CENTRAL RETINAL

Vein Occlusion

Comprehensive PG Exam Summary

Classifications · Pathophysiology · Investigations · Management · Trials

Learn. Grow. Heal.

Viva Pearls | MCQ Traps | Landmark Trials | Surgical Correlates | Emerging Therapies

1. CLINICAL ANALOGY — Building the Concept

*Imagine the central retinal vein (CRV) as the **main drainage pipe of a city** (the retina). The optic nerve head is a narrow underground tunnel through which this pipe must pass. Now imagine the pipe gets **blocked at the tunnel exit** by a blood clot — the entire drainage system backs up. Blood and fluid pour into every district simultaneously. This is CRVO: sudden, panretinal venous hypertension causing flame haemorrhages in **all four quadrants**, disc swelling, dilated tortuous veins, macular oedema, and potentially ischaemic shutdown — the **"thunderstorm fundus."***

2. RELEVANT ANATOMY & SITE OF OCCLUSION

The CRV travels within the optic nerve alongside the central retinal artery (CRA). Both share a **common adventitial sheath** at and just posterior to the lamina cribrosa — the **pathological epicentre** where AV compression initiates thrombus formation.

Structure	Relevance in CRVO
Lamina cribrosa	Primary site of occlusion; rigid collagen lattice compresses CRV
Shared adventitia (CRA + CRV)	Arteriosclerosis of CRA transmits mechanical compression directly to CRV
Cribriform plate pores	Narrowed in glaucoma — raised IOP contributes to venous stasis at lamina
No valves in CRV	No retrograde protection; pressure propagates to entire retinal venous tree
Cilioretinal artery (15–20%)	When present, spares papillomacular bundle → preserved central VA in CRVO

3. PATHOPHYSIOLOGY — Virchow's Triad Applied

Triad Component	Mechanism in CRVO	Key Associations
1. Endothelial damage	AV crossing compression; turbulent flow; vasculitis	Hypertension, atherosclerosis, Behcet's, sarcoidosis
2. Stasis / slow flow	Raised IOP compresses CRV at lamina; hyperviscosity; nocturnal hypotension	POAG, polycythaemia, myeloma, dehydration
3. Hypercoagulability	Defective fibrinolysis; pro-thrombotic states	APLA, Factor V Leiden, Protein C/S deficiency, OCP

Downstream cascade:

- Venous occlusion → raised hydrostatic pressure → plasma + RBC extravasation into all 4 quadrants
- **Macular oedema (cystoid)** — primary driver of visual loss; VEGF-mediated permeability
- Retinal ischaemia → VEGF upregulation → **NVD, NVE, NVI (rubeosis iridis)**
- Cotton wool spots = NFL infarcts (axoplasmic stasis) = marker of concurrent ischaemia

4. CLASSIFICATION — Ischaemic vs Non-Ischaemic

Feature	Non-Ischaemic (Perfused)	Ischaemic (Non-Perfused)
Incidence	75–80%	20–25%
VA at presentation	6/6 – 6/60	**<6/120 (CF/HM)**
RAPD	Absent / minimal	**Present**
FFA: NP areas	<10 disc areas	**>10 disc areas**
ERG b-wave	>60% of normal	**<60% of normal**
Cotton wool spots	Few / absent	Multiple, prominent
Rubeosis (NVI) risk	**Low (<5%)**	**High (45–60% / 3 months)**
VA prognosis	Moderate; 50% improve	**Poor; permanent damage**
Conversion risk	~34% convert to ischaemic	N/A

◆ ***VIVA PEARL: ERG b-wave <60% of normal = ischaemic CRVO (CVOS criterion). Electronegativity pattern (reduced b-wave, preserved a-wave) reflects inner retinal ischaemia at bipolar/Muller cell level — objective predictor of NVI risk.***

5. RISK FACTORS & ASSOCIATIONS

Systemic	Ocular	Haematological / Thrombophilic
Hypertension *(most common, 64%)*	POAG (raised IOP)	Polycythaemia vera
Diabetes mellitus	High myopia	Essential thrombocythaemia
Hyperlipidaemia	Drusen of ONH	Myeloma / paraproteinaemia
Cardiovascular disease	Arteriosclerosis of CRA	Antiphospholipid syndrome
Obesity / metabolic syndrome	Prior fellow eye CRVO	Factor V Leiden mutation
Hyperhomocysteinaemia		Protein C / S deficiency
OCP use (younger women)		Antithrombin III deficiency

