

# VASCULAR OCCLUSIVE DISEASES

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## Anatomy of Retinal Vasculature

1. Retinal arteries and veins - nerve fiber and ganglion cell layer
2. Radial peripapillary capillaries - nerve fiber layer
3. Superficial capillary bed - nerve fiber and ganglion cell layer
4. Deep capillary bed - inner nuclear layer

## Signs of Involvement of Superficial Capillary Bed

1. Superficial retinal edema
2. Flame-shaped or preretinal hemorrhages
3. **Cotton wool spots** - Cotton wool spots are infarcts of the nerve fiber layer due to **obstruction of terminal arteriole** producing axonal destruction or impedance of axoplasmic transport.
  - a. Appearance - Whitish-gray, fluffy areas in the superficial retina, 1/3 disc diameter in size, feathered edges, rarely more than 10 present, generally in the distribution of the radial peripapillary capillaries
  - b. Causes
    - hypertension
    - diabetes mellitus
    - collagen diseases
    - sickle cell retinopathy
    - leukemia
    - bacterial or talc emboli
    - radiation retinopathy
    - Purtscher's retinopathy vasculitis
4. Macular star figures

### **Superficial Retinal Edema**

1. diffuse, misty, white haze
2. dull retinal light reflexes
3. best seen near the disc, appears as separation of nerve fiber layer
4. fades peripherally

### **Signs of Deep Bed Involvement**

1. deep retinal edema
2. microcystic edema of the macula
3. macular cysts
4. dot and blot hemorrhages
5. capillary microaneurysms
6. retinal neovascularization

### **Deep Retinal Edema**

1. in the outer plexiform layer
2. easiest seen at the posterior pole
3. retina is thickened
4. foveal reflex lost

### **Intracellular Retinal Edema - Cloudy Swelling**

1. insufficient retinal blood supply
2. cellular disintegration
3. intracellular water, some extra cellular fluid later
4. transparency returns in two weeks

# ARTERIAL OCCLUSIVE DISEASE

1. **Branch Retinal Artery Occlusion**
2. **Central Retinal Artery Occlusion**
3. **Ophthalmic Artery Occlusion**
4. **Carotid Artery Occlusion - Aortic Arch disease**
5. **Macroaneurysms**
6. **Peripheral Retinal Artery Occlusions**
  - a. **Hemoglobinopathies**
  - b. **Retinopathy of Prematurity**
  - c. **Familial Exudative Retinopathy**

## I. BRANCH RETINAL ARTERY OCCLUSIONS

### Clinical Features

1. majority due to embolism
2. most occur at bifurcations
3. involved retina turns white and opaque -wedge shaped pattern
4. the artery narrows, the blood flow is decreased, may pulsate or be stationary
5. veins darken and have decreased flow
6. rarely, small retinal hemorrhages
7. no visual function in infarcted area
8. **frequency:** 38% of arterial occlusions
  - 57% are central retinal artery
  - 5% are cilioretinal artery

9. **prognosis:** good - about 80% improve to 20/40 or better; neovascularization of the iris is rare, usually **no treatment necessary**; diagnostic work-up indicated

**Cilioretinal Arteries** - occur in **32%** of eyes, **25%** temporal, **7%** nasal.

**Cilioretinal Occlusions- Three Clinical Variants**

1. 40%-Isolated cilioretinal occlusions  
90% improve to 20/40 or better
2. 40%-cilioretinal occlusions with central retinal vein  
70% improve to 20/40 or better
3. 15%-cilioretinal occlusions with ischemic optic neuropathy,  
visual prognosis poor; rule out giant cell arteritis

**Most Common Emboli**

1. cholesterol - from carotid arteries
2. calcified material from diseased cardiac valves
3. platelet-fibrin - from large vessel arteriosclerosis
4. septic valvular vegetation

**Retinal Artery Atheromatosis** - focal endothelial and subendothelial exudates (Kyrieles plaques) - may appear as emboli but don't occlude the lumen of the arteriole - discontinuous angiopathy: assoc. with TB?

### **Differential Diagnosis of Occlusion in Young Patients**

1. emboli from infectious endocarditis
2. emboli from rheumatic valvular heart disease with atrial fibrillation
3. fragments from atrial myxomas
4. amniotic fluid emboli
5. fat emboli from skeletal fractures
6. foreign products from intravenous drug abuse e.g. talc
7. hypercoagulability states i.e. oral contraceptives+ smoking
8. sickle cell disease
9. Hyperhomocysteinuria
10. Vasculitis ie. Behcet's
11. Antiphospholipid antibody syndromes ie. Lupus anticoagulant
12. Migraine related
13. AIDS related ???

