# BDOS SCIENTIFIC HIGHLIGHT

Vol 06 December 2021

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Dr. Aditi Dubey
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BHOPAL DIVISIONAL OPHTHALMIC SOCIETY
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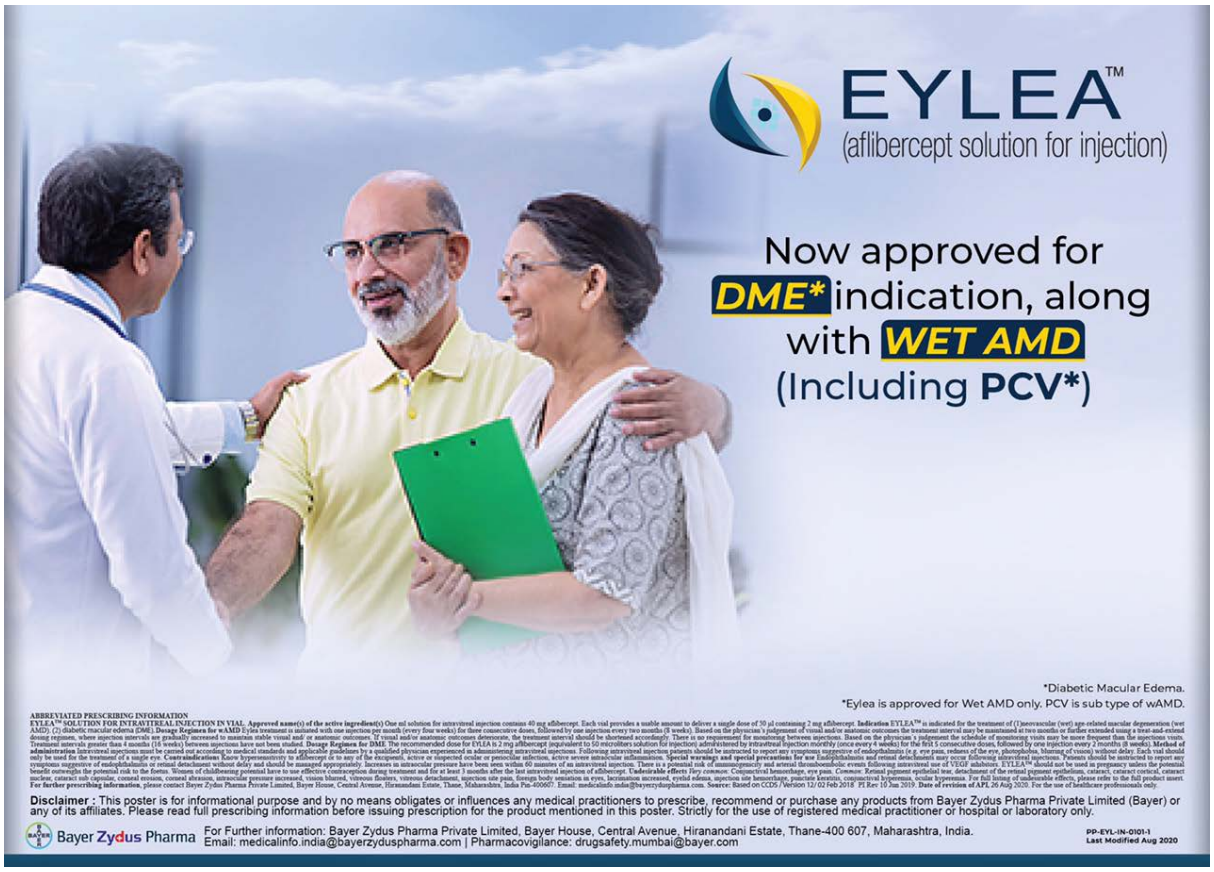


*Diabetic Macular Edema.
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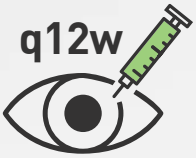


Robust visual gains with a majority of patients (>50%)# on **q12w dosing interval** through week 48[1,*]

**Superior fluid resolution** with **fewer patients with IRF/SRF** at week 48 & 96 (vs aflibercept)[2]

Overall **well-tolerated safety profile**[2]

*Immediately after the loading phase. #q12w; 56% in hawk; 51% in harrier at week 48.
IRF: intraretinal fluid; SRF: subretinal fluid

References:
1. Dugel PU, Koh A, Ogura Y, et al. HAWK and HARRIER: phase 3, multicenter, randomized, double-masked trials of brolucizumab for neovascular age-related macular degeneration. Ophthalmology. 2020;127(1):72-84. 2. Dugel PU, Singh RP, Koh A, et al. HAWK and HARRIER: ninety-six-week outcomes from the phase 3 trials of brolucizumab for neovascular age-related macular degeneration. Ophthalmology. 2021;128(1):89-99.

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**Presentation:** Solution for injection. Each vial contains 27.6 mg of brolucizumab in 0.23 mL solution. **Indications:** Pagenax is indicated for the treatment of neovascular (wet) age-related macular degeneration (AMD).**Dosage regimen and administration:** Single-use vial for intravitreal use only. Each vial should only be used for the treatment of a single eye. Pagenax must be administered by a qualified physician. **Adults:** The recommended dose for Pagenax is 6 mg (0.05 mL) administered by intravitreal injection every 4 weeks (monthly) for the first three doses. Thereafter, Pagenax is administered every 12 weeks (3 months). The physician may individualize treatment intervals based on disease activity as assessed by visual acuity and/or anatomical parameters. The treatment interval could be as frequent as every 8 weeks (2 months).**Special populations: •Renal impairment:** No dose adjustment is required. **•Hepatic impairment:** No dose adjustment is required. **•Geriatric patients:** No dose adjustment is required. **•Pediatric patients:** Safety and efficacy have not been established. **Contraindications: •**Hypersensitivity to the active substance or to any of the excipients. **•**Active or suspected ocular or periocular infection. **•**Active intraocular inflammation.**Warnings and precautions: •Endophthalmitis, retinal detachment, retinal vasculitis and/or retinal vascular occlusion:** Intravitreal injections, including those with Pagenax, have been associated with endophthalmitis and retinal detachment. Proper aseptic injection techniques must always be used when administering Pagenax. Retinal vasculitis and/or retinal vascular occlusion, typically in the presence of intraocular inflammation, have been reported with the use of Pagenax. Patients should be instructed to report any symptoms suggestive of the above mentioned events without delay. **•Intraocular pressure increases:** Transient increases in intraocular pressure have been seen within 30 minutes of injection, similar to those observed with intravitreal administration of other VEGF inhibitors. Sustained intraocular pressure increases have also been reported. Both intraocular pressure and perfusion of the optic nerve head must be monitored and managed appropriately. **•Driving and using machines:** Patients may experience temporary visual disturbances after an intravitreal injection with Pagenax and the associated eye examination. Advise patients not to drive or use machinery until visual function has recovered sufficiently. **Pregnancy, lactation, females and males of reproductive potential Pregnancy:** The potential risk of use of Pagenax in pregnancy is unknown. However, based on the anti-VEGF mechanism of action, brolucizumab must be regarded as potentially teratogenic and embryo/fetotoxic. Therefore, Pagenax should not be used during pregnancy unless the expected benefits outweighs the potential risks to the fetus. **Lactation:** Breast-feeding is not recommended during treatment and for at least one month after the last dose when stopping treatment with Pagenax. **Females and males of reproductive potential:** Women of reproductive potential should use effective contraception (methods that result in less than 1% pregnancy rates) during treatment with Pagenax and for at least one month after the last dose when stopping treatment with Pagenax. **Adverse drug reactions: Common (1 to 10%):** Visual acuity reduced, retinal haemorrhage, uveitis, iritis, vitreous detachment, retinal tear, cataracts, conjunctival haemorrhage, vitreous floaters, eye pain, intraocular pressure increase, conjunctivitis, retinal pigment epithelial tear, vision blurred, corneal abrasion, punctate keratitis, hypersensitivity. **Uncommon (<1%):** Endophthalmitis, blindness, retinal artery occlusion, retinal detachment, conjunctival hyperaemia, lacrimation increased, abnormal sensation in eye, detachment of retinal pigment epithelium, vitritis, anterior chamber inflammation, irirodycitis, anterior chamber flare, corneal oedema, vitreous haemorrhage. **Frequency not known:** Retinal vasculitis, retinal vascular occlusion. **Interactions:** No formal interaction studies have been performed. **Packs:** One 0.23 ml vial, one filter needle Before prescribing, please consult full prescribing information available from Novartis Healthcare Private Limited, Inspire BKC, Part of 601 & 701, Bandra Kurla Complex, Bandra (East), Mumbai – 400 051, Maharashtra, India. Tel +91 22 50243335/36, Fax +91 22 50243010. To be sold by retail on the prescription of an Ophthalmologist only. India BSS dated 6 Jul 2020 based on International BSS dtd 30 Apr 2020 effective from 23 Jul 2020.

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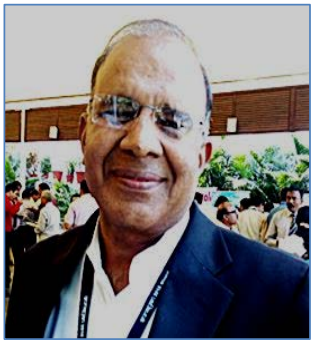

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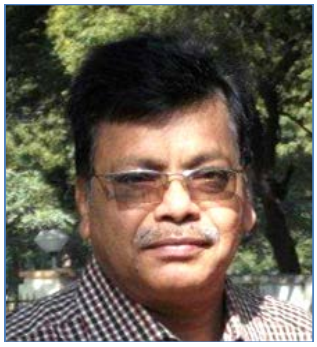

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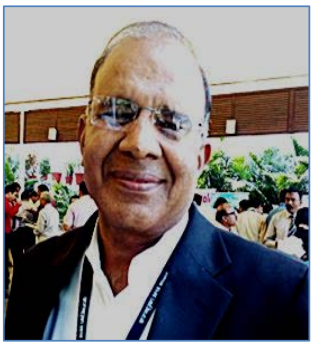

**Dr Lalit Shrivastava**
President, BDOS

Dear members,

It is a matter of great pleasure to release Highlights of BDOS activities.

Team of BDOS, particularly Secretary & Clinical Secretary have been doing a wonderful job and have successfully organised virtual CME on basics as well as on recent advances of ophthalmology, Glaucoma awareness rally , dry eye assessment & awareness programmes.

I hope this issue of BDOS highlights will be beneficial to everyone.

I wish all the success.

Thank you
Best regards to everyone

Dr Lalit Shrivastava
President, BDOS

# MESSAGE FROM BDOS HON. SECRETARY

**Dr Vinita Ramnani**
Hon. Secretary, BDOS

Respected Seniors and Dear Colleagues,

Its matter of immense pleasure to share with you all 6th volume of BDOS Scientific Highlight. BDOS Highlight has come long way since January 2014 when first volume was printed.

I acknowledge the efforts of editor Dr Chaveer Singh Bindra and all esteemed authors for sharing their experiences. Also wants to thank Chief Patron Dr Salil Kumar, President Dr Lalit Shrivastava, all Office Bearers and Executives of BDOS Team for their support.

This issue of BDOS Highlight covers the whole list of activities performed by BDOS office in spite of Covid 19 pandemic with photographs along with achievements of our BDOS members, homage to departed souls and properly designed scientific content.

Covid 19 pandemic changed the way of learning through webinars. The great enthusiasm and involvement of all BDOS members along with participation of many renowned national and international faculties, made our BDOS webinars a grand success. I am really thankful to all for their active participation and hope same for our upcoming activities. Praying to meet all in person in our long awaited physical and social meetings.

Thanks
Warm Regards

Dr Vinita Ramnani
Hon. Secretary BDOS

# CONTENTS

# EDITORIAL

## Recent Updates On Retinopathy Of Prematurity

**Dr Chahveer Singh Bindra**

MS, FVRS, Retina & Uvea Consultant, Matashree Netralaya, Bhopal

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In 1953, Reese et al (1) first described retrolental fibroplasia. The international classification of retinopathy of prematurity (ICROP) was developed in 1984 by 23 ophthalmologists from 11 countries (2) and importance of treating it early was emphasized. In 1987, retinal detachment was also included in the staging of retinopathy of prematurity. In 2005, revised ICROP classification was put forward highlighting aggressive posterior ROP, recognition of "pre-plus" form of disease and anatomical definition of zone 1. (3) The 2015 revision classifies the tractional retinal detachments into extrafoveal (Stage 4A) and foveal (Stage 4B). They are usually circumferentially oriented and described according to the clock hours involved. Recently in 2021, the third revision of the International Classification of retinopathy of prematurity (ICROP3) (4) was done taking into consideration the latest advances and understanding of the disease.

At present, 3 retinal zones are defined centered on the optic disc. The location of the most posterior retinal vascularization or ROP lesion denotes the zone for the eye. The most posterior region, zone I, is defined by a circle with radius twice the estimated distance from the optic disc center to the foveal center. Zone II is a ring-shaped region extending nasally from the outer limit of zone I to the nasal ora serrata and with a similar distance temporally, superiorly, and inferiorly. The committee defined a region of 2 disc diameters peripheral to the zone I border as posterior zone II to indicate potentially more worrisome disease than ROP in the more peripheral zone II. (4) Zone III is the residual crescent of peripheral retina that extends beyond zone II. The term notch is used to describe an incursion by the ROP lesion of 1-2 clock hours into a more posterior zone. The ROP zone for such eyes should be noted by the most posterior zone of retinal vascularization with the qualifier "notch" (e.g., "zone I secondary to notch"). (4) Practically, the temporal extent of zone I may be estimated using a 28-diopter (D) lens. For example, by placing the nasal edge of the optic disc at one edge of the view, the limit of zone I is approximately at the temporal edge of the view.

When no ROP lesion is present, the term "incomplete vascularization" is used along with the zone of vascularization. (4) When acute ROP vascular features develop at the junction of vascularized and avascular retina, the term "stage" is used. Stage of acute disease is defined by the appearance of a structure at the vascular-avascular juncture as stage 1 (demarcation line), stage 2 (ridge - Small isolated tufts of neovascular tissue lying on the surface of the retina, commonly called popcorn may be seen), and stage 3 (extraretinal neovascular proliferation or flat neovascularization). If more than 1 ROP stage is present, the eye is classified by the most severe stage. Stages of retinal detachment are defined as stage 4 (partial: 4A with fovea attached, 4B with fovea detached) and stage 5 (total). Stage 4 ROP may be exudative or tractional, and may occur in treated or untreated eyes. Exudative stage 4 detachments occur most commonly within days after laser treatment and are often localized and self-limited. Stage 5 is subcategorized as stage 5A, in which the optic disc is visible by ophthalmoscopy (suggesting open-funnel detachment); stage 5B, in which the optic disc is not visible because of retrolental fibrovascular tissue or closed-funnel detachment; and stage 5C, in which stage 5B is accompanied by anterior segment changes (e.g., marked anterior chamber shallowing, iridocorneolenticular adhesions, corneal opacification), suggesting closed-funnel configuration. Extent of the disease is described in clock hours using 30° sectors with boundaries along clock-hour positions.

