hypothesis see p. 3785-3786 >>

- constitutive genetic abnormality (i.e. **genomic mutation** - present in all body cells) inherited in autosomal dominant fashion; it is deletion / mutation of **retinoblastoma gene** (tumor suppressor gene located in 13q14).
- **somatic mutation** in allelic 13q14 results in tumor.
- **extraocular extension:**
 - a) through sclera
 - b) along optic nerve
- distant metastases are rare.

DIAGNOSIS

- 90% are diagnosed before age 5 yrs - usually when investigating presenting symptoms - **white pupil reflex** (leukocoria, s. cat's-eye pupil), **strabismus**.

INDIRECT OPHTHALMOSCOPY (with pupils widely dilated, child under general anesthesia) - **gray-white elevations in retina;**

- **ENDOPHYTIC growth** - tumor seeds visible in vitreous; tumor has either no surface vessels or small irregular vessels.
- **EXOPHYTIC (subretinal) growth** - subretinal fluid accumulation and retinal detachment; overlying retinal vessels are increased in caliber and tortuosity.
- **DIFFUSE INFILTRATING growth** (only 1.5% cases) - flat infiltration without discrete tumor mass; grows slowly; may present as pseudouveitis.

CT, MRI, ULTRASONOGRAPHY, X-RAY - **calcification** (in almost all tumors).

Ratio of **aqueous humor LDH / serum LDH** > 1.0.

HISTOLOGY:

- classic findings are **Flexner-Wintersteiner rosettes** and less commonly **fleurettes**.
- **Homer-Wright rosette** can also be encountered, but they are seen in other neuroblastic tumors.

SCREENING

- for immediate family members - **genetic studies** (for detecting asymptomatic carriers);
- if risk of retinoblastoma cannot be ruled out by genetic studies → regular **ophthalmologic examination** under anesthesia:
 - q 3-4 months until age 3-4 years; q 6 months until age 5-6 years and then annually (at age 8 years, most patients tolerate dilated fundus examination in office without anesthesia).

TRILATERAL RETINOBLASTOMA = **bilateral** retinoblastoma + **ectopic intracranial** retinoblastoma (usually pineal gland or parasellar region).

- screen those with hereditary (bilateral or multifocal) disease - **gadolinium-enhanced MRI** or **CT with contrast** every 6 months up to age 5 years.

TREATMENT

ENUCLEATION with removal of as much of optic nerve as possible (> 90% intraocular tumors can be cured!).

BILATERAL disease - vision usually can be preserved with:

- a) unilateral **enucleation** + contralateral **photocoagulation / cryotherapy / radiation***.
- b) bilateral coagulation
 - *radiotherapy has high incidence of local control, but results in bone growth cessation (→ significant midface hypoplasia), increases risk of second cancers 6-fold; so **neoadjuvant chemotherapy** (chemoreduction) has superseded radiotherapy.

Significant local spread → **EXENTERATION**.

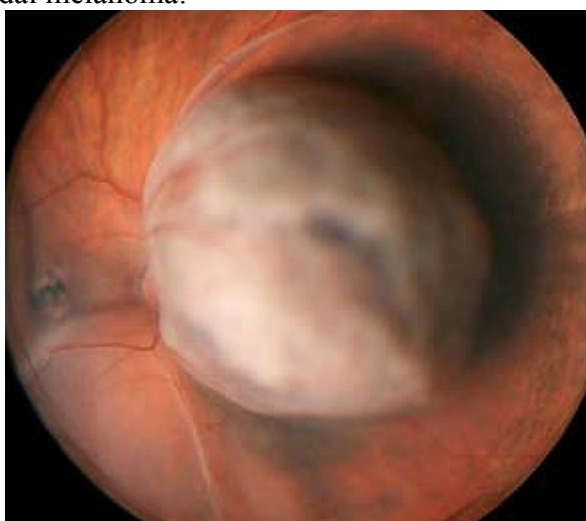
Metastases → systemic **CHEMOTHERAPY** (CARBOPLATIN + ETOPOSIDE + VINCRISTINE ± CYCLOSPORINE).

N.B. combination of *high-dose chemotherapy + radiation therapy + transplantation of blood-producing stem cells* can cure even metastatic retinoblastoma!!! (except in CNS)

FOLLOW-UP, PROGNOSIS

- **ophthalmologic reexamination** at 2-4-mo intervals.
- studies of **CSF & bone marrow** for malignant cells - diagnosis of distant spread.
N.B. primary mode of retinoblastoma spread is hematogenous to bone marrow and back through optic nerve into CSF.
- *overall survival rate* presently is > 85%.
- **death** occurs secondary to intracranial extension
- 70% (i.e. inheritable cases with genomic mutation) develop *second nonocular malignancy* within 30 yrs of diagnosis.

Choroidal melanoma:



COLOR BLINDNESS

suffix "**-anomaly**" = color weakness.
suffix "**-anopia**" = color blindness.

prefixes "**prot-**", "**deuter-**", "**trit-**" =
defects of red, green, blue cone systems.

TRICHROMATS (have all three cone systems, but one may be weak) - norma, protanomaly, deuteranomaly, tritanomaly.

DICHROMATS (only two cone systems) - protanopia, deuteranopia, tritanopia.

MONOCHROMATS (only one cone system).

ETIOLOGY

1. **Inherited** (most frequently - 8% white males, 0.4% white females):
 - **tritanomaly / tritanopia** are rare (more commonly acquired) and show *no sexual selectivity*.
 - genes for **green-sensitive** and **red-sensitive** cone pigments are located near each other in **head-to-tail tandem on Xq**:
 - prone to unequal crossing over → hybrid pigments with shifted spectral sensitivity (≈ 6% males are ANOMALOUS TRICHROMATS).
 - 2% males are DICHROMATS (**protanopia** or **deuteranopia**).
 - these abnormalities are inherited in **recessive X-linked pattern** (females show defect only when both X chromosomes contain abnormal gene; color blindness skips generations and appears in males of every second generation; Turner syndrome patients have ♂ incidence; Klinefelter syndrome patients have ♀ incidence).
2. **Lesions of V8** (*achromatopsia*).
3. **Macular / optic nerve diseases**.
4. **SILDENAFIL** (inhibits retinal form of phosphodiesterase) - transient blue-green color weakness.

BIBLIOGRAPHY for ch. "Ophthalmology" → follow this [LINK >>](#)