### **Differential Diagnosis of Occlusion in Older Patients**

1. carotid artery atherosclerosis
2. mural thrombi after myocardial infarction
3. calcified aortic valve
4. prosthetic aortic valve
5. mitral valve prolapse - Barlow's Syndrome

## **II. CENTRAL RETINAL ARTERY OCCLUSION**

first described by von Graefe in 1859

### **Etiologies**

1. Emboli
2. Thrombosis at lamina cribrosa
3. Trauma or pressure
4. Inflammation - cranial arteritis or polyarteritis  
RARE: syphilis, loa loa, microfilariasis
5. Dissecting aneurysm

### **Clinical Features**

1. Sudden painless, monocular visual loss
2. opaque retina - **cherry red spot**  
opacification resolves in 4-6 weeks
3. Retinal arterial narrowing with segmentation (“Boxcarring”)
4. occasional visual sparing with cilioretinal artery
5. Afferent pupillary defect may precede retinal whitening
6. artery reopens or re-canalizes
  - a. minimal visual recovery
  - b. residual field defects
  - c. LP-NLP
7. 20% visible emboli- cholesterol (Hollenhorst)- most common  
poorer prognosis for longevity  
25% macular cilioretinal artery  
10% foveal sparing  
1-5% neovascularization  
5% have acute ophthalmic artery occlusion  
Wills Eye occurrence rate: 1 in 10,000 outpatient visits;  
Bilateral involvement: 1-2% of cases

8. **ERG**-diminution of the B wave (A wave = photoreceptors).  
If ophthalmic artery occlusion, then the A and B waves are diminished or absent. Visual acuity usually NLP
9. Iris neovascularization - 17-18%, in about 4 weeks (1-12)

### **Associated Diseases in Central Retinal Artery Occlusion**

1. 65% Hypertension
2. 33% Diabetes
3. 20% Carotid stenosis
4. 25% Cardiac valvular disease
5. 1-2% Temporal arteritis, collagen disease, IV drug abuse, hemoglobinopathy, migraine, trauma

### **TEMPORAL, CRANIAL or GIANT CELL ARTERITIS**

1. large and medium-sized arteries involved
2. temporal, occipital, and ophthalmic arteries most commonly affected
3. equal occurrence in males and females over 65 years of age
4. bilateral ocular involvement 20-25%
5. **Symptoms:**
  - a. malaise
  - b. anorexia
  - c. weight loss
  - d. headache
  - e. scalp tenderness
  - f. jaw claudication
  - g. sudden monocular loss of vision
  - h. amaurosis fugax
  - i. occasional diplopia and ptosis
  - j. earache

## **Causes of Cherry Red Spots**

1. Storage Diseases
  - Gangliosidoses ie. Tay Sach's disease, Landring's, Sandoff's
  - Niemann-Pick disease
  - Disseminated Lipogranulomatosis of Faber
  - Gaucher's disease
  - Sialidosis
  - Metachromatic leukodystrophy
2. Central Retinal Artery Occlusion
3. Subacute sclerosing panencephalitis
4. Macular hole with surrounding retinal detachment
5. Short ciliary artery occlusion
6. Macular hemorrhage
7. Traumatic macular edema
8. Preceding Acute macular neuroretinopathy

## **Therapy of Central Retinal Artery Occlusion**

1. Rapid Reduction of IOP by paracentesis and/or massage.
2. Inhalation therapy with Carbogen (95% oxygen and 5% carbon dioxide)
3. Oral acetazolamide
4. Aspirin
5. Topical beta blocker (controversial)
6. Calcium channel blockers ? (investigational)
7. TPA ? (investigational)
8. Sublingual Nitrates ? (investigational)
9. Glutamate receptor antagonists ?- block reperfusion injury

## **Prognosis**

1. 35% improve 3 lines after paracentesis
2. Pan retinal photocoagulation effective for regression of iris neovascularization in 65% of cases

### **III. Ophthalmic Artery Occlusion**

1. May be a cause of Ocular Ischemic Syndrome
2. May be mimicked by CRAO with posterior ciliary artery occlusion
3. **90% results in NLP in contrast to CF or HM with CRAO**

#### **A. Clinical Signs**

1. More intense retinal opacification than CRAO
2. **Absence of cherry red spot in 40%**
3. Mild cherry red spot in 30%
4. Definite cherry red spot in 30% due to re-establishment of choroidal circulation
5. Opacification resolves in few weeks
6. **RPE changes occur late due to choroidal hypoperfusion not seen with CRAO**

#### **B. Fluorescein Angiography**

1. Delayed choroidal filling
2. Delayed arterial filling
3. Prolonged AV Transit time
4. Only segmental filling
5. Late staining of RPE in some cases
6. **ERG shows decrease or absent A & B waves**

#### **C. Etiologies**

1. Similar to CRAO
2. Mucormycosis
3. Retrobulbar injection into optic foramen
4. Steroid injection into nasal turbinates
5. Giant Cell Arteritis

#### **D. Treatment**

1. Same regimen as for CRAO
2. Generally unsatisfactory

## **IV. OCULAR ISCHEMIC SYNDROME**

1. **Ocular manifestations of carotid artery obstruction.**

2. Also known as **Venous Stasis Retinopathy**  
**Hypotensive Retinopathy**  
**Chronic Ischemic Retinopathy**  
(Kearns and Hollenhorst 1963)

**A. Clinical Findings**

1. mean age 65 years
2. males more than females
3. usually unilateral  
(bilateral involvement 20%)

**B. Symptoms:**

1. loss of vision in 90%
2. no visual symptoms in 10%
3. 5% present with amaurosis fugax  
mild 35% 20/20 - 20/40  
moderate 30% 20/50 - 20/400  
severe 35% C.F.. - L.P....
4. pain - 40% have dull headache over eye or brow

**C. Signs**

1. **Anterior Segment**

- a. corneal edema
- b. 2/3 rubeosis iridis (when first present)
- c. 20% iritis (generally mild)
- d. lens opacities at end stage

2. **Posterior Segment**

- a. retinal arterial narrowing
- b. retinal venous dilation but not tortuous
- c. retinal hemorrhages and microaneurysms - 80%
- d. neovascularization of the optic disc and/or retina -8%
- e. cherry red spot - 12% - when visual loss is rapid
- f. cotton wool spots - 5%
- g. spontaneous pulsations of the retinal arteries - 5%
- h. cholesterol emboli
- i. absence of optic disc swelling