The term "plus disease" was used in 1982 in association with severe disease (5). The recent understanding of the disease states that the plus disease spectrum should be determined by the tortuosity and dilation of vessels in zone 1. The terms "plus" and "preplus" can be used but they indicate the continuous spectrum of the activity of the disease. (4)

The term “aggressive posterior ROP” (earlier was referred as rush disease) has also been replaced by “aggressive ROP” as this condition has been increasingly seen in larger premature infants with vasculature beyond zone 1. (4) It is characterized by rapidly progressing vascularization without typical stages seen usually in ROP and can cause retinal detachment within few days. Among all infants demonstrating aggressive ROP, lower birth weight, lower gestation age (<29.5 weeks) and preretinal hemorrhages are at the greatest risk for unfavorable outcome. (6) Although staged ROP and aggressive ROP are different, ridge tissue (simulating staged ROP) and flat neovascularization (simulating aggressive ROP) may coexist in the same eye. Hybrid ROP has a preponderance of posterior zone 2 disease and comparatively higher birth weight and gestational age as compared to aggressive ROP. (7) The differences in staged ROP and aggressive ROP can be made by the pattern of vessels which are dichotomously branched in staged ROP as compared to loops and shunting seen in aggressive ROP. Also, in staged ROP new vessels start at junction of vascular and avascular retina and they grow vertically in vitreous while in aggressive ROP new vessels can start at any place (especially nasally) with no definitive junction enclosing multiple pockets of avascular retina and are flat and ill defined.

The retinal vascular development comprises of initial vasculogenesis, responsible for formation of four major arcade vessels, and the second phase, angiogenesis, which completes the rest of the vasculature. Interference in vasculogenesis results in aggressive ROP, while the classical staged ROP is correlated with disruption of angiogenesis. Flynn and Chan-Ling have described a hybrid form of ROP where normal vascularisation was present along upper temporal arcade and abnormal vessels simulating aggressive ROP were present along lower temporal arcade. (8) They hypothesised that there may be an overlap between vasculogenesis and angiogenesis and both may be disrupted at the same time. This hypothesis may explain the simultaneous presence of abnormal flat new vessels (disrupted vasculogenesis) and ridge tissue (disrupted angiogenesis).

In 2005, randomised trials of early stages of ROP showed better outcomes than treating at threshold ROP stage. Prethreshold ROP was divided into two types. (9) Type 1 high risk prethreshold ROP was defined as zone 1 plus with any stage, zone 1 stage 3 with no plus and zone 2 stage 2 or 3 plus. All eyes with type 1 prethreshold ROP are currently recommended for immediate treatment. Type 2 low risk prethreshold ROP was defined as zone 1 stage 1 or 2 without plus disease and zone 2 stage 3 without plus disease and follow-up is recommended for such eyes. The standard treatment in type 1 ETROP is by near confluent laser therapy. The main challenge is treatment of aggressive ROP in which despite laser treatment the outcomes are poor, with unfavorable structural outcomes ranging from 14.3% to 28.6%. (10) In some cases, fibrovascular traction usually begins 1 to 3 weeks after laser treatment, with a rapid progression to retinal detachment, despite adequate laser treatment. Although no clear guidelines exist, eyes with limited traction may be followed up closely for either spontaneous separation of traction or progression requiring vitrectomy. Laser treatment is also associated with risk of high myopia and limited field of vision. (11) Primary or adjunctive intravitreal anti-vascular endothelial growth factor (anti-VEGF) therapy and early vitreous surgery have shown promising results in such cases (12, 13). The use of intravitreal anti-VEGF injection results in prompt regression of ROP, with the potential for further retinal vascular development. This may reduce the need for ablation of the peripheral avascular retina, decreased treatment time and induce less myopia. However, recurrence and reactivation of disease requiring longer follow up is the main concern with anti VEGF monotherapy. Thus, in patients with aggressive ROP especially in zone 1, combination of anti VEGF injection and laser have favorable structural outcome. (14)

There is still a debate on early vs deferred laser after anti VEGF injection in aggressive ROP. Though, eyes undergoing deferred laser require a fewer number of laser spots and have less myopia at 6 months after laser. Also, posterior zone I aggressive ROP can be managed with combined treatment with anti VEGF injection and zone I sparing laser ablation (after around 4 weeks of injection) in order to preserve large part of central retina. (15) However, eyes planned for the deferred laser after anti VEGF injection requires regular vigilant follow up for early identification and treatment of recurrence. Several factors influence the ‘ideal’ timing of laser intervention after anti VEGF injection including response to the drug, recurrences, vascular growth into the retina beyond zone 1, weight of the baby, post menstrual age, systemic conditions and follow-up compliance (especially in rural areas). In some cases, vascularization can progress into more peripheral zones before they either stop or show signs of recurrence or worsen. Ideally, if compliant follow-up is ensured and enforced, a schedule of weekly imaging until a postmenstrual age of 44 weeks, fortnightly until 52 weeks and monthly thereafter may help to detect the growth of vascularization as well as any recurrence that requires early intervention. Laser is performed if there is active flat neovascularization (confirmed on angiography), arrest of vascularization or unwillingness to follow-up further. With this approach larger part of retinal area can be spared from laser ablation. (16)

Up till now most of the classification laid stress of classifying the stages and treatment, but no guidelines addressed the regression or reactivation of disease which has become increasingly important after introduction of anti VEGF agents. (17) The term "regression" refers to disease involution and resolution while term "reactivation" refers to recurrence of acute phase. The regression occurs much earlier after anti VEGF injection (1-3 days) as compared to laser photocoagulation (7-14 days) or spontaneous regression. After regression, vascularization may be complete or incomplete upto ora serrate (termed as "persistent avascular retina"). (4)

Reactivation is more common after anti VEGF injection (more commonly between 37-60 weeks) than after laser photocoagulation or spontaneous regression. Reactivation may occur in form of dilation, tortuousity or extraretinal neovascularization which may not progress through classical stages and are more prone to bleed. When reactivation of ROP stages occurs, the modifier reactivated (e.g.,"reactivated stage 2") is recommended. (4)

Long term sequelae or ROP includes retinal detachment (18), retinoschisis, foveal maldevelopment (19, 20), retinal vascular changes (inform of falciform retinal fold or macular dragging), vitreous hemorrhage, retinal holes or tear (especially in persistent avascular retina (21)) and glaucoma (22).

In India, wide field imaging (WFI) is the recommended method for ROP screening as enlisted in its current national ROP screening guidelines. (23) Also, it can bridge the gap between large number of premature babies to be screened and handful of available specialists. The trained imagers serve as the first line of expertise that ensures that rural babies are provided with the standard of care, even in the absence of specialists whose telemedicine reports are returned to the center within a short period of time. The photo documentation provides a definite advantage over meticulously recorded indirect ophthalmoscopy findings in medico-legal cases, though both are considered in current jurisprudence. Understanding the current pathophysiologic features and treatment modalities available, management of ROP can be done in a much rational way. This can improve the quality of ROP care and standardization of treatment worldwide. Further collaboration with ROP specialists and caregivers can lay the foundation for improving research and clinical care in the future.

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# EXPERT VIEWS ON PROLIFERATIVE DIABETIC RETINOPATHY

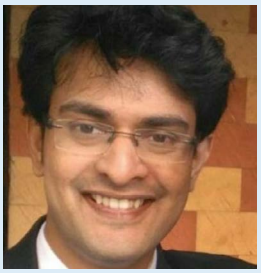
## Expert Panelists

**Dr. Gajendra Chawla (GC)**
Director and Consultant,
Vision Care Center

**Dr. Vivek Som (VS)**
Professor, Eye Dept,
Gandhi Medical College

**Dr. Mansi Kishnani (MK)**
Assistant Professor,
CHCM

**Dr. Amit Shrivastava (AS)**
Retina Consultant,
Sankalp Eye Hospital



**Dr. Ganesh Pillay (GP)**
Retina Consultant,
ASG Eye Hospital

**CASE:** A 57 year old male walks into your clinic with chief complaints of diminution of vision in right eye since 2 days. His BCVA in right eye was 1/60 and in left eye was 6/24.He had history of DM since 10 years. On investigating, patient had proliferative diabetic retinopathy (PDR) with pre retinal hemorrhage over the macular area in right eye while PDR with diabetic macular edema with epiretinal membrane (ERM) in left eye. Also, patient was pseudophakic in both eyes.

**Q1: What are the initial ocular and systemic investigations to be done?**

**GC:** My ocular investigations include Fundus fluorescein angiography and OCT in left eye while B-scan in right eye to rule out traction on macula behind pre retinal hemorrhage. My systemic investigations include complete haemogram including CBP, ESR, FBS, PPBS, HBA1c, renal profile, lipid profile etc.

**VS:** My preferred initial investigations are - HbA1c, CBP, Renal profile and OCT.

**MK:** In Ocular investigations, I prefer fundus photo and OCT, B-scan RE for documentation. In Systemic investigations I advise blood pressure and other parameters. I also enquire about any history of blood thinners, cardiac disorder/MI, stroke and nephropathy.

**AS:** My preferred systemic investigations are HbA1c, FBS, PPBS, Renal Function Test, Lipid profile and blood pressure. In ocular investigations, I would advise OCT in Left Eye and FFA.

**GP:** I look for NVI in anterior Segment and get a random glucose level and blood pressure done. I advise for lipid profile and HbA1c in systemic examination. In ocular investigation, I advise for Fundus photo, FFA and OCT. In case of vitreous hemorrhage along with dense pre retinal bleed an USG B-scan is also advised.

**Q2: What is the treatment of choice to begin with?**

**GC:** For right eye - depends on B scan. If no traction is seen then I prefer conservative treatment and laser PRP to available retina. If traction is present then I prefer vitreous surgery. In left eye, I will prefer intravitreal injection and laser PRP.

**VS:** I would go ahead with right eye Pan retinal photocoagulation and laser hyaloidotomy and in left eye intravitreal injection of Ranibizumab along with PRP laser.

**MK:** If in right eye periphery is clear with no traction, I prefer PRP in 3 sittings. In left eye, I will prefer PRP in 3 sittings and anti VEGF injection after 2 weeks of PRP laser completion.

**AS:** I would prefer panretinal photocoagulation in both eyes with Intravitreal antivegf in between for left eye. Strict DM control is must.

**GP:** Intravitreal anti- VEGF is treatment of choice. Patient is asked to follow up physician for good blood sugar, blood pressure and cholesterol management.

**Q3: Which intravitreal injection would you prefer in your practice?**

**GC:** I will prefer Anti VEGF in left eye. However, Ozurdrex implant can also be considered in this case (pseudophakia) after explaining risk of raised IOP.

**VS:** I will prefer Ranibizumab injection.

**MK:** I prefer Accentrix inhection.

**AS:** I prefer Antivegf Accentrix or Razumab.

**GP:** Ranibizumab is preferred but I do give option of bevacizumab to non-affording patients.

**Q4: In high risk PDR cases, in how many sittings would you prefer to do laser panretinal photocoagulation and at what interval?**

**GC:** We do laser PRP in 4 sittings in such high risk cases. In above mentioned case, I will prefer PRP in 4 sitting at interval of 3 days in left eye. For right eye - if no traction behind pre retinal hemorrhage then I prefer doing laser to available retina and do more laser in follow up as and when hemorrhage is absorbing.

**VS:** I prefer laser in three sittings on consecutive days or gap of 1 day between sittings.

**MK:** I prefer doing PRP in 3 Sittings – on 3 consecutive days or alternate day.

**AS:** If we have pascal it can be completed in one sitting otherwise I prefer PRP in 3 sittings with 3 to 5 days interval.

**GP:** In high risk PDR I always give Anti-VEGF followed by 3 sitting laser. It takes care of both risk of hemorrhage as well as macular edema.

**Q5: How long will you wait before planning for vitreous hemorrhage surgery in right eye?**

**GC:** If B-scan shows traction, then early vitrectomy, of course after control of systemic parameters (mean while I complete laser PRP in left eye). If no traction - then depends on patient's profession and needs. I usually do not opt for surgery before 4-6 weeks (in this period we complete laser PRP in left eye, as well as ask for control of systemic parameters also).

**VS:** If Vitreous haemorrhage shows no sign of resolution for more than a month I plan for surgery after consent of patient.

**MK:** I wait for 3 months before planning for vitreous hemorrhage surgery.

**AS:** I wait for maximum 1 month with current instrumentation but only after 3 days prior antivegf.

**GP:** In case of associated traction on USG on vitrectomy on immediate basis but in case of no traction, I would prefer anti-VEGF followed by LASER.

**Q6: What is your note of caution while doing diabetic vitrectomy in such cases and which instruments would you prefer for dissecting membranes while doing the surgery?**

**GC:** I usually use 25/ 23 gauge MIVS system for vitreous surgery. After vitrectomy, I do segmentation of proliferative tissue which can be done with cutter itself. In case of flat & plastered tissue bimanual surgery (forceps and scissors) is preferred using chandelier light from 4th port. I don't do ILM peeling in diabetic vitrectomy. Word of caution- Diathermised all bleeders as soon as possible before it form another new membrane on the retina. If proliferation is highly vascular, inject anti VEGF 3-5 days before surgery. Here a word of caution - Do not inject anti VEGF until and unless physicians fitness for surgery is obtained.

**VS:** DR VS: For me note of caution is to evaluate retina with extremely careful retinal examination to find out the type and extent of proliferation. In instrumentation my preferred choice is: In case of simple vitreous haemorrhage - 23G Vitrectomy with PVD and Endolaser PRP while in case with complicated proliferation and TRD - Intravitreal injection Ranibizumab followed by 23G vitrectomy with Band with membrane peeling (curved intravitral scissors wherever required) with Endolaser with or without Silicone oil/ C3F8.

**MK:** DR MK: I use Avastin 3 days before surgery if florid NVE is present to reduce intraocular bleed. Secondly, membranes become taut post injection and it helps to get the dissection plane easily. I use only cutter for dissection of membranes. I rarely use forceps for the surgery.

**AS:** DR AS: I always treat such eyes with prior PRP with or without Antivegf before going for vitrectomy. For surgery, I prefer bimanual peeling for membranes with chandelier. My instruments of choice are 25 G cutters and scissors (horizontal and vertical).

**GP:** DR GP: Not all traction needs to be aggressively dissected it may cause more bleeding. I prefer to inject Anti-VEGF 3 days prior to diabetic vitrectomy to get a relatively bloodless field. A chandelier with bimanual dissection is preffered. Alternatively propotional reflux in constellation along with ILM forceps also helps to get a good cleavage plane.

**DISCLAIMER** – All the answers are recommendations by the practicing consultant and are not in accordance with standard practice pattern.

# REVIEW ARTICLE

## Review on Benign Intracranial Hypertension

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### INTRODUCTION

Benign Intracranial Hypertension also known as Idiopathic Intracranial Hypertension(IIH) or Pseudotumor Cerebri is an idiopathic condition associated with increased CSF pressure, normal or small ventricles, normal CSF composition and papilledema (usually bilateral, which may be severe).[1]

The first case of IIH was reported by Quincke in 1897and the term Benign Intracranial Hypertension was coined by Foley in 1955.[2]

### EPIDEMIOLOGY

Annual incidence is 0.9/100000 persons with 3.5/100000 in females between 15 to 44 years of age and is concurrent with obesity with the incidence increasing upto 19 per 100000 in females between 20-44 years of age that are 20% or more over the ideal weight .[3]Obesity is the most important contributing factor as more than 90% of patients are obese and over 90% are women of childbearing age with asymptomatic elevated intracranial pressure that may persist for year.[4] The peak incidence is in 3rd decade of life.[5]

### CLINICAL FEATURES

- Headache (94%) worse in the morning aggravated by Valsalva's maneuver.[6]
- Transient visual obscurations (68%) usually preceeded by headache caused by transient ischemia of the optic nerve head related to increased tissue pressure.
- Tinnitus synchronous with pulse rate(58%).
- Photopsia (54%)
- Retrobulbar pain (44%)
- Diplopia (38%)[5]{cranial nerves II,VI,VII most commonly affected}[7]
- Visual loss (30%).[8]

Benign intracranial hypertension may be associated with:-

(a) Obstruction /impairment of cerebral venous drainage (tumors, septic thrombi, radical neck dissection).