Thrombophilia Screen Indications: Age <50 years · Bilateral CRVO · Recurrent CRVO · Family history of thromboembolism · No identifiable systemic cause

6. CLINICAL FEATURES

6a. Symptoms

- Sudden, **painless**, unilateral visual loss (hours to days)

- Often noticed **on waking** — nocturnal hypotension + horizontal posture → venous stasis
- Metamorphopsia when macula involved (CMO distorts foveal architecture)
- **Pain = late sign = neovascular glaucoma — "90/100-day glaucoma"**

6b. Fundoscopy Signs — All 4 Quadrants

Sign	Description	Significance
Flame haemorrhages	All 4 quadrants, radiating from disc; NFL-level	Hallmark; distinguishes CRVO from BRVO (1 quadrant only)
Disc swelling	Hyperaemic, oedematous; blurred margins entire disc	Venous congestion + axoplasmic stasis
Dilated tortuous veins	All 4 branch veins; "sausage-link" tortuous course	Pathognomonic; absent in AION
Macular oedema	CMO pattern; loss of foveal reflex; petaloid on FFA	Primary cause of VA loss; treatment target
Cotton wool spots	White NFL infarcts near disc and temporal arcade	Marker of ischaemia; predict conversion
NVD / NVE / NVI	Late (~3–4 months); frond-like vessels	**Ischaemic CRVO; urgent PRP + anti-VEGF**
Optociliary shunts	Dilated retinociliary collaterals at disc	Chronic CRVO; also optic nerve sheath meningioma; no FFA leak

7. INVESTIGATIONS

7a. Ocular Investigations

Investigation	Key Findings	Purpose
FFA	Delayed venous filling; blocked fluorescence; NP areas; disc/CMO leakage (petaloid)	**GOLD STANDARD** — classify ischaemic vs non-ischaemic; guide PRP
OCT Macula	CMO; SRF; ELM/EZ disruption; DRIL; hyperreflective foci; CMT	**GOLD STANDARD** for CMO monitoring and treatment response
OCT-A	FAZ enlargement; capillary dropout; NV flow maps	Non-invasive ischaemia mapping; replacing FFA in some centres
ERG	b-wave reduction; b/a wave ratio; electronegativity	Objective ischaemia — b-wave <60% = ischaemic (CVOS)
Gonioscopy	NVI, angle NV, PAS assessment	**Mandatory at every visit — ischaemic CRVO**
IOP	Baseline and ongoing monitoring	Risk factor; NVG develops ~90 days post-CRVO

7b. Systemic Investigations

- **BP, fasting glucose, HbA1c, lipid profile** — all patients; cardiovascular risk screen
- **CBC, ESR, serum protein electrophoresis** — hyperviscosity syndrome
- **Thrombophilia screen** (if indicated): Factor V Leiden, Protein C/S, ATIII, APLA, homocysteine
- **Carotid Doppler** — OIS differential; bilateral disease or poor anti-VEGF response
- **Echo + 24h Holter** — cardioembolic source in younger patients

8. OCT FEATURES IN DETAIL (Exam Favourite)

OCT Finding	Interpretation	Prognostic Value
Intraretinal cysts (CMO)	Fluid in OPL / INL / ONL — cystoid spaces	Responds to anti-VEGF and steroids
Subretinal fluid (SRF)	RPE pump dysfunction; fluid under neurosensory retina	Good anti-VEGF response; can self-resolve
ELM disruption	Photoreceptor stress and degeneration	Poor VA outcome; structural compromise
EZ (IS/OS) disruption	Photoreceptor outer segment loss	**Worst VA prognosis — irreversible**
Hyperreflective foci	Activated microglia or lipid exudates	Active ischaemia / inflammation marker
DRIL	Disorganisation of Retinal Inner Layers — loss of distinct band pattern	**Strong independent predictor of poor VA**
FAZ enlargement (OCT-A)	Macular ischaemia; capillary dropout around fovea	Predicts limited response to any therapy

9. MANAGEMENT ALGORITHM

9a. General Principles

- CRVO has **no proven acute reversal treatment** — management targets complications
- Aggressively control systemic risk factors: HTN, DM, hyperlipidaemia, obesity
- Avoid dehydration, excessive diuretics, beta-blockers (all worsen venous stasis)
- **Anticoagulation: No proven role** in CRVO management
- Aspirin: reasonable for cardiovascular risk; no direct CRVO benefit proven

9b. Macular Oedema — Pharmacological Treatment (First Line)