**D. Fluorescein Angiography**

1. prolonged arm to choroid/retina circulation (95%)
2. delayed or patchy choroidal filling >5 seconds to completion
3. staining of retinal vessels, especially arteries
4. increased retinal arterial-venous transit time
5. macular edema
6. microaneurysms
7. retinal capillary non-perfusion
8. ERG shows decreased AB wave  
on carotid angiogram - 90% occlusion

**E. Differential Diagnosis**

1. non-ischemic central retinal vein obstruction
2. diabetic retinopathy
3. chronic ophthalmic artery insufficiency

**F. Systemic Associations**

1. 50% have ischemic heart disease
2. 25% have had previous CVA
3. 5 year mortality = 40%  
leading causes: heart disease,  
then stroke

## **G. Treatment of Ocular Ischemic Syndrome**

1. carotid artery endarterectomy
2. superficial temporal artery to middle cerebral artery bypass
3. Pan retinal photocoagulation for rubeosis

\*Clue to less severe carotid disease:  
Asymmetric diabetic or hypertensive retinopathy

## **V. MACROANEURYSMS**

A macroaneurysm is a fusiform or asymmetrical enlargement of a retinal artery. This may be enlarged up to three times the normal caliber. First reported by Loring in 1880, defined clinically by Robertson in 1973.

1. arise at major branching sites or A-V crossings
2. usually solitary; in 20% of cases, more than one in an eye
3. 10% - 25% incidence of bilaterality,  
right more than left eye ?
4. occur in elderly hypertensive (75% Gass) females
5. MASQUERADE SYNDROME

### **Clinical Course of Macroaneurysms**

1. asymptomatic, or may present with visual loss secondary to exudation or hemorrhage
2. may spontaneously sclerose
3. visual loss may persist because of
  - a. preretinal fibrosis
  - b. retinal pigment epithelial changes
  - c. persistence of blood or macular arterial occlusion

### **Angiographic Findings in Macroaneurysms**

1. widening of capillary free zone
2. small areas of capillary non-perfusion
3. capillary dilatation
4. microaneurysms
5. intra-arterial collaterals

### **Differential Diagnosis of Macroaneurysms**

1. Age related maculopathy, hemorrhagic RPE detachments
2. Leber's and Coats'
3. retinal angioma
4. collateral vessels (e.g. branch vein occlusion)
5. Eales' disease
6. Background diabetic retinopathy
7. Venous macroaneurysms
8. Cavernous hemangioma
9. Idiopathic epiretinal membrane
10. Malignant melanoma

### **Therapy of Macroaneurysms**

1. Indicated for deterioration due to macular edema or exudate
2. Direct vs indirect treatment
3. Complications include BRAO, BRVO, macular pucker, paracentral scotomas, SRN, foveal burns, optic disc damage

## **IV.a SICKLE CELL RETINOPATHY**

Sickle cell retinopathy is a vascular retinopathy in which fibrovascular proliferation occurs in response to retinal ischemia

Hemoglobin A = 2 alpha peptide chains and 2 beta peptide chains  
alpha chain = 141 amino acids  
beta chain = 146 amino acids