(b)Endocrine and metabolic dysfunction

- Elevated estrogen levels
- Pregnancy(esp.2nd and 5th month due to decreased corticoids and increased estrogen).[4]
- Hypoparathyroidism and hypocalcemia (interferes with transport of CSF through arachnoid granulation).

(c)Exogenous agents

- Systemic corticosteroids(suppression of adrenal cortex)
- Antibiotics(Tetracycline, Nalidixic acid)
- Anti-inflammatory drugs(Indomethacin, Ketoprofen)
- Vitamin A overdose(1 lakh units per day for a few months)
- Lead encephalopathy (causing cerebral edema and increased intracranial tension).

(d) Systemic illnesses

- Meningitis,Encephalitis (blockage of ventricular system)
- Status Epilepticus (cerebral hypoxia and cerebral edema)
- Vascular hypertension
- Thrombocytopenic purpura
- Chronic respiratory insufficiency.

(e)Familial Benign Intracranial Hypertension.[9]

## INVESTIGATIONS

• Fundus examination

Papilledema or optic disc edema[Figure 1] due to increased intracranial pressure is the most important sign of benign intracranial hypertension that may even lead to visual loss. The higher the grade of the papilledema, the worse the visual loss.[10]

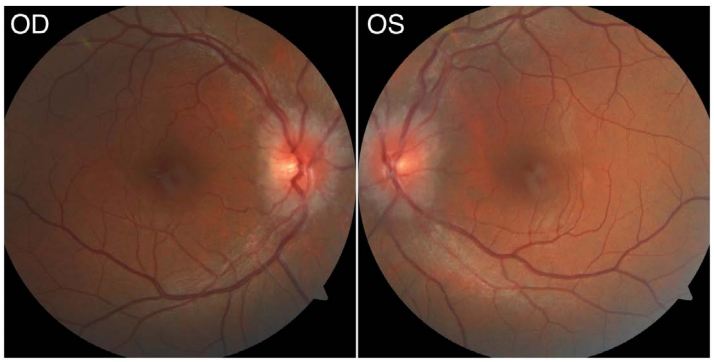


Figure 1. Papilledema or optic disc edema

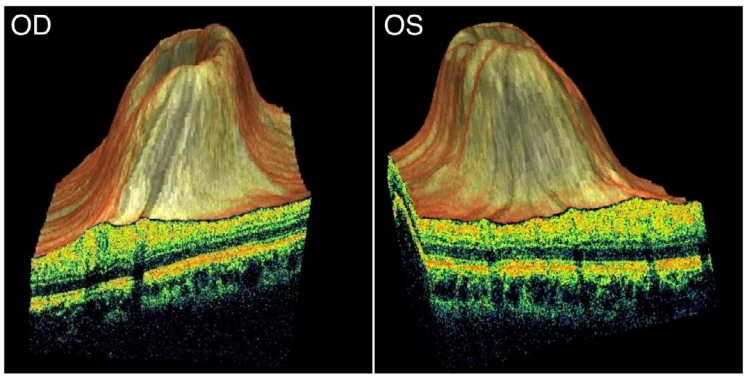


Figure 3: 3-D display of optic nerve

• Perimetry

Inferior nasal step defect is the earliest visual field defect followed by peripheral nasal loss. Arcuate defects may appear next followed by a gradual depression of the entire field, most pronounced peripherally along with blind spot enlargement[Figure 2] which is usually present.[11]

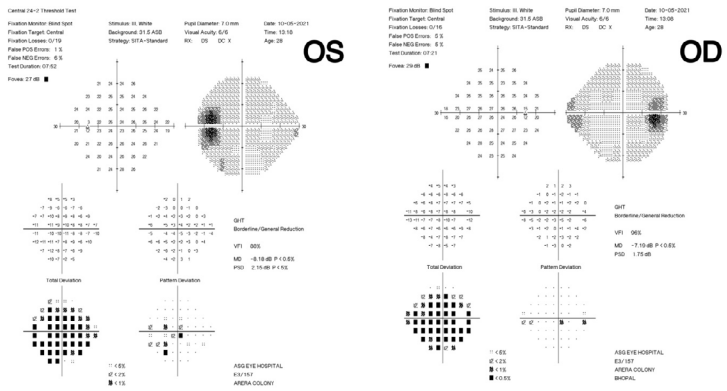


Figure 2. Blind spot enlargement

• Optical Coherence Tomography

Important for both diagnosis as well as monitoring the condition. There is an upward deflection of Bruch's membrane.Also,elevated optic nerve head with smooth internal contour and subretinal hyporeflective space (SHYPS) with recumbent "lazy V" pattern can be seen[12] with 3-D display of optic nerve[Figure 3] being very helpful.

• Neuroimaging

MRI Brain and Orbit may reveal-

- Distension of perioptic subarachnoid space
- Partial empty sella
- Flattening of posterior sclera
- Vertical tortuosity and elongation of orbital Optic Nerve
- Bilateral transverse sinus stenosis.[1,13]

5)Diagnostic Lumbar Puncture

For CSF opening pressure.[1-4]

## DIAGNOSTIC CRITERIA

First given by Walter Dandy in 1937.Later modified by Smith in 1985 and by Digre and Corbett in 2001.

- Signs and symptoms of raised intracranial pressure(headache, nausea, vomiting, papilledema)

- No localizing findings on neurological examination(except false localizing signs such as CN VI or VII palsy)
- Awake and alert patient
- Increased CSF opening pressure of >25 cm or 250 mm of water measured in left lateral decubitus position
- Normal CSF cytological and chemical composition
- Normal CT/MRI/MR Venography findings and normal neurological examination except papilledema with no evidence of dural sinus thrombosis
- No other cause of increased intracranial, pressure found.[1-4]

**MANAGEMENT**

**(A) Medical Management**

1) Weight loss

Weight loss in the range of 5-10% of total body weight can cause reversal of signs and symptoms.[14]

2) Acetazolamide

Considered as treatment of choice. In adult patients,it is usually started at 1 g daily (250 mg QID or 500 mg BID), with a maximum recommended daily dose of 4 g. Adverse effects of acetazolamide include paraesthesias, lethargy and altered taste. Hypokalemia is an important adverse effect and hence, electrolytes must be monitored. Idiopathic Intracranial Hypertension Treatment Trial reports improved quality of life outcome with use of acetazolamide at 6 months.[15]

3) Furosemide

Lowers the intracranial pressure by causing diuresis and reducing sodium transport into the brain. Dose of 20 mg p.o. b.i.d. to a maximum of 40 mg p.o. t.i.d can be given. Potassium supplementation is given as needed.[16]

4) Topiramate

Acts by inhibiting carbonic anhydrase and can also suppress appetite. The dose of is from 25 mg to 50 mg bd with side effects like depression, cognitive slowing and potential teratogenic risks.[17]

5)NSAIDs

Paracetamol may be used for headache. Indomethacin has an advantage of reducing ICP.[18]

6)Corticosteroids

Short term course can also be used pre operatively before CSF shunting procedure.[19]

7)Therapeutic Lumbar Puncture

Has only a short-lived effect on CSF pressure with a return of pressure to pre-tap level after only 82 minutes.[20]

**(B) Surgical Management**

1) Subtemporal /Suboccipital decompression

Long term success rates are reported.Complications include seizures, otorrhea, and subdural hematoma.

2) Optic nerve sheath decompression/fenestration

Preferred for patients with progressive visual loss with mild or easily controlled headaches.Has good efficacy.

3) CSF Shunting

Lumbar subarachnoid-peritoneal shunts, ventriculoatrial, ventriculojugular and ventriculoperitoneal shunts can be done for a failed medical therapy or intractable headache and has been increasingly used nowadays.[21]

4) Gastric exclusion surgery

Useful in treating co morbid conditions with obesity such as arterial hypertension, diabetes mellitus, and sleep apnea. Complications include major wound infection and stenosis at the gastrojejunal anastomosis.Has been successful for morbid obese patients.[22]

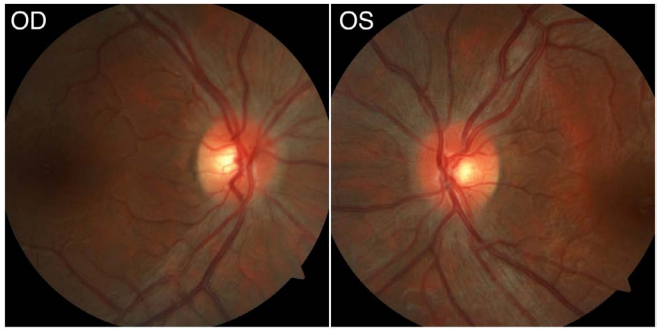


Figure 4

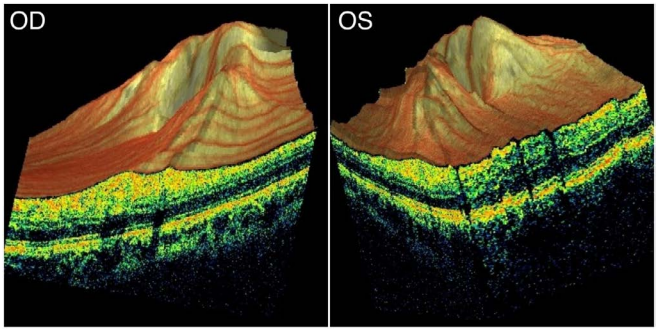


Figure 5

5) Venous Sinus stenting

Novel method,tried in cases of transvers sinus stenosis and requires further study.[23]

## CONCLUSION

Benign intracranial hypertension is characterized by elevated CSF(intracranial) pressure of unknown cause. It is predominantly a disease of women in the childbearing years with complaints of severe headache, papilledema,visual disturbances and patient may even progress to blindness if untreated. Serial perimetry and optic disc grading or fundus photography are crucial for management. Modified Dandy criteria is a very important guide for diagnosis and prompt management of the condition, however, there is no evidence based data to guide therapy, hence,there are still ongoing randomized double blind controlled treatment trials investigating diet and medical therapy.

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# REVIEW ARTICLE

## Surgical Approach of Chemical Injuries

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Surgical Management of Chemical Injuries -

1. Amniotic membrane transplant

Amniotic membrane helps in ocular surface reconstruction, promotes rapid epithelial healing and partially restores limbal stem cell function.[1] Amniotic membrane seems to be an efficient adjunct for ocular surface reconstruction in chemical burns with partial limbal stem cell deficiency. When performed in conjunction with limbal stem cell transplantation, it is also effective in most cases of total limbal stem cell deficiency

Tseng et al reported that amniotic membrane transplantation is effective in promoting re-epithelialization and reducing inflammation, thus preventing scarring squeal in the late stage. In mild to moderate burns, AMT alone rapidly restores both corneal and conjunctival surfaces. In severe burns, however, it restores the conjunctival ocular surface without debilitating symblepharon and reduces limbal stromal inflammation, but does not prevent limbal stem cell deficiency, which requires further limbal stem cell transplantation.[2]

Role of amniotic membrane in grade 4 chemical injuries is not clear. Mellor et al reported that amniotic membrane transplant alone was effective in reducing limbal stromal inflammation, restoring the conjunctival surface and preventing symblepharon formation in patients with grade 4 burns.[2]

However Dua et al reported failure of amniotic membrane transplant for ocular surface reconstruction in patients with severe acute chemical and thermal burns. He concluded that prognosis of patients with 100% limbal ischemia is much worse than patients with just over 50% limbal ischemia thus highlightning the inadequacy of the Ropper Hall classification.[3]

Use of suture less amniotic membrane (ProKera; Bio-Tissue, Inc, Miami, Florida) in acute alkali burns has also been reported.[4]

2. Conjuctival /Tenon's advancement

In severe chemical injuries, the development of anterior segment necrosis due to loss of limbal vascular blood supply ,as well as certainty of failure to re-epithelialize are the primary concern. Tenonplasty has been almost uniformly successful in preventing anterior segment necrosis or sterile corneal ulceration. The access of vascular derived collagenase inhibitors may be of clinical significance in the prevention of collagenolytic –related ulceration of the corneal stroma prior to the re-establishment of an intact epithelium.

As described by Teping and Reim, in tenonplasty, all necrotic conjuctival and episcleral tissue is excised, followed by blunt separation of tenon's tissue from the equatorial region of the globe and from the extraocular muscles. The tenon's flap with its carefully preserved vascular supply, is then advanced to the limbus and sutured tightly to the sclera.[5]

This technique, however has not worked as well in establishing appropriate phenotypic reepithelization of the cornea.

3. Limbal Stem Cell Transplantation

Limbal stem cell transplantation was proposed by Kenyon and Tseng.[6] It has an advantage of restoring normal corneal epithelial phenotype after chemical injury. Successful limbal stem cell transplantation early in the clinical course is also an effective means of supporting repair and minimize ulceration.

Limbal stem cell transplantation has proven extremely useful in the management of unilateral chemical injury and recent innovations in regenerative medicine focusing on tissue –engineered techniques has opened a new clinical field ,particularly in cases of bilateral chemical injuries. In particular ,cultivated mucosal epithelial transplantation using well –differentiated ,stratified epithelial sheets on amniotic membrane allows a rapid epithelial cover over the entire corneal surface, resulting in early reduction of inflammation and cicatrization. Tissue –engineered strategies using autologus corneal or oral mucosal epithelial sheet transplantation avoid the risk of rejection and complications associated with immuno-suppresive treatments.[7]

More recently, simple limbal epithelial transplantation (SLET), in which the affected cornea is seeded with multiple small pieces of limbal tissue harvested from the contralateral normal eye, was shown to produce outstanding short-term results in chemical injured eyes.

Limbal stem cell transplantation is primarily focused on the reconstruction of the epithelial layer or, at the most, on the anterior corneal stroma, but does not directly deal with the deep corneal stromal opacification. To recover corneal clarity and to improve vision, a penetrating keratoplasty is necessary[8-9]

However, chemical and thermal burns usually cause heavy and deep neovascular invasion into the cornea, the incidence of immunologic graft rejection and graft failure after Penetrating Keratoplasty is high.[10-11] The prognosis is virtually hopeless if there are intraocular abnormalities such as glaucoma, hypotony, anterior chamber membrane formation and retinal detachment.[12]

If the severity of intraocular abnormalities does not preclude penetrating keratoplasty, the prognosis of penetrating keratoplasty can be improved by rehabilitation of ocular surface with the appropriate combination of limbal stem cell, conjunctival or mucosal membrane transplantation.