Agent	Mechanism	Landmark Trial	Key Outcome
Ranibizumab *anti-VEGF*	Anti-VEGF-A all isoforms; reduces vascular permeability	**CRUISE 2010**	**+14.9 ETDRS letters** at 12 months vs +0.8 sham; FDA approved
Aflibercept *anti-VEGF*	Traps VEGF-A, VEGF-B, PlGF; higher binding affinity	**GALILEO / COPERNICUS 2012**	**+17.5 letters** (GALILEO) at 24 weeks; FDA approved 2012
Bevacizumab *off-label*	Full-length anti-VEGF-A; off-label widely used	**SCORE2 2017**	Non-inferior to ranibizumab; 73% vs 77% gained ≥15 letters
Ozurdex 0.7mg *Dex implant*	Biodegradable steroid; reduces VEGF + inflammatory cytokines	**GENEVA 2010**	+9 letters at 60 days; effect wanes by 6 months; retreatment effective
IVTA 4mg *Triamcinolone*	Non-biodegradable depot steroid	**SCORE-CRVO 2009**	4mg superior to sham; BUT IOP rise 35% + cataract acceleration

Anti-VEGF vs Steroid — Decision Logic:

- ▶ **Anti-VEGF first line:** phakic patient, normal IOP, no steroid responder history, monthly follow-up feasible
- ▶ **Ozurdex preferred:** pseudophakic, vitrectomised, poor compliance, anti-VEGF non-responder, inflammatory CMO
- ▶ **SCORE pearl:** 4mg IVTA effective in CRVO-CMO — but anti-VEGF safety profile is superior for long-term use

9c. Panretinal Photocoagulation (PRP) — Ischaemic CRVO

- **Indication:** Confirmed NVI, NVE, NVD, or >10 DA non-perfusion on FFA
- **CVOS key recommendation:** Do **NOT** give prophylactic PRP — treat only when NVI confirmed
- **Mechanism:** Destroys hypoxic outer retina → reduces VEGF → NV regression
- **Parameters:** 200–500 µm spots, 0.1–0.2 sec, 2–3 burn widths apart, 1200–1500 burns total
- **Combine** intravitreal anti-VEGF at same sitting for faster NVI regression

9d. Neovascular Glaucoma (NVG) Management

- **Early NVG** (open angle, NVI only): Intravitreal anti-VEGF + aggressive PRP
- **Advanced NVG** (synechial closure): **Ahmed valve (GDD)** — preferred over trabeculectomy
- Medical: Maximum topical IOP-lowering; **avoid prostaglandins** (pro-inflammatory in NVG)
- Cyclodiode laser: Palliation for blind painful eye (end-stage NVG)

10. LANDMARK TRIALS — MUST KNOW

Trial (Year)	Design	Key Finding	Clinical Impact
CVOS (1995)	RCT: Prophylactic PRP vs observation in ischaemic CRVO	No benefit of prophylactic PRP; NVI equally common in both arms	Established watchful waiting + monthly gonioscopy protocol
SCORE-CRVO (2009)	1mg vs 4mg IVTA vs sham in CRVO-CMO	4mg IVTA > sham; 1mg = sham; IOP rise 35%	Proved steroids work; safety concerns favoured anti-VEGF
CRUISE (2010)	Ranibizumab 0.3mg vs 0.5mg vs sham (6 injections)	**+14.9 letters** (0.5mg) vs +0.8 (sham) at 6 months	First major RCT proving anti-VEGF superiority; FDA approval
GALILEO / COPERNICUS (2012)	Aflibercept 2mg q4w vs sham in CRVO-CMO	GALILEO: **+17.5 letters** at 24 weeks	Established aflibercept; FDA approved 2012
GENEVA (2010)	Ozurdex 0.7mg vs sham in combined RVO	Peak +9 letters at 60 days; wanes by 6 months; retreatment effective	Established Ozurdex; pseudophakic preferred group
SCORE2 (2017)	Bevacizumab vs ranibizumab in CRVO/ HRVO-CMO	Bev non-inferior; 73% vs 77% gained ≥15 letters	Supported off-label bevacizumab as cost-effective option

11. CRVO vs BRVO — KEY DIFFERENTIATOR

Feature	CRVO	BRVO
Site of occlusion	At / behind lamina cribrosa	AV crossing (superotemporal 60%)
Quadrants involved	**All 4 quadrants**	1 quadrant only
Disc swelling	Whole disc	Absent / sector only
NVG risk	**High (45–60% ischaemic)**	**Low (~2%)**
Main associations	HTN, POAG, glaucoma	HTN, AV nicking, arteriosclerosis
VA prognosis	Worse overall	Better; 50% achieve 6/12
Systemic risk	Higher CVS mortality	Lower systemic risk