Hemoglobin variants

alpha chain = same in A, S, and C

beta chain = #6 position varies

Variant hemoglobins believed to offer protection against malaria

Advantage for survival in endemic regions

**AFRO-AMERICANS - 10% Abnormal Hemoglobin**

AS	8-11%	
AC	2- 3%	
SS	1/600	0.4%
SC	1/1500	0.2%
CC	1/6000	
Sthal	Rare	

**ALSO PRESENT IN MEDITERRANEAN POPULATIONS**

**NON-PROLIFERATIVE SICKLE CELL RETINOPATHY**

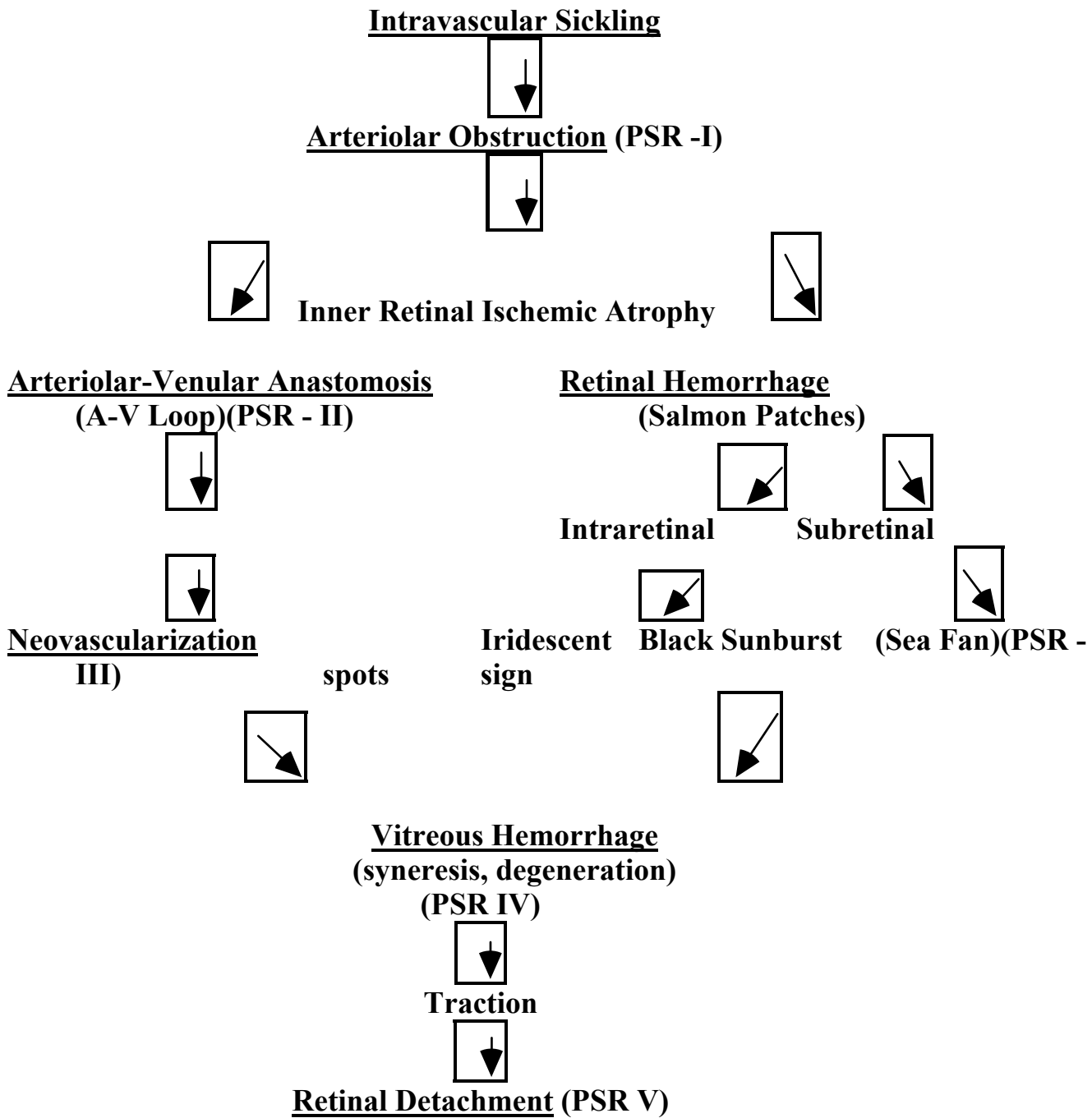
**( Background changes - Arteriolar Occlusion**

1. Retinal Hemorrhages- **Salmon Patches**
2. **Refractile Iridescent Spots**-old, re-absorbed hemorrhages with **hemosiderin** deposits within the retina in acquired schisis cavities beneath internal limiting membrane secondary to sudden blowout. Hemosiderin appears within **macrophages** as yellow-copper colored granules
3. **Black Sunburst** - localized areas of RPE hypertrophy, hyperplasia and migration into the retina in a perivascular location secondary to intraretinal hemorrhage 1/2 - 2 DD in size
4. Major vessels usually appear normal but may show **increased tortuosity** due to peripheral A-V shunts
5. Anterior Segment Signs include **comma-shaped capillaries** in the conjunctiva, **Iris atrophy**, Anterior and posterior **synechiae** and **cell & flare**



**Proposed Pathogenesis of Sickle Retinopathy**  
**(Morton F. Goldberg, M.D.)**

Summary of proposed sequence of events and pathogenesis of sickle retinopathy....



## **THERAPY OF SICKLE CELL RETINOPATHY**

1. spontaneous regression of sea fans in 60% of the lesions
2. eight year incidence of significant visual loss is 12%
3. photocoagulation
4. cryopexy or diathermy
5. scleral buckle with or without vitrectomy
6. Hydroxyurea - increases HbF
7. Clotrimazole - may decrease sickling by blocking deoxygenation induced cell shrinkage produced by the Gardos channel (K<sup>+</sup>/Cl<sup>-</sup> cotransporter)

### **Photocoagulation of Sickle Cell Retinopathy**

#### **A. Indications**

1. recurrent vitreous hemorrhage from neovascularization
2. vitreal traction on new vessels
3. retinal holes or tears, if in areas of traction need scleral buckling

#### **B. Method**

1. recurrent feeder vessel and the neovascular frond
2. spot size larger than caliber of vessels
3. intense burns
4. repeat fluorescein angiogram to confirm vessel closure

5. **AVOID**
  - a. treating venous side
  - b. treating in a traction detachment

### **C Contraindications To Photocoagulations**

1. tears in areas of significant vitreous traction
2. traction retinal detachments
3. vitreous or lens opacifications

### **Complications of Feeder Vessel Photocoagulation**

Chorioretinal, choriovitreal neovascularization

Vitreous hemorrhage, macular hole

Pre-retinal membrane, subretinal fibrosis

### **D. Complications of Photocoagulation**

1. retinal hemorrhages
2. choroidal hemorrhages
3. peripheral choroidal ischemia
4. choroidal neovascularization
5. retinal breaks
6. retinal detachment, traction or rhegmatogenous
7. vitreous hemorrhage