Lamellar procedures like Deep anterior lamellar keratoplasty (DALK) avoids the risk of immunologic allogrft rejection. DALK combined with autologus limbal transplantation can restore a healthy, stable ocular surface, besides providing a clear cornea that remarkably improves the visual acuity, in patients with unilateral, late stage, severe chemical injury[13]

4.Tissue adhesives like cyanoacrylate glue are effective tool for management of impending or actual perforation related to sterile ulceration of the corneal stroma following chemical injury.The application of tissue adhesives is best reserved for impending perforations or actual perforations of less than 1 mm. If the defect is more than 1 mm, tectonic keratoplasty may be required.[14-15]

5. Keratoprosthesis

Keratoprosthesis like Boston keratoprsthesis are indicated for restoring vision in bilateral blindness resulting from chemical injury. Long term visual outcome can be compromised by complications like infections, retroprosthetic membranes, and extrusion of keratoprosthesis.

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## REVIEW ARTICLE

# Optic Disc Pit Maculopathy: A Review

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Introduction

Optic disc pit (ODP) is a rare congenital abnormality of the optic nerve head first described by Weithe in the year 1882.It belongs to the spectrum of congenital cavitary anomalies of the optic disc which encompasses extrapapillary cavitation, optic disc coloboma and morning glory.1The estimated incidence of ODP is 1 in 10,000 with no obvious gender predilection.1 Although ODPs are typically unilateral, they may be bilateral in 15% of cases.2 The usual presentation is between 3rd -4th decade of life.2 Majority of cases are sporadic but autosomal recessive inheritance has been suggested in some family pedigrees.3No specific genetic association has been identified.

Clinically ODPs appear as single grayish, round or oval hypopigmented depressions at the optic disc, most commonly seen at the inferotemporal or temporal segment of the disc but may be located elsewhere including centrally.4Occcasionally there may be more than one pit.

Histologically, an ODP is defined as a herniation of dysplastic retina into a collagen-rich excavation, extending into the subarachnoid space through a defect in the lamina cribrosa.5-7This anatomical abnormality is commonly seen in all congenital cavitary anomalies of the optic disc and leads to a non-physiological communication between intra and extra ocular spaces.8

ODP although usually asymptomatic can produce visual field defects.8,9,10 When an ODP is complicated by maculopathy, it may cause significant visual deterioration.

The exact pathogenesis of ODP maculopathy is unclear. Approximately 25% to 75% of patients develop Optic disc pit maculopathy (ODP-M) at some stage of their life. 2,8,9,11, A drop in Visual acuity is consistent with development of serous macular detachment and/or retinoschisis of the central macula.

Despite the adverse effects of ODP-maculopathy on vision, there is no clear consensus on the optimal treatment modality.

Pathogenesis

The etiology of subretinal and intraretinal fluid in ODP-M is poorly understood.

The first possible source of fluid is the vitreous humor. It is postulated that vitreous traction on the retina, underlying the area of Martegiani and the bursa premacularis, leads to the development of a negative pressure gradient that draws vitreous fluid in through the optic pit and into the submacular space.12 As progressive vitreous liquefaction usually occurs in the third or fourth decade of life it may coincide with typical presentation of ODP-M.

The second possible source of fluid is the cerebrospinal fluid (CSF), which has been proposed to enter the intra- and sub-retinal spaces from the subarachnoid space through the ODP defect. Several optical coherence tomography

(OCT) studies have shown direct communication between the subarachnoid space and the subretinal space.13 Also supported by the fact that intracranial migration of silicone oil and gas has been reported in patients with optic disc pit who had underwent pars plana vitrectomy for retinal detachment.14

The concept of leaking blood vessels at the ODP has also been suggested which may be seen as late hyperfluorescence and macular elevation on Fundus Fluorescein angiography.15 However this feature is not present in all cases. Another explanation is that the fluid is derived from the choroid via the Bruchs membrane and peripapillary atrophy.9 This is however unlikely as subretinal fluid is not always seen in pathologies causing chorioretinal atrophy.

Presenting symptoms and clinical signs

ODPs are usually asymptomatic and may be an incidental finding on fundus examination. However they have shown to cause visual field defects such as an enlarged blind spot or a paracentral arcuate scotoma.8-10

When OPD-M is present, visual acuity is usually 20/70 or worse.2,11 The coexisting macular detachment may be accompanied with lamellar or full-thickness macular holes, cystoid changes, retinal pigment epithelium atrophy and eventually cause irreversible loss of vision with VA poorer than Snellen 20/200 in long standing cases.16

Imaging

Fundus Autofluorescence

A study by Hiraoka et al using infrared and autofluorescence imaging in eyes with disc pit maculopathy pre and post vitrectomy showed that areas of serous detachment and schisis appeared dark preoperatively and changed to brighter areas after resolution of serous detachment and schisis post operatively.17 The study also observed an increase in granular hyperfluorescence accompanied by an increase in the number of subretinal precipitates.

Optical Coherence Tomography

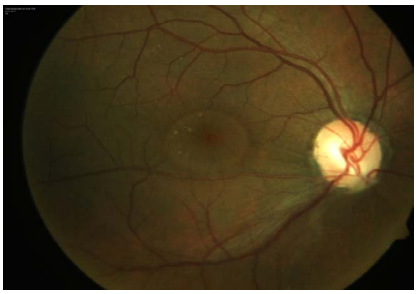
The morphology of ODP-M has been well characterized by the use of optical coherence tomography (OCT). ODP-M has a typical bilaminar appearance of retinal schisis and neurosensory detachment, but, commonly, either one of the features exists in isolation.18 Spectral-domain OCT has also shown that the fluid mainly accumulated in the outer nuclear layer (94%), followed by the inner nuclear layer (81%), the ganglion cell layer (44%), and the sub-internal limiting membrane (13%). Outer retinal holes or dehiscence are uncommon findings in ODP-M, reported to occur in only 27% of cases.18

A 3-dimensional spectral-domain OCT scans revealed a 3-fold connection: between subretinal and intraretinal space, perineural space, and the vitreous cavity suggesting that intraretinal or subretinal fluid in ODP-M may have both a vitreous and cerebrospinal origin.19

Fluorescein Angiography and Indocyanine Green Angiography

A study by Theodossiadis et al reported early hypofluorescence and late staining of the pit with no extension of the dye towards the macula on FFA. All eyes had a clearly delineated area of late hyperfluorescence representing the macular elevation and absolute hypofluorescence of the ODP on ICG during all phases of the study.15

Current approach in the management of optic disc pit maculopathy



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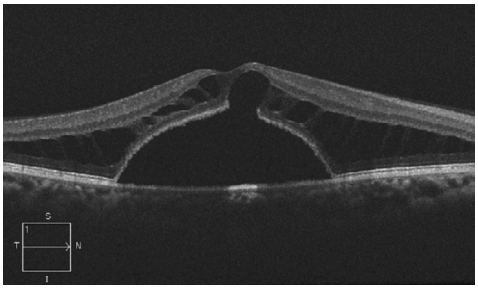

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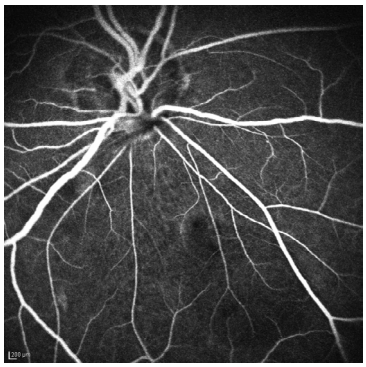

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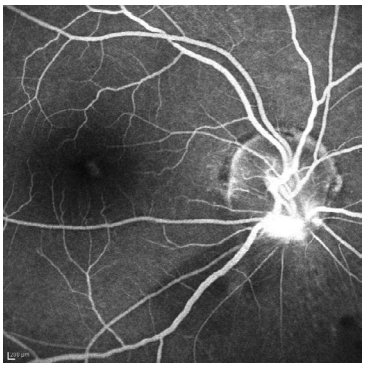


Fig.1.(d)

Fig.1.(a) RE Fundus photograph of a 45 yrs old patient showing optic disc pit at the inferior margin of the disc along with neurosensory detachment at the macula(ODP-M).(b) Optical coherence tomography showing showing serous macular detachment, schitic changes with outer macular hole.(c) & (d) FFA showing early hypofluorescence and late staining of pit respectively.

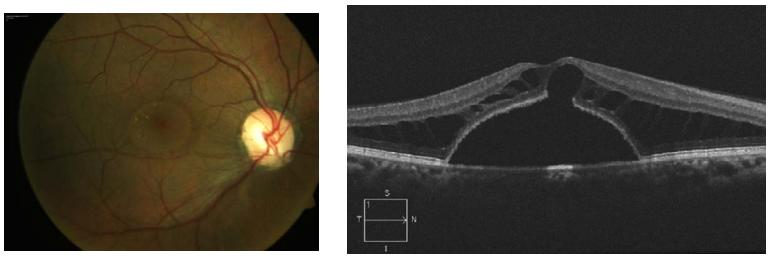
Pars Plana Vitrectomy(PPV)

PPV is the mainstay of treatment of ODP-M. PPV can be done in combination with laser treatment, gas tamponade, and/or internal limiting membrane (ILM) peeling. 20 A complete PVD induction is essential to relieve the traction leading to macular reattachment. ILM peeling can also be carried out and laser can be applied to the temporal margin of the pit.
Vitrectomy has shown promising results and long-term visual improvement with anatomical success rate was between 50% and 95%, whereas the VA improvement in approximately 50% of cases.21The concept of using inverted ILM flap to cover the disc including the ODP and excluding the fovea has demonstrated favourable results. However, the evidence remains low and more studies are warranted.22

Pneumatic Tamponade With or Without Laser Photocoagulation
Another current proposed therapeutic approach for ODP maculopathy is the intravitreal gas tamponade alone or combined with laser.23 Pneumatic tamponade may cause PVD and alleviation of vitreomacular traction, which is considered an essential factor in the pathogenesis of the disease. Laser application contributes to the sealing of the route of the ODP to the fovea. The technique was reported to have a 50% success rate using SF6 alone, but more than one injection was often necessary.24 Another study has reported higher success rate by combining laser photocoagulation and intravitreal gas tamponade.25

Macular Buckling

Macular buckling has shown to be an effective treatment for more than a decade, with long-term visual improvement and low rates of complications or recurrences. This surgical technique involves a sponge implant fixation to the posterior segment of the globe along the 6-to-12 o'clock meridian, providing a buckling effect under the macula. No application of additional gas, laser, or cryotherapy is required.26This technique showed long-term success rate of approximately 85%, with complete resolution of fluid, and improved VA and visual fields (within 30° of fixation). Despite the impressive results of this technique, it is rather difficult to apply and has a long learning curve.



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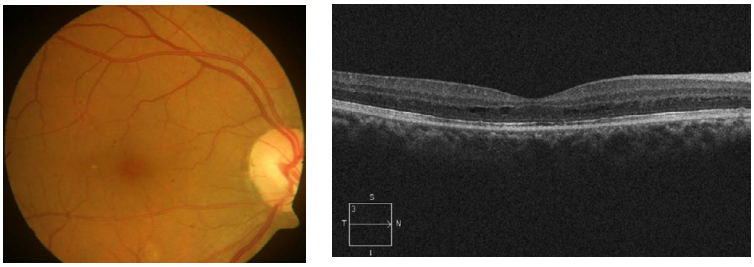

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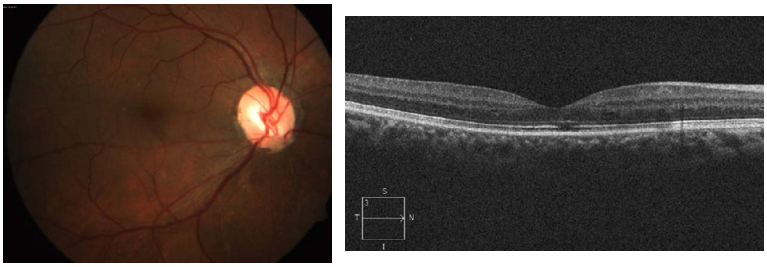

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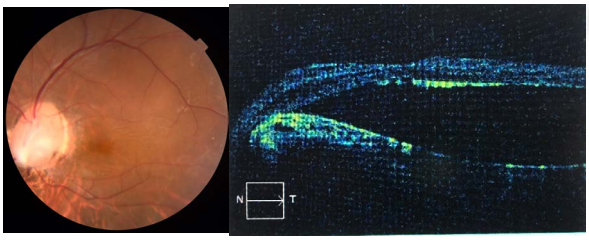

Fig.3.(a)

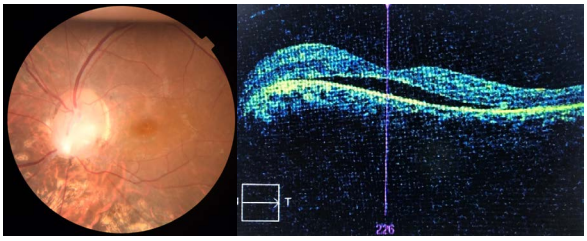

Fig.3.(b)

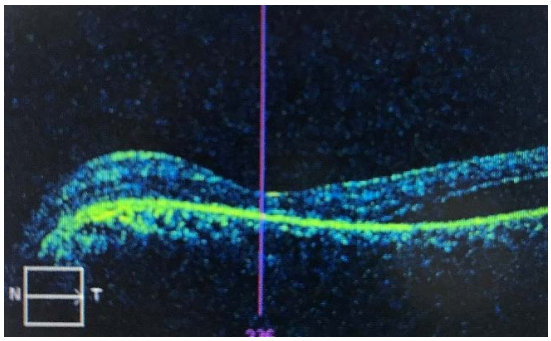

Fig.3.(c)

Fig.2 (a) Preoperative RE Fundus and OCT images of the same patient in fig.1 , BCVA-20/126. (b) 2 months post PPV + gas tamponade shows resolution of macular detachment , BCVA- 20/50 (c) 4 months follow up showing complete resolution of macular detachment, BCVA- 20/30.

Fig.3.(a) Fundus photo and OCT of a 24 yr old patient showing temporal disc pit with serous macular detachment,BCVA- 20/200. (b) 1 week follow up post gas tamponade and laser barrage to pit showing significant decrease in macular detachment (c) 4 week followup showing foveal reattachment with small residual pocket of fluid temporal to fovea, BCVA- 20/100

Other Techniques

Other approaches have produced promising results. Vitrectomy with radial inner retinal partial-thickness fenestration is a newer surgical technique that has been shown to completely resolve subfoveal fluid in 94% of eyes.27 Autologous fibrin injection over the ODP after PPV has been successful in treating a patient with persistent ODP-related macular detachment.28

PPV and temporal-side single radial optic neurotomy is thought to create a barrier to fluid passage by creating scar tissue and is associated with fluid resolution in 86% of eyes.29

Sealing of ODPs with autologous scleral flaps has been reported to be ef¬fective in inducing retinal reattachment and improving VA.13

The removal of glial tissue at the temporal segment of the ODP appears to also be beneficial without recurrence of the maculopathy at a 10-year follow-up.30

Conclusion

ODPs are rare cavitations of the optic nerve that may be asymptomatic or may be complicated by ODP-M, leading to significant visual loss. Although a rare condition the management of optic disc pit maculopathy still remains a challenge for all vitreoretinal surgeons particularly in absence of adequate published data.

Surgical management of ODP-M often leads to good visual outcomes. However if ODP-M is left untreated, the prognosis is generally poor and the final visual outcome unfavourable.