12. FOLLOW-UP PROTOCOL

Time Point	Non-Ischaemic CRVO	Ischaemic CRVO
Initial	FFA, OCT macula, gonioscopy, systemic workup	Same + ERG; immediate PRP if NVI present
1 month	VA, OCT, IOP; anti-VEGF if CMO present	VA, OCT, IOP, **gonioscopy**; anti-VEGF injection #1
3 months	OCT; anti-VEGF PRN; FFA if conversion suspected	Gonioscopy mandatory; complete PRP; FFA if NV suspected
6–12 months	3-monthly if stable; monitor fellow eye	Monthly gonioscopy for 6 months; then 3-monthly lifelong

13. COMPLICATIONS & NATURAL HISTORY

- **Chronic CMO:** → cystoid macular degeneration; EZ disruption = permanent VA loss
- **Neovascular Glaucoma:** "100-day glaucoma"; NVI in 45–60% ischaemic CRVO by 3 months; synechial closure → intractable IOP
- **Vitreous haemorrhage:** From NVD/NVE — may require pars plana vitrectomy
- **Tractional RD:** Late fibrovascular proliferation in advanced ischaemic CRVO
- **ERM / Macular atrophy:** Chronic sequelae affecting central VA irreversibly
- **Fellow eye risk:** ~10% CRVO in fellow eye over 5 years

14. EVOLVING CONCEPTS & EMERGING THERAPIES

- **Faricimab (bispecific anti-VEGF-A + Ang-2):** BALATON/COMINO trials — non-inferior to aflibercept with fewer injections; vessel stabilisation via Ang-2 blockade; CRVO trials ongoing
- **Brolucizumab:** Anti-VEGF-A 165; high concentration, longer durability; Phase 3 RVO trials underway
- **Port Delivery System (PDS):** Sustained-release ranibizumab implant; RVO phase 3 data awaited
- **OCT-A:** Replacing FFA in some centres for NP area mapping and FAZ monitoring
- **Radial Optic Neurotomy (RON):** Largely abandoned — inconsistent results, significant risks
- **AAV gene therapy:** VEGF antagonist delivery — early phase trials; sustained suppression potential

15. VIVA PEARLS — 12 HIGH-YIELD FACTS

1. Site of CRVO = posterior to the lamina cribrosa — NOT at the disc surface. The lamina is the site of mechanical CRV compression.

2. CVOS: Prophylactic PRP = NO benefit. Monthly gonioscopy; treat only when NVI confirmed. Classic exam trap.

3. SCORE-CRVO: 4mg IVTA effective but IOP rise 35% + cataract — anti-VEGF remains safer first-line choice.

4. NVG = "90/100-day glaucoma" — 45–60% of ischaemic CRVO develop NVI within 3 months without treatment.

5. Optociliary shunts = chronic CRVO collaterals OR optic nerve sheath meningioma. Do NOT leak on FFA (unlike NVD).

6. RAPD in affected eye = ischaemic CRVO until proven otherwise. Absent RAPD = non-ischaemic type.

7. ERG b-wave <60% = ischaemic type. Electronegativity (reduced b, preserved a) = inner retinal ischaemia.

8. FFA: "blocking" fluorescence early (haemorrhages); NP areas = dark non-filling zones in venous phase.

9. DRIL on OCT = strongest functional predictor of poor VA — more sensitive than CMT alone.

10. Bilateral CRVO in young patient = mandatory thrombophilia screen + haematology referral + stop OCP immediately.

11. Cilioretinal artery present → papillomacular bundle spared → central VA may be preserved despite complete CRVO.

12. ~34% of non-ischaemic CRVO convert to ischaemic — repeat FFA if VA worsens or new cotton wool spots appear.

16. CONSULTANT-LEVEL MCQ TRAPS

Q1. CVOS randomised ischaemic CRVO patients to prophylactic PRP vs observation. The result was:

- A. PRP prevented NVI in 80% of cases
- B. No difference in NVI incidence; prophylactic PRP did not prevent NVG
- C. PRP significantly reduced vitreous haemorrhage
- D. Observation led to more tractional RD

✓ B — No benefit of prophylactic PRP. NVI appeared equally in both arms. Take-away: watchful waiting + monthly gonioscopy; treat only when NVI confirmed.