### **Precautions - Surgical Risks**

Pre-op closure of sea fans

Local anesthesia

Avoid Epinephrine, phenylephrine

Low IOP during surgery

Minimal use of CAI/mannitol to avoid hemoconcentration

Cryo better than diathermy

Scleral buckling may compromise circulation

## **HYPHEMAS**

Significantly poorer prognosis

Sickle RBC's clog the TM

IOP increased to 35 - may be risk for CRAO

**Recommend - paracentesis to control IOP**

## **VI.b RETINOPATHY OF PREMATURITY**

### **(RETROLENTAL FIBROPLASIA)**

#### **History:**

- 1942 Terry described disease
- 1951 Campbell in Australia and Evans in England  
incriminate the role of oxygen
- 1953 Ashton and Patz produced retrolental  
fibroplasia in experimental animals
- 1984 Lucy and Dangman oxygen's role reevaluated

#### **Clinical Course**

1. Exposure to oxygen concentration over 40%
2. Low birth weights -1500 gm
3. oxygen toxicity produces severe retina  
vasoconstriction
4. following return to normal oxygen levels
  - a. retinal vasodilatation and tortuosity
  - b. retinal hemorrhage, retinal edema
  - c. preretinal neovascular formation
  - d. retinal detachment
  - e. vitreous hemorrhage
  - f. cicatricial phase with increased retinal  
detachment and disorganization

**Ocular findings depend on severity**

1. dragging of retinal vessels temporally
2. ectopic macula
3. tilted disc
4. myopia
5. partial or total retinal detachment
6. retrolental mass

**Retinopathy Of Prematurity - Committee For Classification**

**LOCATION:**

**Zone I: posterior retina within 60° circle  
centered on the optic nerve**

**Zone II: from the posterior circle (zone I) to the  
nasal ora anteriorly**

**Zone III: remaining temporal retina**

**EXTENT: Number of clock-hours involved**

**SEVERITY:**

**Stage 1: Demarcation line**

**Stage 2: Ridge**

**Stage 3: Ridge with extraretinal fibrovascular proliferation**

**Stage 4: Subtotal retinal detachment**

**a. Extrafoveal**

**B. Retinal detachment including fovea**

<b>Stage 5:</b>	<b>Total retinal detachment</b>	
<b><u>Funnel:</u></b>	<b><u>Anterior</u></b>	<b><u>Posterior</u></b>
	<b>Open</b>	<b>Open</b>
	<b>Narrow</b>	<b>Narrow</b>
	<b>Open</b>	<b>Narrow</b>
	<b>Narrow</b>	<b>Open</b>

**Changes associated with Regressed ROP**

**Transient disease in majority of infants**  
**Spontaneous regression in 85% of eyes**

**PERIPHERAL CHANGES**

**Vascular**

1. failure to vascularize peripheral retina
2. abnormal, non-dichotomous branching of retinal vessels
3. vascular arcade with circumferential interconnection
4. telangiectatic vessels

**Retinal**

1. pigmentary changes
2. vitreo-retinal interface changes
3. thin retina
4. peripheral folds vitreous membranes with or without attachment to retina
6. lattice-like degeneration
7. retinal breaks
8. traction/rhegmatogenous retinal detachment

**POSTERIOR CHANGES**

**Vascular**

1. vascular tortuosity
2. straightening of blood vessels in temporal arcade
3. decrease in angle of insertion of major temporal arcade

**Retinal**

1. pigmentary changes
2. distortion and ectopia of macula
3. stretching and folding of retina in macular region
4. vitreo-retinal interface changes
5. vitreous membrane
6. dragging of retina over disc
7. traction/rhegmatogenous retinal detachment

## **Histopathological Features - depend on stage of disease**

**Early:** ridge-like thickening of the retina at the junction of vascularized and non-vascularized zones, involving endothelial cell and spindle-shaped mesenchymal cell proliferation

**Neovascularization** develops at the junction between the vascularized and non-vascularized areas of the peripheral retina, proliferating on the surface of the retina at vitreo-retinal interface. Capillary-like vessels extend into the vitreous cavity along with fibro-glial tissue. The new vessels leak and bleed eliciting more fibro-glial proliferation

**Fibrovascular and glial tissue** contract producing dragging of the macula and the retinal vessels from the optic nerve

**If traction and fibrovascular proliferation** is progressive it leads to a total retinal detachment with a mass of tissue behind the lens and the clinical appearance of leukocoria

## **Therapy**

- A. Primary goal is to **avoid occurrence** of the disease by carefully monitoring oxygen levels in the newborn or premature nursery. However, respiratory distress and increasingly immature newborns makes prevention impossible.
- B. **Monitoring - High risk infants( less than 36 weeks or 2000 grams) need evaluation at discharge from the nursery and again at 3 to 6 months of age. The optimal examination time is 7 to 9 weeks of age. Particular attention to infants 1000 grams or less. Those with prethreshold disease should be seen every 2 weeks.**
- C. **Vitamin E therapy** - precise value is unclear, many newborns have a deficiency; **may reduce the severity but not the incidence of the disease.** High levels of vitamin E (greater than 3.5 mg) may be associated with necrotizing enterocolitis, sepsis and death.