Currently PPV either alone or combined with other procedures ((eg gas tamponade, laser photocoagulation) is the treatment of choice. Macular buckling can be equally efficient regardless of the fluid origin however it is a laborious procedure with a long learning curve.

Other surgical techniques include inner retinal fenestration, autologous fibrin, and glial tissue removal presenting promising results. However more studies are required to confirm these results.
Although OPDs are rare, it is important for ophthal¬mologists to be aware of this condition and to monitor ODP patients for signs of developing ODP-M.

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# REVIEW ARTICLE

## Medical Management for Ocular Surface Restoration – A Review

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The Ocular Surface is a complex microsystem. It includes the corneal epithelium, limbal epithelium, conjunctival epithelial cells, conjunctival goblet cells, mucoepidermal junction of the lid, meibomian glands, lacrimal glands. The other components like immune cells, matrix cells, hormones, neural networks, and microbiome also regulate the homeostasis of the ocular surface. [1]

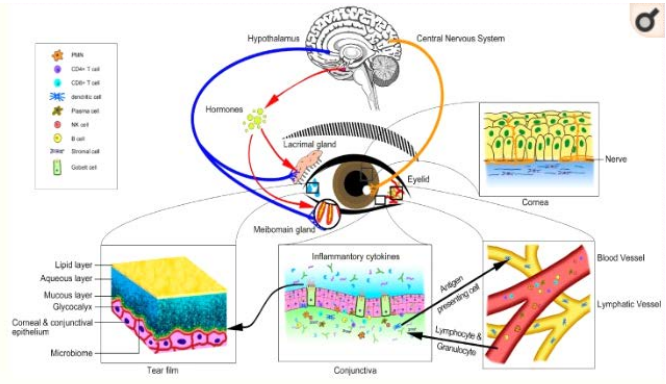


Figure 1: Schematic representation of ocular surface microenvironment components.[1]

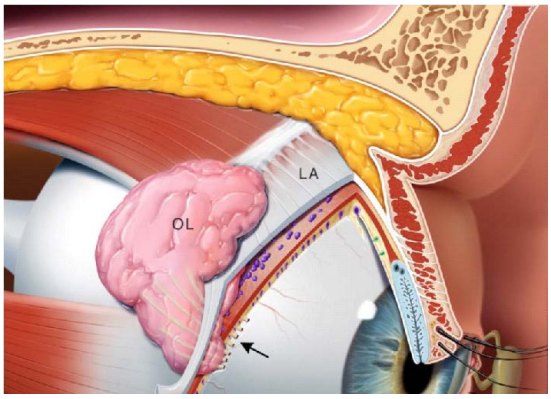


Figure 2: The main lacrimal gland is divided into the orbital lobe (OL) and palpebral lobe by the lateral horn of the levator aponeurosis (LA). [7]

**Role of various components forming ocular surface and the disorders associated:-**

**Cornea**:- The tight intracellular junction resist the entry of harmful pathogens. The microvilli of the superficial epithelium help in anchoring the tear film. The growth factors and cytokines secreted by epithelial cells help in wound healing. The keratocytes in the stroma are capable of synthesizing collagen and glycosaminoglycans which maintain the extracellular matrix. [2] Dry eye disease (DED) simulates an inflammatory response that causes an imbalance between the matrix metalloproteinases (MMPs) and their inhibitors causing degradation of the extracellular matrix resulting in corneal thinning. [3]

**Conjunctiva**:- It covers two-third of the ocular surface. The goblet cells present in the conjunctiva secrete mucin and the dentritic Langerhans cells help in the immune defense mechanism. Their density has been found to change in certain ocular surface immune/inflammatory conditions and targeted by cytokines and chemokines. [4] DED causes chronic inflammation of the conjunctiva causing squamous metaplasia. The tear breakup time is found to be reduced in pterygium causing DED. [5]

**Lacrimal glands**:- It contributes to the normal homeostasis of the ocular surface through secreting the aqueous layer that includes water, electrolytes, protein, mucus and maintains the moisture content of the ocular surface. [6] Dysfunction of the

lacrimal gland is seen in various conditions such as aging, prolonged exposure to visual display, dry environments, radiation therapy, contact lenses, refractive surgery, hormonal imbalance, ocular cicatricial pemphigoid, Sjögren's syndrome, systemic disorders autoimmune disorders like Sjögren's syndrome. [1][7]

**Meibomian glands**:- It secretes lipid, which maintains osmolarity, stability and prevents evaporation of tears. [8] Meibomian gland disease (MGD) is characterized by progressive obstruction of ducts leading to tear-film instability, hyper-osmolarity, and excessive evaporation of tears. [9]

**Eyelids**:- The mobile mucosal lining covers the ocular surface and uniformly distributes the glandular secretion into the tear film protecting the ocular surface. [1] Age-related degenerative changes, trauma, facial palsies, lagophthalmos, proptosis, or the floppy eyelid syndrome influence the eyelid laxity resulting in inefficient and infrequent blinking. [10] Blepharitis, inflammation of the eyelid caused by infections with Staphylococcus aureus, S. epidermidis, and Corynebacterium spp leads to hyperemia, edema, and ulceration of eyelids obstructing the meibomian glands leading to DED.[11]

**Tear film**:- It is a highly specialized and ordered fluid layer covering the ocular surface and forming an integral part of the ocular surface. The tear film has 3 layers, the outermost lipid layer, the middle aqueous tears, and the innermost mucous layer. [12] The outermost lipid layer is secreted by meibomian and Zeiss glands. It reduces evaporation of the underlying aqueous layer. The aqueous layer is secreted mainly by the lacrimal gland, and also by the glands of Krause & Wolfring. It contains various proteins including cytokines, immunoglobulins, and growth factors. Therefore has a crucial role in cell signaling and rehabilitation of the ocular surface. Lastly, the mucin layer, secreted by goblet cells of conjunctiva act as a surfactant and converts the hydrophobic surface of the cornea to hydrophilic. This layer is chiefly composed of mucin, immunoglobulins, salts, urea, enzymes, glucose, and leukocytes. The mucin layer harbors the commensals of the ocular surface and depletion of the mucin alters the microbiome of the ocular surface. [13] Compromise in any layer of the tear film can potentially disrupt the ocular surface health.**Meibomian glands**:- It secretes lipid, which maintains osmolarity, stability and prevents evaporation of tears. [8] Meibomian gland disease (MGD) is characterized by progressive obstruction of ducts leading to tear-film instability, hyper-osmolarity, and excessive evaporation of tears. [9]

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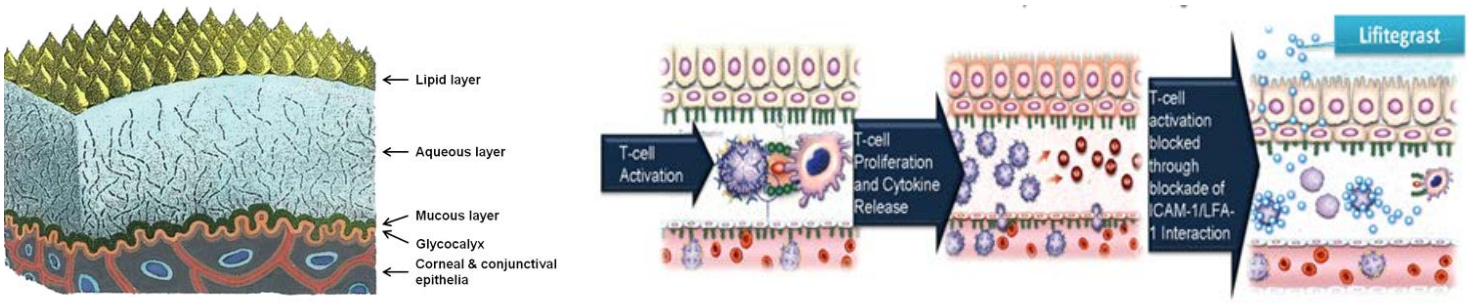



Figure 3:The precorneal tear film consists of four complex layers of tissue secretions and epithelia. [14]

**Immune system**:- The Antigen-presenting cells (APCs) like the macrophages, B-cells, and the fibroblasts form the part of innate immunity and act as the first line of defense and coordinate the adaptive immune response. The adaptive immunity of the ocular surface is mediated by the T-cells and the humoral defense is mediated by the immunoglobulins secreted by the plasma cells. Any external insult to the ocular surface stimulates the corneal and conjunctival APCs resulting in the production of Th effector cells which release inflammatory cytokines amplifying the process of immune response and leading to ocular surface epithelial damage. The conjunctiva-associated lymphoid tissue (CALT) consists of natural killer cells (NK cells), CD4+ CD25+ Foxp3+ T cells, CD8+ T cells, γδ T cell which protects against autoimmunity. [15] T-helper cells are involved in the secretion of cytokines which are associated with increased MMP levels and are involved in the corneal barrier dysfunction in DED. [16][17]

**Neural regulation of ocular surface:-** The ocular surface is innervated by nerve fibers which are branches of the trigeminal nerve which maintain the action of blinking and tear reflex. Nerve endings secrete neurotransmitters and nerve growth factors (NGF) which are essential for maintaining epithelial integrity, proliferation, and wound healing. [17] The parasympathetic nerve supply to the lacrimal gland releases acetylcholine which leads to the secretion of proteins, electrolytes, and water. The conjunctival goblet cells contain muscarinic and adrenergic receptors playing an important role in maintaining their physiological functions. [18] Therefore, the innervations of the ocular surface contribute to the major components of the tear film. Some ocular surgeries like refractive surgery and cataract surgery lead to corneal nerve transection causing decrease feedback to the lacrimal gland leading to reduced tear production. [19][20]

**Hormones:-**The systemic hormones play a role in maintaining ocular surface homeostasis, as lacrimal and meibomian glands possess the sex hormone receptors. [21] The androgens are capable of exerting a significant effect on the gene expression, protein synthesis, and immune response of the cornea, conjunctiva, and the secretory functions of the meibomian gland. [22] Androgen deficiency could lead to obstructive MGD with a lack of lipids at the lid margin and in the tear film, and altered lipid profile, and dry eye symptoms. [23] While estrogen deficiency is related to post-menopausal DED by initiating tissue-specific apoptosis. [24]

**Vascular supply**:-The ocular surface vasculature is mainly observed in the conjunctival, episcleral layers, and the limbal region, and it is maintained by VEGF. [25][26] The prime function is to mediate the transport of growth factors, immune response, and oxygen supply.

**Ocular surface microbiome**:- Dong et al. observed 24 genera including pathogenic and non-pathogenic bacteria in the ocular surface which helps in maintaining homeostasis and removing the pathogenic organism. [27] Chronic use of ocular antibiotic affect the ocular surface by decreasing the number of commensals. [28] Compromise in the ocular microbiome is seen in conditions such as DED, contact lens wear, keratoprosthesis, antibiotic exposure, and infectious states.

**Management of ocular surface disorders:-**

The management of ocular surface disorders can be done by medical and surgical methods depending upon the type and severity of the disease. The medical line of management aims for restoration of the ocular surface microenvironment which differs with various components of the lacrimal functional unit.

Artificial tears, gels, ointments, and inserts, replenish the tear film. Tears can also be conserved by punctal plugs, cautery, and moisture chamber eyewear. Lid hygiene, warm compresses, and massage are necessary for patients with blepharitis/ MGD to facilitate secretions. [29]

Anti-inflammatory and immune-modulatory agent options include cyclosporine, steroids, and nutritional supplements, such as omega-3 fatty acids. In addition to the classical treatments for the ocular surface disorder, innovative treatment options including compounded formulations of agents are also available. [29]

Dry eye disease:- It is a multifactorial disease of the tear film and ocular surface resulting in symptoms of ocular discomfort, visual disturbance, and tear film instability with potential damage to the ocular surface. This is associated with hyperosmolarity of the tear film and inflammation of the ocular surface. [30]

Treatment is based primarily on patient symptoms and signs. Disease severity was considered the most important factor for treatment decision-making and was categorized into 4 levels. Severity was assessed based on tear substitute requirements, symptoms of ocular discomfort, and visual disturbance. Also, the clinical signs present in lids, tear film, conjunctiva, and cornea were used for the categorization of severity. [31]

**Preservatives:-**Multi-dose artificial tears contain preservatives to prevent microbial growth. Benzalkonium chloride (BKC)

is the most frequently used preservative in topical ophthalmic preparations, as well as in topical lubricants. BKC is found to be epitheliotoxic. It damages the corneal and conjunctival epithelium, affecting cell-to-cell junctions and cell shape and microvilli, eventually leading to cell necrosis with sloughing of 1-2 layers of epithelial cells. The single most critical advance in the treatment of dry eye came with the elimination of preservatives. [30]

The widespread availability of non-preserved preparations allows patients to administer lubricants more frequently without concern about the toxic effects of preservatives.

**Nutritional supplements**: Diet rich in omega-3 fatty acids is associated with a reduced chance of developing and also improvement in symptoms of dry eye. [32] A diet rich in omega-6 fatty acids which is a precursor for pro-inflammatory mediators is associated with an increased risk of dry eye.

**Topical Cyclosporine:** It is a peptide derived from a fungal origin. It acts as an anti-inflammatory agent with immunosuppressive properties. Topical application of cyclosporine (0.05%) to the ocular surface is indicated to increase tear production in patients who have decreased tear production due to inflammation associated with dry eye. [33]

**Tetracycline class agents:** They suppress the production of staphylococcal lipases, required for antimicrobial activity. Bacterial lipases produce free fatty acids and diglycerides with the potential to disrupt the tear film lipids and cause ocular irritation. [34]

**Vitamin A**: It is essential for the development and maintenance of goblet cell levels in the conjunctiva. Commercially available ointment preparation replenishes goblet cells and helps in the healing of corneal injury and damage. [35]

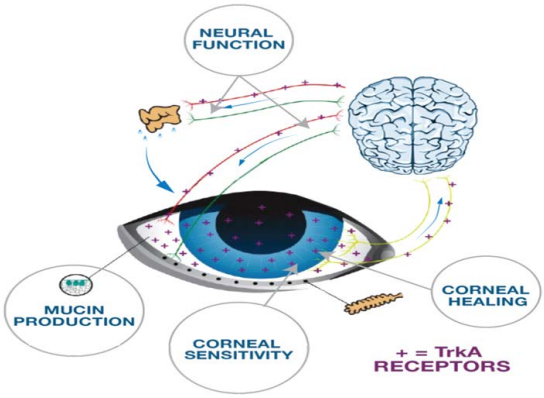
**Autologous serum**: It mimics the composition of natural tears and contains components like immunoglobulins, enzymes, and growth factors. It is available, a 20–50% preparation, diluted in artificial tears and used as a therapeutic option, and applied four to eight times a day to restore the ocular surface. [36]

**Newer drugs in dry eye:-**

**LIFITEGRAST** [37]

A potent Tetrahydroisoquinoline derivative, developed in 2012 was approved by the FDA in July 2016. The dosage form: 5% (50 mg/mL) in single-use container. It is a small molecule that blocks the interaction between Lymphocyte Function associated Antigen (LFA-1) and Intercellular Adhesion Molecule – 1 (ICAM-1) of immunologic synapse which in turn is responsible for cytokine release resulting in chronic inflammation and ocular surface damage. It has low systemic absorption following ophthalmic administration.