Q2. Painful eye at 3 months post-CRVO. IOP 48 mmHg. Gonioscopy: NVI + PAS in 270 degrees. Best management:

- A. Trabeculectomy with mitomycin-C
- B. Topical pilocarpine + systemic acetazolamide
- C. Intravitreal anti-VEGF + maximum medical therapy + Ahmed valve planning
- D. Emergency PRP alone

✓ C — NVG with synechial closure. Anti-VEGF regresses NVI rapidly. Maximum medical IOP lowering. Ahmed valve is preferred (GDD). Pilocarpine CONTRAINDICATED — worsens angle closure, induces inflammation.

Q3. TRAP: Optociliary shunt vessels at the disc in longstanding CRVO represent:

- A. Neovascularisation of the disc (NVD) — urgent PRP needed
- B. Enlarged cilioretinal artery
- C. Pre-existing retinociliary collaterals that have dilated — NOT true NV
- D. Early papilloedema with venous dilation

✓ C — Optociliary shunts are pre-existing connections between retinal and choroidal circulations. They dilate as collateral bypass channels in chronic CRVO. Do NOT leak on FFA. Also seen in optic nerve sheath meningioma.

Q4. Worst OCT prognostic sign for VA in CRVO-CMO:

- A. Intraretinal cysts in OPL
- B. Subretinal fluid
- C. EZ (ellipsoid zone / IS-OS) disruption
- D. Hyperreflective foci in INL

✓ C — EZ disruption = photoreceptor outer segment loss = irreversible damage. DRIL also predicts poor VA but EZ disruption is the strongest independent predictor. SRF paradoxically responds well to anti-VEGF.

Q5. Letter gain with ranibizumab 0.5mg vs sham in CRUISE at 6 months was:

- A. +9.0 letters (GENEVA — Ozurdex figure)
- B. +14.9 letters
- C. +17.5 letters (GALILEO — aflibercept figure)
- D. +5.9 letters

✓ B — +14.9 letters (CRUISE, ranibizumab). GALILEO = +17.5 (aflibercept). GENEVA = +9 (Ozurdex at 60 days). Examiners deliberately swap these numbers — know the agent-to-trial-to-outcome mapping.

Q6. 35-year-old woman on OCP with sequential bilateral CRVO. Most critical systemic next step:

- A. Carotid Doppler bilateral
- B. Thrombophilia screen + haematology referral + OCP cessation
- C. 24-hour ambulatory BP monitoring
- D. Fasting glucose and HbA1c

✓ B — Young + bilateral = prothrombotic state until proven otherwise. Screen for Factor V Leiden, Protein C/S, ATIII, APLA, homocysteine. Stop OCP immediately. BP/glucose still needed but secondary priority.

17. CONSULTANT-LEVEL EXTENSION QUESTION

Advanced Clinical Scenario:

A 62-year-old pseudophakic patient with confirmed ischaemic CRVO has received 6 monthly intravitreal ranibizumab injections for persistent CMO. Central macular thickness remains 480 µm. OCT shows persistent intraretinal cysts with intact ELM but developing DRIL. IOP = 22 mmHg (medically controlled). Gonioscopy is clear. FFA confirms >10 disc areas of capillary non-perfusion.

Question: What is your next therapeutic decision, and what specific OCT and FFA parameters influence your choice between switching to aflibercept, adding Ozurdex, or considering vitreoretinal surgical intervention? Justify with trial evidence and mechanistic reasoning.

Framework: (1) Anti-VEGF switch: aflibercept traps PlGF — rationale for switching in ranibizumab non-responders. (2) Ozurdex: pseudophakic = safe; DRIL = ischaemic + inflammatory CMO; VEGF ceiling likely reached. (3) Faricimab (Ang-2 dual block): emerging rescue for persistent ischaemic CMO. (4) Vitrectomy + ILM peel: controversial but some evidence for refractory CMO — improved oxygenation + drug distribution. DRIL progression = guarded prognosis regardless of therapy escalation; counsel patient.

Kanski's Clinical Ophthalmology 9th Ed | Yanoff & Duker 5th Ed | Ryan's Retina 6th Ed | Shields Glaucoma | Atul Kumar Ophthalmology | CRUISE 2010 | GALILEO/ COPERNICUS 2012 | CVOS 1995 | SCORE-CRVO 2009 | GENEVA 2010 | SCORE2 2017