**D. Cryoretinopexy**

**Cryo-ROP Study:** 50% reduction in unfavorable events  
43% to 21.8%

1. **Unfavorable outcomes:**
  - a. retinal fold involving the macula
  - b. retinal detachment involving posterior pole
  - c. total retrolental mass
2. **Threshold disease**, zone 1 or 2, Stage 3+ in 5 contiguous clock hours or 8 cumulative clock hours

**Plus disease** - increased dilatation and tortuosity of retinal vessels at the posterior pole, iris, vascular engorgement, pupillary rigidity, vitreous haze

**Rush disease** - Plus disease located in zone I or posterior zone II is at risk for rapid progression

**Risk of blindness in infants reaching threshold approaches 50%**  
**Threshold disease is thus defined as risk of blindness = 50%**

3. **Pre-threshold** Zone I any stage  
Zone II Stage 2+  
Zone III Stage 3
4. cryocoagulation carried out within 72 hours  
contiguous single applications begin at ora  
and move posteriorly, entire anterior  
avascular retina treated to anterior edge of ridge

**E. Photocoagulation - Equivalent regression of neovascularization to cryo with less morbidity**  
**May produce less late myopia**

**F. Vitrectomy** Stage 5 disease - long term results must be evaluated

**G. Supplemental Oxygen Therapy (SOT)** - animal studies suggest the possibility of moderating revascularization by controlled hypoxia. Refinement may lead to a noninvasive therapy

## **VI.c FAMILIAL EXUDATIVE VITREO-RETINOPATHY (FEVR)**

1. **Autosomal Dominant** affects young patients  
presents with late signs - cataracts, strabismus, nystagmus
2. Cause - **failure of the temporal retina to vascularize**
3. may be mistaken for R.O.P.
  - a. full term, no oxygen
  - b. normal respiratory status
  - c. no peripheral mesenchymal shunt
  - d. no myopia
  - e. no lattice
4. traction exudative detachments - may occur in infancy or later
5. may be asymptomatic in adults  
73% of patients are asymptomatic

### **Fundus Appearance**

**Mild** -limited to the periphery

Earliest signs excessive white with and without pressure and  
abnormal retinal vessels of excessive size extending to the ora

**Moderate** - includes periphery + posterior pole  
Periphery shows dilated, tortuous peripheral blood vessels, neovascularization, hemorrhages, and retinal tears  
Posterior pole shows dragging of the disc and macular ectopia

**Severe** Total retinal detachment, PVR, and optic atrophy

**Vitreous Appearance** - diffuse haze, large most intense at base  
snow flake appearance with fibrovascular membrane in periphery like ROP  
liquefaction infrequent  
Posterior Vitreous Detachments present that do not involve disc or macular

Vitreous exudation, contraction, condensation at the base  
white with pressure and  
peripheral cystoid present

**Vitreous contraction = constant sign**

**Differential diagnosis** - appearance similar to **ROP**,  
**Pars Planitis, Coat's disease,**  
**peripheral uveitis, PHPV,**  
**Eales, Angiomatosis Retinae**  
(often bilateral also)but none of these have a + **Family History**

**Treatment - pars plana vitrectomy**

## **VENOUS OCCLUSIVE DISEASE**

1. **Branch Retinal Vein**
2. **Central Retinal Vein**
3. **Periphlebitis**

### **I. BRANCH RETINAL VEIN OCCLUSIONS**

#### **Clinical Features**

1. Patients age 50-70 years
2. 50% of patients are hypertensive
3. symptoms depend on location of the occluded vein in the retina and site of occlusion in the involved vein

#### **Vessel Involvement**

- |    |                          |     |     |
|----|--------------------------|-----|-----|
| 1. | superior temporal branch | 60% |     |
| 2. | inferior temporal branch | 30% |     |
| 3. | all other vessels        |     | 10% |

## **Clinical Findings**

### **A. Acute Stage**

1. segmental distribution of retinal hemorrhage
2. retinal edema
3. cotton wool spots (nerve fiber layer infarcts)
4. tortuous vein with darkened blood column

### **B. Chronic Stage**

1. persistent retinal hemorrhage
2. capillary bed tortuosity and leakage
3. capillary bed non-perfusion
4. fatty exudate
5. retinal edema
6. collateral vessel formation
7. neovascularization

### **C. Late Stage**

1. halo sheathing of vein
2. ghost vessels
3. remodeling of collateral vessels
4. hemorrhage from neovascularization
5. preretinal gliosis (epiretinal membrane)

## **Mechanism of Obstruction - Mechanical**

The **A-V crossings** have a **common adventitial sheath**. **70%** of the time the artery crosses over the vein. Contraction of the sheath and increased rigidity of the crossing artery, features of arteriolar sclerosis, are thought to result in compression and narrowing of the vein, turbulent blood flow, endothelial cell damage, and thrombotic occlusion of the vein

### **A-V Crossing Changes**

1. loss of transparency
2. tapering of vein
3. deflection of vein
4. flow changes
5. **banking** – Post-crossing dilation and darkening
6. **Bonnet's sign** - hemorrhages surrounding crossing
7. microaneurysms, transudations, hemorrhages

### **Proposed Pathophysiology**

1. mechanical compression
2. turbulence of flow
3. endothelial damage
4. platelet adherence and aggregation
5. thrombus formation

### **Risk Factors for BRVO**

1. Systemic hypertension
2. Cardiovascular disease
3. Increased body mass index at 20 years of age
4. Glaucoma
5. Elevated serum levels of alpha-2- globulin ( inflammation?)  
(The Eye Disease Case-Control Study Group,  
AJO 116:286-296, September, 1993)
6. Shorter axial length - both BRVO and CRVO
7. Increased plasma viscosity and hematocrit

### **Factors which Decrease Risk for BRVO**

1. Higher levels of alcohol consumption
2. Higher levels of high density lipoproteins  
(The Eye Disease Case-Control Study Group,  
AJO 116:286-296, September, 1993)