| SEVERITY | SIGNS AND SYMPTOMS | RECOMMENDED TREATMENT |
|---|---|---|
| 1 | • Mild to moderate symptoms; no signs<br>• Mild to moderate conjunctival signs | Patient counseling, preserved tears, environmental management, use of hypoallergenic products, water intake |
| 2 | • Moderate to severe symptoms<br>• Tear film signs<br>• Mild corneal punctate staining<br>• Corneal staining<br>• Visual signs | Unpreserved tears, gels, ointments, cyclosporine A, secretagogues, topical steroids, nutritional support (flaxseed oil) |
| 3 | • Severe symptoms<br>• Marked corneal punctate staining<br>• Central corneal staining<br>• Filamentary keratitis | Tetracyclines, punctal plugs |
| 4 | • Severe symptoms<br>• Severe corneal staining and erosions<br>• Conjunctival scarring | Systemic anti-inflammatory therapy, moisture goggles, acetylcysteine, punctal cautery, surgery |



| COMPONENT | PROPERTIES | ADVANTAGES | DISADVANTAGE |
|---|---|---|---|
| **CELLULOSE ESTERS**<br><br>**( HYPROMELLOSE,**<br><br>**HYDROXYETHYLCELLULOSE,**<br><br>**CARBOXYMETHYL-CELLULOSE)** | VISCOELASTIC,<br><br>INCREASE THE VISCOSITY OF TEARS | GOOD RETENTION TIME ON THE OCULAR SURFACE.<br><br>BLINKING DOESN'T AFFECT THE VISCOSITY | BENEFITS ONLY IN AQUEOUS TEAR DEFICIENCY.<br><br>HYPROMELLOSE CAN CAUSE CRUSTING OF EYELIDS. |
| **POLYVINYL ALCOHOL** | SYNTHETIC POLYMER | GOOD RETENTION TIME ON THE OCULAR SURFACE | BLURRING OF VISION<br><br>UNCOMFORTABLE TO THE PATIENT |
| **POVIDINE**<br><br>**(POLYVINYL-PYRROLIDONE)** | SYNTHETIC POLYMER.<br><br>SUPERIOR WETTING ABILITY WHEN CO-FORMULATED WITH POLYVINYL ALCOHOL | BENEFICIAL IN MUCIN LAYER DEFICIENCY | LITTLE CLINICAL EXPERIENCE |

SONATA (Safety Of a 5.0% coNcentrATion of lifitegrAst ophthalmic solution)- multicenter, randomized, prospective, double-masked study, the primary objective was percentage and severity of Treatment-Emergent Adverse Events ( TEAEs) and secondary objective was ocular safety measures like fluorescein stain, drop comfort, BCVA, IOP over 7 visits. Overall, 53.6% of participants receiving lifitegrast experienced ≥1 ocular TEAE versus 34.2% in the placebo group.

**TAVILERMIDE (MIM-D3)** [38]

MIM-D3 (developmental code name) is a small cyclic peptide-mimetic of Nerve Growth Factor (NGF). NGF is a naturally occurring protein in the eye responsible for the maintenance of corneal nerves and epithelium. It activates the tropomyosin-related kinase (TrkA) receptor and the p75NTR receptor, a member of the tumor necrosis factor superfamily.

Tavilermide demonstrated significant improvements in both signs and symptoms along with strong safety, comfort, and tolerability profiles. Few adverse events were reported like reduction of visual acuity, instillation site pain, and eye irritation. All adverse ocular events were mild and transient.

**TREHALOSE** [39]

It is a naturally occurring disaccharide found to have an anhydrobiotic function due to its lubricative and water-retaining properties in biological systems. It is available as a preservative-free eye drop. It can be used alone as Trehalose (3%) OR in combination with Sodium hyaluronate (0.15%) OR above two plus Carbomer gel (0.25%).

**REBAMIPIDE** [40]

Rebamipide is a novel quinolinone derivative available as 2% ophthalmic suspension. Rebamipide increases gastric endogenous prostaglandin E2 and I2, promotes gastric epithelial mucin, behaves as an oxygen-free radical scavenger and it has other anti-inflammatory action. In the eye it increases both secreted and membrane-associated mucin, it prevents damage to microvilli, and also increases proliferation and thereby density of goblet cells. Therefore, it ensures firm adhesion and good stability of tear film.

**CHLOROQUINE PHOSPHATE** [41]

It is available as 0.03% eye drops. It has anti-inflammatory property which prevents the release of inflammatory mediators due to desiccation of cornea and conjunctival epithelial cells in dry eyes. It is effective, safe, and well-tolerated in patients with moderate dry eye syndrome. Due to its long duration of action, it is not preferred for severe dry eyes.

**OTHER DRUGS IN DRY EYE PIPELINE**

| NAME | MECHANISM OF ACTION | STATUS |
|---|---|---|
| DEXAMETHASONE PHOSPHATE | ANTI-INFLAMMATORY | PHASE III COMPLETED |
| RIMEXOLONE (1%) [42] | INHIBITS CYTOKINE PRODUCTION & T-CELL PROLIFERATION | PHASE III COMPLETED<br>(OFF LABEL RX FOR DRY EYE) |
| BROMFENAC (0.07/0.09%) [43] | NON-STEROIDAL ANTI-INFLAMMATORY | PHASE III COMPLETED |
| EBI-005<br>(5MG/ML) [44] | INTERLEUKIN-1 ANTAGONIST | PHASE III |
| TOCILIZUMAB | INTERLEUKIN-6 INHIBITOR | PHASE III UNDERWAY |
| AZITHROMYCIN (1%) | INHIBITS MRNA TRANSLATION | PHASE IV COMPLETE |
| DIQUAFOSOL TETRASODIUM (3%) [45] | P2Y2 RECEPTOR AGONIST (↑ MUCUS SECRETION) | APPROVED IN JAPAN AND KOREA |
| HAPORINE-S (CYCLOSPORINE AS A NANOPARTICLE) - ↑ ABSORPTION RATE | T-CELL INHIBITOR | PHASE III COMPLETE |
| CYCLOKAT (PRESERVATIVE-FREE CYCLOSPORINE 0.1% CATIONIC EMULSION) | IMMUNOSUPPRESSIVE | PHASE III/RECOMMENDED FOR APPROVAL BY EMA |

## CONCLUSION :

Numerous diseases can cause ocular surface disorder and accurate diagnosis can be difficult and time consuming. Therefore, identifying and treating the functional effects of the underlying disorder on ocular surface can be beneficial.

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# REVIEW ARTICLE

## How To Read A Visual Field Chart?

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**Introduction:**
Visual field assessment and optic disc changes are important tools in diagnosis of glaucoma. Structure versus functional changes in glaucoma has always been a point of debate. Functional changes or field defects appear when 20-30 % axons are already lost but at the same time in advanced glaucoma from view point of progression and floor effect, visual field assessment sounds more relevant. In early glaucoma, OCT plays an important role but we should be cautious about misinterpretation in presence of anatomical variants.
Now how to read a visual field chart ? It's interpretation of humphrey's visual field chart. Single field analysis printout is divided into 10 zones which can be divided into 2 groups:

**Zones independent of normative data and statpac analysis**
**Divided into 4 zones**
**Zone 1** Patient data / test data
**Zone 2** Reliability indices/foveal threshold
**Zone 3** Raw Data
**Zone 4** Grey Scale
Zones dependent on normative data and statpac analysis ( 4 zones)
**Zone 5** Total deviation numerical plot
**Zone 6** Total deviation probability plot
**Zone 7** Pattern Deviation numerical plot
**Zone 8** Total deviation probability plot
**Zone 9** Global Indices –
- Mean deviation( MD )
- Pattern standard deviation(PSD )
- Corrected pattern standard deviation( CPSD) &
- Short term fluctuation( SF )

**Zone 10** Glaucoma hemifield test
- Outside normal limits
- Border line
- Abnormally low sensitive
- Abnormally high sensitivity
- Within normal sensitivity

**Zone 1 Patient data and test data**
- Apart from name, correct age is important otherwise patient's raw data will be compared with mean threshold values of wrong age group thus wrong total deviation plot.
- Pupil size should be 3 -4 mm and should be same for present and previous test as media opacities can reduce field with pupil less than 2 mm.
- Proper near correction .
- Fixation target could be central, small diamond or large diamond .
- Size 3 for routine and in advanced glaucoma size 5 is used to know macular split

**Zone 2 Foveal threshhold and reliability indices**

- Foveal threshold is measured at the beginning, if patient is not properly focussed foveal sensitivity will be reduced along with remaining field. If VA is good and threshold is low correction is not proper
- Fixation losses should not be more than 20%. If patient fixes at central fixation target he should not respond to 5 % stimuli presented on blind spot.
- If false positive rate exceed 33% in print out XX is printed next to the rate. In established and advanced glaucoma 20% of false positive, false negative and fixation losses are acceptable
- Unusual cause for fixation losses is that selected fixation target is central and patient fixes at diamonds

**Zone 3 Raw data**

- The raw data is the exact retinal sensitivity in db units of the selected points calculated by field ` analyser. Only numerical values are displayed and db units are omitted.
- " 0 " indicates absolute scotoma i.e. no response to max.intensity of light i.e.10,000 asb units in Humprey's analyser. 40 is response to 1asb units
- Raw data is strategy specific, hence for follow ups, same strategy should be used.
- Whether measured sensitivity is normal or decreased can be assessed by total deviation plot not by raw data. Retinal sensitivity at 5 degree is higher than sensitivity at 10 degree so slope of vision is smooth.

**Zone 4 Grey scale**

- The conversion of raw data to grey scale does not involve any statistical calculation or normative analysis
- The sensitivity from 50 db to 0 db is divided into 10 zones. 1st column includes 50 db to 41 db and then each step corresponds to a change of 5db . Highsensitivity areas are represented by lighter shades while low sensitivity areas are represented by darker shades.
- The grey scale just gives rough idea of the pattern of visual field loss.
- In high false positive, white zones appear while high false negatives gives clover leaf appearance.
- Colour is imparted as per numerical value and that value could be normal at one location and abnormal at another so its misleading.

**Zone 5 Total deviation numerical plot ( TDNP)**

- Raw data is compared with normative data of same age group and calculates the difference between the measured sensitivity and the normative data at each point and plots the deviation as TDNP.
- If measured sensitivity is less than normal, ( -) sign is allotted and if measured sensitivity is better than mean normal value of the same age group, no sign is given and "0" deviation indicates no loss of sensitivity
- Higher (-db ) indicates deep scotomas and lower (-db) values indicates superficial scotomas.. If there is no significant field loss, TDNP contains deviation values in the range of 0 to -2 db.
- If there is uniform field lossTDNP contains almost similar (- ve db) values all over and difference between highest and lowest values is minimal.
- If irregular loss of sensitivity is there difference between highest and lowest values will be high.

**Zone 6 Total deviation probability plot ( TDPP)**

- The loss of retinal sensitivity is now expressed in terms of it's p value and p value is given a symbol. ***Darker the symbol the greater the probability of abnormality as indicated by p value. So higher the P value lesser the chances of field being abnormal.***
- STATPAC calculates the p value for the points where there is loss of sensitivity. If the loss of sensitivity has P value 0.5 %, it simply means that loss of sensitivity of that point seen is one in 200 normal population for that age but it doesn't tell whether it is abnormal or diseased.

**Zone 7 Pattern deviation numerical plot (PDNP)**

- The pattern deviation plot is created to know the pattern and the extent of deep scotomas masked by generalised depression in the total deviation probability plot.
- The 7th best sensitivity point of TDNP is selected and the db value that converts it into 0 deviation is worked out .Now this db value is added to all points of total deviation numerical plot to convert it into PDNP. The generalised depression is removed by elevating the value of sensitivity of each point by certain db value to form the new numerical plot and corresponding probability plot and this will expose deep scotomas.

**Zone 8 Pattern deviation probability plot( PDPP)**

- Pattern deviation probability plot is nothing but symbolic representation of P value of PDN plot.
- If pattern deviation probability plot does not show any scotoma, we consider the generalised depression as uniform generalised depression.
- In irregular generalised depression, the pattern and the extent of the deep scotomas masked inTDPP, are highlighted in PDPP.
- If TDPP shows generalised field defect and the PDPP shows shows localised scotoma, It indicates (cataract +glaucoma).
- If TDPP shows generalised field defect and normal pattern deviation plot, it indicates no evidence of glaucoma in a case of cataract.

**Zone 9 Global indices**

- **Mean deviation (MD)**
  - Mean deviation index signifies the average of overall severity of field loss. **It is the average of all the numbers shown on TDNP except two points in area of blindspot.** Thus the points with low variance that is closer to the fixation affect the MD value more than do the eccentric points which have a higher variance .
  - The sensitivity of normal visual field is depicted by the solid diagonal lines and general depression is depicted by broken lines.
  - With suspicious disc

  ( a) A difference of mean deviation of 2 db between two eyes

  (b) An average 1.5 db difference must be maintained between two eyes on two consecutive tests

  ( c) An average difference of 1db must be maintained between 2 eyes on 4 consecutive tests.
  - The increase in MD >0 .08 db per year should be considered abnormal.
  - The MD Index is higher in generalized field defects and value of MD index in localized field defect depends on the extent and the depth of the field defects
  - TheMD Index is expressed by the change in height of hill of vision and PSD is expressed by changes in smoothness of the contour of hill of vision.
- **Pattern standard deviation (PSD)**
  - **PSD** is an index to express dissimilar deviation values in the total deviation numerical plot or in other words to express contour of hill of vision whether is smooth or rough.
  - If roughness is not significant, PSD will be a simple number without P value
  - So PSD with significant P value indicates the numbers in the TDNP are not similar to each other. PSD helps to diagnose glaucoma at an early stage, once the glaucoma is diagnosed PSD has very minimal role in management of glaucoma as the field defect covers most of the tested area as in advanced field loss. **Hence, this indicator loses its value in advanced disease. Such patients can be followed up with the MD.**
  - Higher the irregularity in the loss of sensitivity, higher the PSD value.
  - In localised defects, contour is irregular without affecting the height
  - When there is irregular generalised defect, height of hill is decreased as well as contour. No change in PSD indicate there is a progression of the field defect and it is uniform generalised type. PSD will be high in localised and irregular generalised field defects. ( high MD and high PSD)
  - In uniform generalised depression contour of hill is smooth and height of hill is decreased ( Low PSD and high MD )
- **Short term fluctuation(SF) :**

  The **SF** and and **corrected pattern standard deviation (CSPD)** will Be calculated by full threshold and FAST PAC strategies. SITA Strategies donot calculate SF and hence CSPD cannot be calculated. SF value is always less than 3 db.and is a indicator of reliability.
- **Corrected pattern standard deviation( CPSD)**

  Intra testing variability is removed from PSD to produce CPSD .CPSD is not calculated if SF is not estimated.

**Zone 10 Glaucoma hemifield test**

GHT is refined PSD. GHT is developed to pick up the dissimilarity among the sensitivities of the corresponding points on either side of horizontal axis to diagnose glaucoma at an early stage. GHT evaluates five zones in the upper field and compares these zones to mirror image zones in the lower field . Grading is as follows:

- Out side normal limits
- Borderline
- General reduction of sensitivity
- Abnormally high sensitivity
- Within normal limits

Apart from this we should know about strategies also and in follow ups we should keep in the mind about staratégy followed earlier. As the standard threshold strategy takes longer time to perform, now new strategy (SITA – Swedish interactive threshold Algorithm) strategies are available without really compromising the results. So correct interpretation of visual field analysis is an important tool and always correlate clinically.

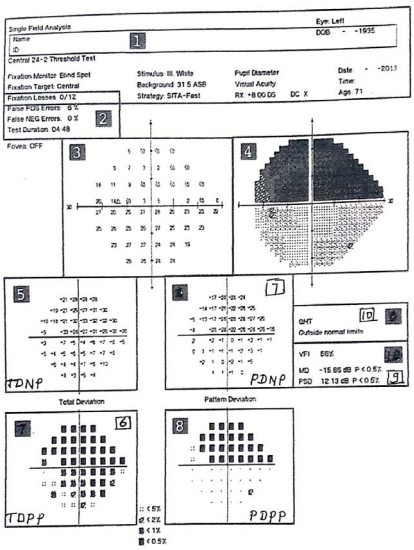


Fig 1 Field chart marked in 10 zones as described

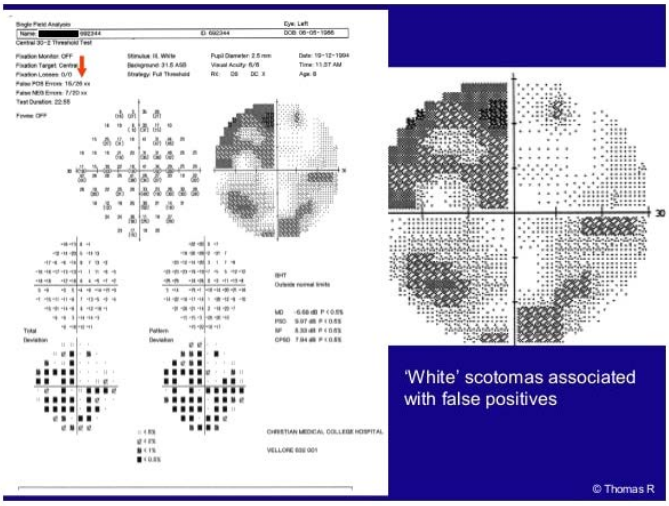



Fig 3 White scotomas ( check false positives)

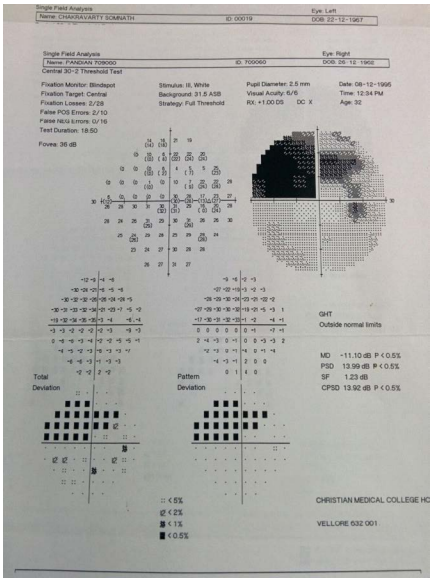
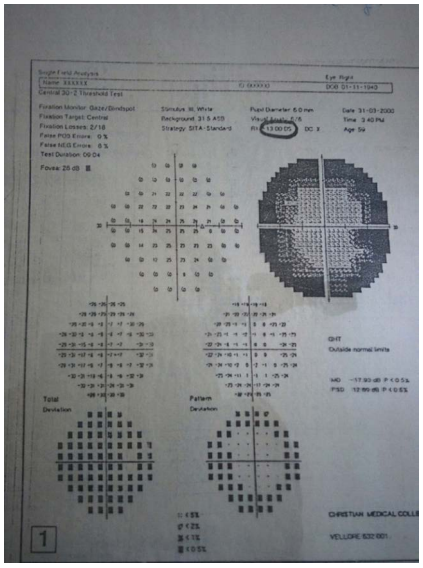


Fig 2 Superior arcuate defect



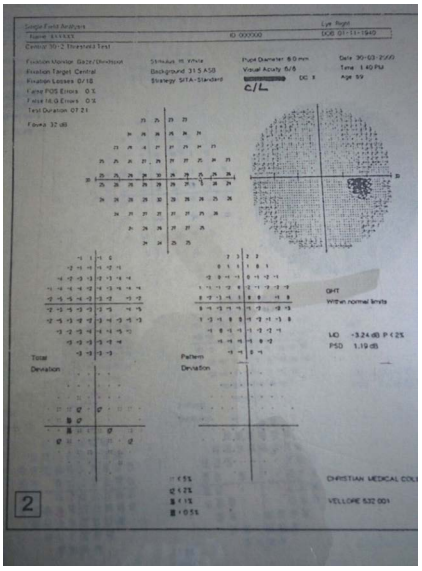


Fig 4 ( A & B)
A. Classic Ring Scotoma due to Ahakic glasses
B. Cotoma vanished with contact lens

# WHAT'S NEW

## POST COVID 19 ORBITAL MUCORMYCOSIS: ALL WE NEED TO KNOW

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**INTRODUCTION:** A COVID-19 pandemic has affected millions and millions of lives in the world. In India also it has become a matter of immediate concern since the early part of year 2020. Post covid many new complications like hypercoagulability, pulmonary fibrosis, deranged glucose metabolism, mesenteric ischemia, and secondary bacterial and fungal infections have surfaced. Mucormycosis is one of these which has attracted the ophthalmologist attention in recent past. Literature review shows a few sporadic cases reported after the first wave of covid 19. There has been an exponential increase in incidence of mucormycosis in India, in sync with the soaring second wave of COVD-19. Mucormycosis, a subtype of a larger category of diseases known as zygomycoses, is an aggressive opportunistic infection which tends to show a proclivity for, the lungs, gastrointestinal tract, and the rhino-orbital cerebral tract. While rhino-orbital cerebral mucormycosis [ROCM] is typically associated with Rhizopus species, a number of other species have also been implicated, including Mucor, Rhizomucor, Absidia, Apophysomyces, Saksenaea, Cunninghamella, Cokeromyces, and Syncephalastrum. ROCM caused by filamentous fungi involving the nose, paranasal sinuses, and brain. It is an opportunistic pathogen commonly found in immunocompromised individuals. The fungus grows rapidly and aggressively, causing a well-defined fulminant and life-threatening disease. Early intervention is a must to save lives and prevent complications. It is an acute fungal infection in most cases, but chronic presentations have also been described, which is indolent and slowly progressive, occurring over several weeks.

**RISK FACTORS AND PATHOGENESIS:** Commonly associated risk factors include uncontrolled diabetes with or without diabetic ketoacidosis, severe burns, steroid therapy, solid organ transplantation, prolonged corticosteroid therapy, hemochromatosis, patients with HIV, neutropenia, malnutrition, hematologic malignancies, toclizumab use, mechanical ventilation, Covid 19 infection.

The infection starts in the nasal cavity and extends to adjoining paranasal sinuses. It gets implanted and grows in the nasal cavity and sinuses. The humid environment of the nose and paranasal sinuses favours the growth and invasion of fungi. The most common site involved in mucor is middle turbinate, followed by middle meatus and septum. Invasion of blood vessels by fungal hyphae damages the endothelium causing blood clots that occlude the blood vessels leading to ischemia and necrosis of surrounding tissue. In ROCM invasion of brain and orbit is through the involvement of sphenopalatine and internal maxillary arteries. Involvement of orbit can be by various routes:

Involvement of medial orbit via nasolacrimal duct or in continuation with ethmoid sinus.
Involvement of inferior orbit via inferior orbital fissure nerves and vessels.
Involvement of orbital apex or superior ophthalmic fissure in cases of ethmoid sinusitis and sphenoidal sinuses.
Involvement of 6th and 7th cranial nerves if the disease is predominantly in pterygopalatine fossa, infratemporal and surrounding skull base soft tissue.
Retrograde from the internal carotid artery to ophthalmic artery ultimately resulting in Central retinal artery occlusion.

**CLINICAL PRESENTATION:** The ocular involvement and presentation depend upon the route by which it has reached the orbit. Depending upon the site of entry of infection into the orbit and the structure involved it can be unilateral or bilateral (fig 1). Mostly, unilateral cases are common than bilateral involvement.

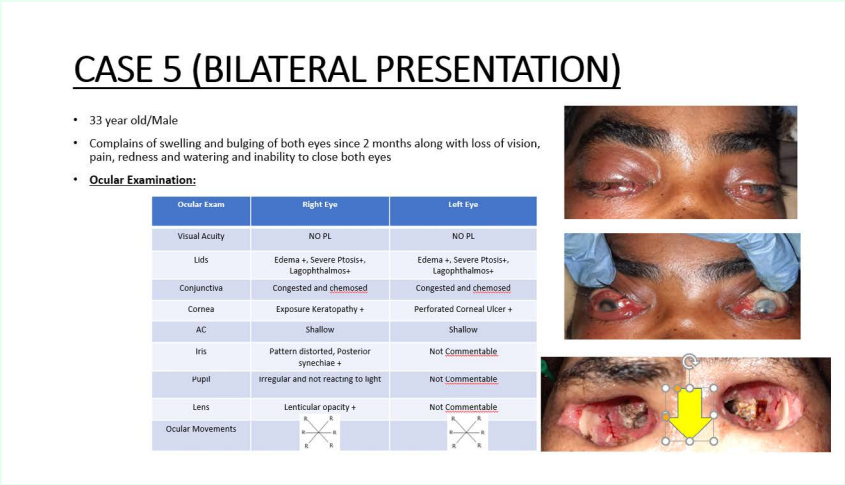


Fig 1: ROCM with bilateral presentation

Cases may present with -

- Sudden painless diminution of vision
- Mono-muscular palsy leading to diplopia
- Inability to move the eyeball (ophthalmoplegia)
- Ptosis
- Eyelid, periocular or facial edema
- Eyelid, periocular, facial discoloration
- Facial paresthesia, anesthesia or facial pain
- Proptosis and chemosis
- Lagophthalmos
- Neurotropic ulcers (fig 2)
- Central retinal artery occlusion ultimately resulting in optic atrophy
- Orbital apex syndrome
- Orbit, paranasal sinus or dental pain

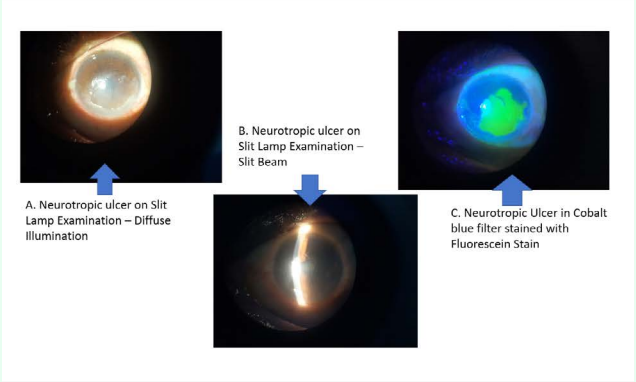


Fig 2: ROCM with neurotropic corneal ulcer

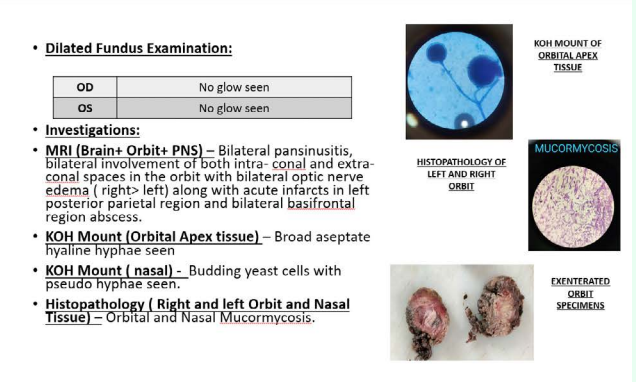


Fig 3: KOH mount and HP showing Fungus

Further spread intra-cranially may lead to headache, altered consciousness and even death.

Possible ROCM: high risk cases with clinical suspicion of ROCM
Probable ROCM: Possible + radiological (Gd enhanced MRI or CT scan) evidence of ROCM
Proven ROCM: microbiologically (KOH or H/P) proven ROCM (fig 3)

**DIAGNOSIS AND ROLE OF IMAGING**: Early diagnosis is the key. High degree of clinical suspicion coupled with appropriate investigations should be done at the earliest in high-risk patients. Nasal endoscopy with biopsy and swabs for KOH mount and fungal culture are the most economical and easily available tools for diagnosis. In addition, MRI of paranasal sinus with orbit and brain aid in surgical planning and extent of resection. Gd enhanced MRI is a better predictor of disease in comparison to CT scan as soft tissue signs can be under rated in CT scan. Renal function tests and electrolytes should be closely monitored in the peri-operative period as these patients are treated with adjuvant Amphotericin-B, which is potentially nephrotoxic.

**TREATMENT OPTIONS:** Multimodality team approach for treatment should be there including otolaryngologists, ophthalmologist, maxillofacial surgeon, intensivist, neurologist, endocrinologist and a nephrologist. In cases of naso-sinus the treatment is straight forward. Injection liposomal amphotericin B (1 mg/kg/day for a total dose of 2–3 g) is the gold standard along with adjuvant surgical debridement of dead and necrotic tissues. Surgical debridement of all the accessible necrotic tissues should be done as far as practicable. Supportive anti-inflammatory therapy with good glycemic control is also important aspect of management. The mode of administration of Amphotericin B is parenteral and four formulations are available commercially. These are:

Conventional Amphotericin-B

Amphotericin-B Colloidal Dispersion

Liposomal Amphotericin-B

Amphotericin-B Lipid complex.

Liposomal Amphotericin-B is considered the best in terms of therapeutic efficacy and safety margin. Posaconazole

is a new triazole that has been shown to have good efficacy against some strains of Mucorales. However, when the orbit is involved the decision making is not as direct. In cases of probable ROCM with orbital involvement systemic antifungal with naso-sinus debridement should be started along with Retrobulbar Inj Amphotericin B 3.5mg/ml in dose of 1ml can be given in cases of segmental orbital involvement with preserved vision for a maximum of 5-7 doses. If the disease is still progressing or is extensive at initial presentation with no visual potential early exenteration should be done. The decision to either preserve the eye or exenterate it as a part of surgical debridement has to be taken jointly by the otolaryngologists and the ophthalmologists. The scoring system is based on 3 main criteria, namely: (1) clinical signs and symptoms. (2) Direct and Indirect Ophthalmoscopy. (3) Imaging. The Sion Hospital Scoring System is an accurate and promising measure to solve the dilemma that is associated with orbital exenteration in ROCM. In cases of doubt and patients with good vison endonasal endoscopic medial orbital wall debridement can be done and retrobulbar fat inspection and demonstration of broad septate fungal hyphae on KOH mount can solve the dilemma. In cases of proven mucor with orbital and CNS involvement if visual prognosis is guarded then decision for exenteration should be taken to decrease the necrotic and inflammatory load.

**CONCLUSION:** Post COVID-19 patients with high-risk features should be kept under surveillance. A slightest degree of suspicion must prompt early diagnosis and initiation of treatment. Clinicians should not hesitate to initiate Amphotericin B therapy when there is reasonable suspicion of ROCM. Underlying risk factors such as diabetes should be managed promptly. Radical debridement of all necrotic tissue, with special attention to the critical surgical areas of affection must be done as far as practicable, to decrease the inflammatory burden and increase the drug penetration.