### **Possible Associated Conditions**

#### **A. Changes in blood constituents**

1. dysproteinemias
2. polycythemia
3. leukemia
4. malaria
5. sickle cell disease

#### **B. Inflammatory Obstruction**

1. periphlebitis as in Eale's Disease
2. toxoplasmosis
3. non-specific uveitis
4. pars planitis
5. sarcoidosis
6. Behcet's Disease

### **Management of Branch Vein Occlusion**

A. **Acute** marginal value of fluorescein angiogram

B. **Chronic** do fluorescein angiogram

To detect macular edema  
collaterals  
capillary bed non-perfusion  
neovascularization

### **Retinal Collateral Vessels**

1. vessels which develop within the framework of the existing vascular network
2. originate from the retinal capillary bed joining obstruction to non-obstructed adjacent vessels to bypass obstruction in a single vessel]
3. flow generally slower than normal
4. clinically visible at three months
5. distinguished by fluorescein from neovascularization

## **Retinal Neovascularization**

new vessels originating from and continuous with the pre-existing retinal vascular bed located either within or adjacent to the retina in areas where vessels are not abnormally present, usually from venules

## **Complications of Branch Retinal Vein Occlusion**

1. Macular edema 50%
2. Capillary non-perfusion 5dd's or greater 40%  
develop neovascularization, of these 60% will develop vitreous hemorrhage when neovascularization develops, argon laser photocoagulation will reduce the rate of bleeding from 60% to 30%
3. Epiretinal macular gliosis - 21%
4. Retinal tears due to vitreous contraction at site of occlusion

## **NATURAL COURSE**

### Visual Acuity

20/40 or better	53%
20/50 - 20/100	28%
20/200 - or worse	19%
<i>OR</i>	
20/50 or better	60%
20/25 or better	30%

## **Extent of Permanent damage related to:**

1. degree of venous obstruction
2. extent of damage to capillary bed
3. amount of secondary ischemic and hemorrhagic infarction
4. adequacy of collateral channels

## Treatment of Branch Vein Occlusion

1. macular edema                      laser grid
2. collaterals                            no, avoid
3. neovascularization    yes
4. medical control of hypertension    yes
5. anticoagulants, dextran, etc            probably of no value
6. surgical decompression (sheathotomy)            investigational

## Recommendations for Treatment

1. Wait 3-6 months for clearing of retinal hemorrhages, this will allow for a high quality angiogram
2. Evaluate angiogram for macular edema versus macular non-perfusion (**Macular edema criteria = fluorescein leakage, as opposed to CSME from ETDRS**)

If vision 20/40 or worse and edema is responsible, give laser grid to macula. Carefully avoid collaterals.

If macular non-perfusion is responsible, laser not helpful

If area of retinal involvement is greater than 5dd's, wait for retinal hemorrhages to clear

If capillary bed non-perfusion is present, follow carefully

If neovascularization develops, treat with argon laser photocoagulation. Carefully avoid collaterals.

### **Summary of Clinical Finding in Branch Vein Occlusion**

1. vein peripheral to obstruction dilates, darkens and becomes more tortuous (banking)
2. deep and superficial edema in the drainage bed
3. dot and blot deep retinal hemorrhages
4. cotton wool exudates
5. fatty exudates after two months
6. early vein wall haze, then help sheathing
7. ghost veins or segments with obliterated lumens
8. collaterals - occur in two placed
  - a. point of obstruction
  - b. either side of macula
9. increased arteriosclerosis of accompanying artery
10. low grade epiretinal gliosis
11. neovascularization

## **II. CENTRAL RETINAL VEIN OCCLUSION**

### **Classification (Stuart Fine, M.D.)**

- A. **Severe = Hemorrhagic Retinopathy of Hayreh**
- B. **Mild = Venostasis Retinopathy of Hayreh**
- C. **Optic Disc Vasculitis or Papillophlebitis (Lyle-Wybar)**

## **Ophthalmic Findings - A spectrum of vascular obstruction**

- A. **Severe type**
  - 1. extensive hemorrhage and edema
  - 2. engorged retinal veins
  - 3. cotton wool spots
  - 4. microaneurysms
  
- B. **Mild type**
  - 1. scattered hemorrhages
  - 2. macular edema
  - 3. engorged retinal capillaries
  - 4. some microaneurysms
  
- C. **Optic Disc Vasculitis**
  - 1. peripapillary hemorrhages
  - 2. mild papilledema

### **\*\*\*\*\*CRVO Rules of Thumb-**

- 1/3 ischemic , 2/3 non-ischemic**
- 2/3 of ischemic develop neo ( rubeosis , NVD, NVE)**
- 2/3 of neo is rubeosis, 1/3 is 2/3 NVD,1/3 NVE**
- 2/3 of rubeosis results in Neovascular Glaucoma**

### **Clinical Indicators of Ischemia**

- 1. Severe visual loss - usually < 20/200**
- 2. Afferent pupillary defect**
- 3. Confluent retinal hemorrhages with multiple CWS**
- 4. Extensive capillary non-perfusion - 10DD**
- 5. ERG B/A wave amplitude ratio <1**
- 6. Constriction of peripheral visual fields**
- 7. Reduced CV blood velocities by Color Doppler**
- 8. Rubeosis**

### Ocular Disease with Predisposing Effect on Central Vein Occlusion:

- A. glaucoma 20%
- B. papilledema
- C. optic nerve drusen
- D. optic nerve hemorrhage
- E. subdural hemorrhage

(Green et al., Retina 1:27-55, 1981)

### Associated Systemic Diseases

- 1. hypertension 50%-70%
- 2. diabetes mellitus 15%-20%
- 3. cardiovascular disease 25%-50%
- 4. hematological disorders e.g. leukemia

## THE CENTRAL VEIN OCCLUSION STUDY

### Baseline and Early Natural History Report

- 1. 728 eyes of 725 patients
- 2. 4 groups- **Perfused** ( 547/728 or **75%**),  
**Non-perfused**( 181/728 or **24.8%**),  
**Indeterminate**(52/728 or **7%**),  
**Macular edema** (155/728 or 21%)
- 3. **16%** (81/522) of **perfused** eyes became **ischemic**
- 4. **83%** of **indeterminate** eyes became **ischemic**  
(Central Vein Occlusion Study Group,  
AJO 1993;111:1087-1095)

### Grid Pattern Photocoagulation for Macular Edema in CRVO

- 1. **155 eyes with visual acuity of 20/50 or worse** randomized to treatment or not with grid laser therapy
- 2. **No difference** in final acuity results between groups
- 3. Treatment **reduced angiographic evidence** of macular edema  
(Central Vein Occlusion Study Group, Ophthalmology 1995;102: 1425-1433)

## **Prophylactic Panretinal Photocoagulation in Ischemic CRVO**

**1. 180 eyes with at least 10 disc areas of nonperfusion** were randomized to immediate prophylactic treatment or close observation

**2. Two clock hours of iris neovascularization or angle neovascularization (TC-INV/ANV)** developed less often in eyes treated prophylactically but the difference was not statistically significant.

**3. Prompt regression of (TC-INV/ANV) in response to PRP was more likely to occur in eyes that had not been previously treated** (Central Vein Occlusion Study Group, Ophthalmology 1995;102: 1434-1444)

## **Complications of Central Retinal Vein Occlusion**

1. Rubeosis - anterior segment neovascularization 20 - 33%
2. Optic disc neovascularization 1-3%
3. Chronic macular edema 20%

## **Collateral Vessels on the Disc - Opticociliary Veins** (Elschnig)

### **Differential diagnosis:**

1. Central Retinal Vein Obstruction
2. Chronic Papilledema
3. Optic Nerve Glioma
4. Perioptic Vascular Malformation
5. Spheno-orbital Meningiomas
6. Meningiomas of the optic nerve sheath
7. Chronic glaucoma

## **Opticociliary Veins and Central Vein Occlusion**

1. Found in 7.4% of eyes within 1 Years of CVO
2. Found as late development in 30.4% of eyes 1 year after CVO
3. No difference in incidence between ischemic vs. non-ischemic eyes
4. No difference in visual acuity in eyes with or without OCVs
5. No prognostic significance

(Giuffrè et al, BJO 1993; 77: 774-777)

## **Treatment**

- A. **Medical**
  1. anticoagulants, etc., of questionable value
  2. steroids - controversial
  3. TPA - clinical trials in progress
- B. **Photocoagulation** indicated for disc neovascularization and anterior segment neovascularization. May be of value prophylactically in eyes with large areas of capillary non-perfusion ( ischemic CRVO's) and for macular edema
- C. **Surgical decompression** - Posada Procedure - no value, others ?
- D. **Laser Chorioretinal Venous Anastomosis**- investigational

## **III. PERIPHLEBITIS**

Periphlebitis is an inflammation of the venous wall characterized by white, segmental sheathing of the vein.

### **Causes of Periphlebitis:**

1. Eales' Disease
2. multiple sclerosis
3. non-specific uveitis
4. toxoplasmosis
5. sarcoidosis
6. Behcet's Disease
7. peripheral uveitis (pars Planitis)

### **Rare Causes of Periphlebitis**

1. brucellosis
2. Cryptococcus neoformans
3. infectious mononucleosis
4. leprosy
5. syphilis

### **Eales' Disease (primary idiopathic retinal vasculitis)**

1. 1880 Henry Eales described primary recurrent retinal hemorrhage, originally associated with epistaxis and constipation
2. currently periphlebitis, idiopathic occlusive vasculopathy with recurrent vitreous hemorrhage
3. predominantly young, rarely over 40 years of age
4. begins more frequently in left eye
5. periphlebitis usually first appears in periphery, sparing the macula, but may progress to tractional detachment
6. Rare in North America, widespread in India, Pakistan, Afghanistan
7. Equal prevalence males and females
8. May rarely affect the retinal arterioles

### **Findings in Eales Disease**

1. darkening and irregularity of a venous branch
2. deep retinal edema in drainage bed
3. within several days, cuffing of veins and hemorrhages
4. signs of venous impedance - may improve in 2-3 weeks with resolution in 3 months and halo sheathing
5. may progress and extend along the vein
6. capillary bed closure - non-perfusion
7. retinal neovascularization
8. Multifocal areas of vitreoretinal adhesions reported in 83%(Liggett)

### **Prognosis in Eales Disease**

1. 54% final vision 2//50 or better
2. 20% final vision less than 20/200

### **Clinical Course**

- 1 Periodic exacerbations
2. Duration 6 months to 14 years  
average 2.9 years (Elliott 1954)

### **Treatment**

Pan retinal photocoagulation  
Pars plana vitrectomy  
Good visual return in majority of cases

### **Vascular Endothelial Growth Factor (VEGF)**

Angiogenic protein  
Produced by several retinal cell types in response to hypoxia  
May induce and control intraocular neovascularization in a variety of ischemic retinal conditions