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# CASE REPORT

## MANAGEMENT OF POLYPOIDAL CHOROIDAL VASCULOPATHY BY ANTI VEGF- STRUCTURAL AND FUNCTIONAL OUTCOME

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**ABSTRACT**

Polypoidal Choroidal Vasculopathy (PCV) is characterized by subretinal polypoidal vascular lesions associated with serous and hemorrhagic pigment epithelial detachments (PED). The classical features of PCV are presence of sub-retinal reddish orange nodules and serosanguineous maculopathy, with the exudation being disproportionately larger than the size of lesion. Indocyanine green angiography (ICGA) is the gold standard for detection and evaluation of PCV. Treatment modalities are photodynamic therapy (PDT), anti-vascular endothelial growth factor (anti-VEGF) agents and thermal laser (TL) or combination. The choice of specific treatment modality and prognosis depend upon multiple factors.

We present the case of 67-year-old diabetic female with diminution of vision in both eyes more in left eye from past 2 years. Left eye macula showed multiple subretinal hemorrhages of various duration and elevated reddish orange nodule in paramacular area. Diagnosed with right eye operable cataract and mild diabetic retinopathy and left eye Polypoidal choroidal vasculopathy. Right eye cataract surgery was performed after control of sugar and left eye Intravitreal Anti-VEGF (brolucizumab)were given. We describe the detail management of Polypoidal choroidal vasculopathy and its structural and functional outcome.

**Keywords**: Choroidal neovascularization; Idiopathic polypoidal choroidal vasculopathy; Retinal pigment epithelial detachment

**INTRODUCTION**

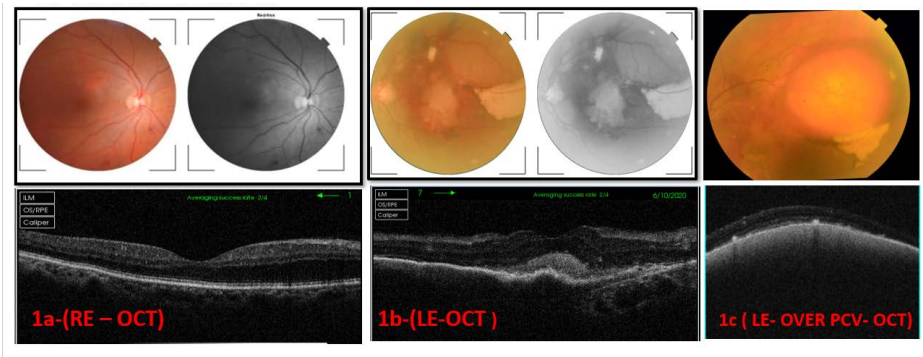
Polypoidal Choroidal Vasculopathy (PCV) has subretinal polypoidal vascular lesions associated with serous and hemorrhagic pigment epithelial detachments (PED). It is an important cause of exudative maculopathy in Asian eyes as Wet age-related macular degeneration in Caucasians eyes. It was thought first that PCV preferentially affect pigmented individuals like African or Asian descent.[1] PCV been described in people of European descent as well, although prevalence is higher in Asian people than in whites.[2]

The classical features of PCV are presence of sub-retinal reddish orange nodules and serosanguineous maculopathy, with the exudation being disproportionately larger than the size of lesion. Hemorrhagic pigment epithelial detachment, submacular hemorrhage and neurosensory retinal detachment in the peripapillary or macular retina are other common findings. Indocyanine green angiography (ICGA) as gold standard for detection and evaluation of PCV.[4] while Spectral-domain OCT is a useful imaging modality for diagnosis and follow-up of PCV. The treatment for PCV is photodynamic therapy (PDT), anti-vascular endothelial growth factor (anti-VEGF) agents and thermal laser (TL) or combination. The choice of specific treatment modality and prognosis depend upon multiple factors such as visual acuity, the location and size of PCV lesion, presence or absence of leakage on fundus fluorescein angiography, presence or absence of polyp with residual abnormal vascular network and amount of submacular hemorrhage. According to some authors Anti -VEGF treatment is less effective in idiopathic PCV than for CNV secondary to AMD[5].

The ultimate visual acuity improvement depends on subretinal blood and resultant subfoveal fibrosis. Visual prognosis of PCV is generally better as compared to wet ARMD, mainly due to spontaneous regression and the containment of PCV lesions under the RPE preventing intrusion and leakage in the subretinal space. A recent multicenter randomized controlled trial titled "EVEREST" (i.e., efficacy and safety of verteporfin photodynamic therapy) in combination with ranibizumab or alone versus ranibizumab monotherapy in patients with symptomatic macular PCV showed that treatment of PCV with a combination PDT plus ranibizumab injections were well tolerated and highly effective in achieving complete regression of the polypoidal lesions in symptomatic PCV.[6]

**CASE REPORT**

A 67-year-diabetic female presented with visual acuity in the right eye of 6/36 and left eye close to face with history of progressively worsening vision in both eyes which was more in left eye from past 2 years. She is diabetic from past 2 years with fasting blood sugar of 216 mg%, post prandial sugar 319 mg% and glycosylated hemoglobin (HBAIC -7.9). Both eyes anterior segment showed nuclear and cortical cataract which was more in right eye. Color fundus photograph revealed few deep retinal hemorrhages and microaneurysm right eye and areas of subretinal and sub-RPE hemorrhages of variable duration in left eye with reddish orange nodule in paramacular area. On SD-OCT (3D OCT-1Maestro; Topcon Medical Systems) the appearance of the pigment epithelial detachment subretinal fluid, PEDs was suggestive of PCV in left eye only and right was normal (Figure 1). Intravenous fluorescein angiography in right eye showed few dot hemorrhages with no leak while in left eye showed blocked fluorescence owing to subretinal hemorrhage and hemorrhagic pigment epithelial detachment with hyper fluorescence owing to leakage from the polyps (Figure 2).




(Figure 1) 1a - fundus photo and OCT of right eye, 1b- fundus photo and OCT of left eye, 1c- Photo & OCT over PCV

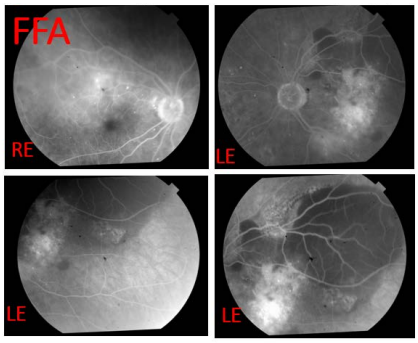



Figure- 2- LE - Polypoidal choroidal vasculopathy (PCV)

We did B Scan to rule out amelanotic choroidal melanoma (Figure 3), as ICGA facilities were not available to confirm the presence of PCV. Diagnosis of right eye operable cataract with mild NPDR and left eye Polypoidal choroidal vasculopathy was made and patient was counselled for diagnosis and treatment options available. We advised right eye cataract surgery after control of sugar and left eye intravitreal Anti-VEGF injection of ranibizumab (Razumab - Intas). After two consecutive monthly intravitreal injections, her visual acuity in the left eye improved to finger counting one foot only. Clinically, the polypoidal lesions were regressed little with decreased hemorrhage with flattening of the PEDs (Figure 4). We were not satisfied with results and after proper counselling injection brolucizumab (Pagenex- Novartis) was given as third Anti- VEGF injection with encouraging results (Figure 5). After a total of five injections (2 ranibizumab and 3 brolucizumab injections) visual acuity in the left eye improved to 6/36p and the sub-RPE blood had resolved (Figure 6). At her most recent follow- up, 11 months after the last injection, the visual acuity in the left eye was stable and the patient was delighted with the improvement from her baseline and does not require further injections (Figure 7). Her right eye following cataract surgery and sugar control is maintaining BCVA of 6/6p N/6.

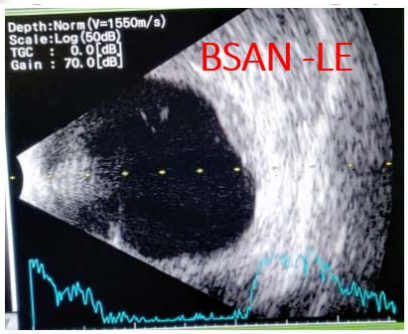



Figure 3 - LE – ultrasonography

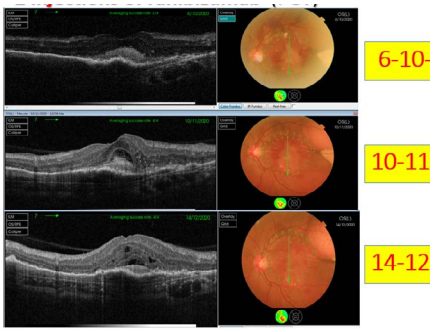



Figure 4- LE- Comparison left eye after 2 injections of ranibizumab (PCV)

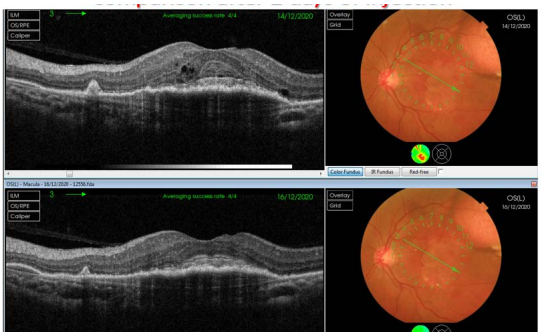


Figure- 5- first brolucizumab (15th December 20) comparison after 2 days of injection

**DISCUSSION-**

Age-related macular degeneration (AMD) is a leading cause of visual impairment in developed countries and AMD is divided into two subtypes: geographic atrophy and neovascular AMD (nAMD) which is associated with choroidal neovascularization (CNV). CNV progresses more rapidly than geographic atrophy is divided into types 1 and 2 depending on its histopathological location. Type 1 CNV grows beneath the retinal pigment epithelium (RPE). Type 2 CNV grows into the subretinal space, thereby penetrating the RPE. While type 3 CNV is retinal angiomatous proliferation is a specific type of nAMD associated with intraretinal neovascularization.[7] Polypoidal lesions is type 1 CNV is called as PCV incidence of which is higher in Asian than in Caucasian populations. Idiopathic polypoidal choroidal vasculopathy is a hemorrhagic disorder of the macula which is characterized by a vascular network in the inner choroid ending in an aneurysmal bulge. This outward projection is visible clinically as a reddish-orange polyp-like structure. Bleeding from polypoidal lesions causes massive submacular haemorrhage, leading to significant visual deterioration.[8,9]

The disease follows a remitting-relapsing course and is associated clinically with chronic recurrent serosanguineous pigment PED. In eyes with PCV using ICGA and OCT, Tsujikawa and colleagues[10] found that polypoidal lesions are located at the margins of the PED. Fluid from the lesions can cause these lesions to detach from Bruch's membrane and appear to be located inside the PED. In eyes with a PED, en face OCT shows protrusions of the RPE corresponding to polypoidal lesions seen on ICGA.[11,12] In eyes without a PED, en face OCT shows distinctive rings of a highly reflective RPE line corresponding to polypoidal lesions seen on ICGA. Anti-VEGF therapy has become the standard of care for the management of macular neovascularization. Each anti-VEGF agent which is currently in use offers certain unique advantages. While bevacizumab is the most economical choice, ranibizumab has been FDA-approved for the past 14 years and has the most evidence in the literature. Aflibercept acts against multiple molecular targets including VEGF-A, VEGF-B, and placental growth factor and has the advantage of a bi-monthly dosing schedule. Brolucizumab is a very durable agent primarily due to its low molecular weight allowing for higher molar dosing and offers the advantage of ≥12 weekly dosage in nAMD. Ranibizumab and aflibercept are anti-VEGF agents approved for ophthalmic use. In vitro studies have shown that aflibercept has higher anti-VEGF efficacy than ranibizumab.[13]

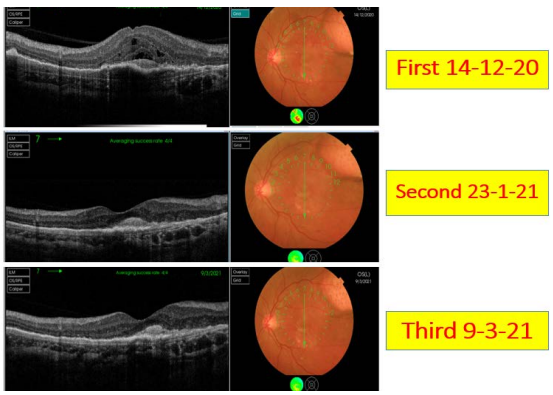



Figure- 6 Comparison after 3 injections of Brolucizumab

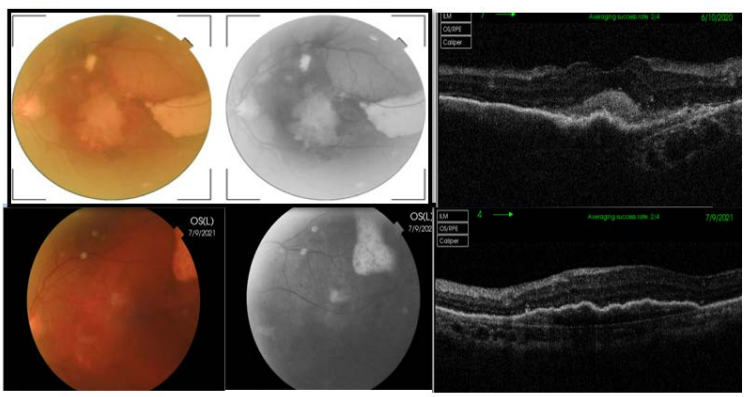


Figure 7 - First and last presentation of left eye

Recently, brolucizumab was approved as a new anti-VEGF agent for the treatment of nAMD based on HAWK and HARRIER, worldwide phase 3 clinical trials.[14,15] These trials proved q12/q8 week dosing intervals for intravitreal brolucizumab to be effective for improving and maintaining visual acuity for 96 weeks, results not inferior to those of a q8 week dosing interval for intravitreal aflibercept. Intravitreal brolucizumab provided better control of intraretinal, subretinal and sub-RPE fluid than intravitreal aflibercept. The result of trial indicates that brolucizumab might be the most effective approach to treating nAMD among the anti-VEGF agents approved for ophthalmic use. There are significant concerns about intraocular inflammation like retinal occlusive vasculitis, after intravitreal brolucizumab which can result in permanent loss of vision[16.] With regard to anatomic results, fewer PCV patients experienced intra-retinal (IRF) and/or sub-retinal fluid (SRF) with brolucizumab 6mg compared with aflibercept at weeks 16, 48 and 96. In addition, a greater reduction in central subfield thickness (CST) was observed with brolucizumab 6mg vs aflibercept. The overall safety profile of brolucizumab was consistent to aflibercept. Researchers concluded, "Robust BCVA gains were observed in the PCV population, across all treatment arms. Brolucizumab monotherapy works well in typical AMD and PCV patients."[17]
In our real-world retrospective cohort, the mean baseline V/A was comparatively worse at 0.81 LogMAR. Despite the fact that the current study's participants had poor baseline vision, considerable visual improvement was observed at the last visit. These visual benefits were sustained after stratification in the eyes that had been switched from other anti-VEGF medications, in contrast to the SHIFT and BREW studies, which looked at real-world data on brolucizumab after switching, and found no significant visual improvements.[18] Study of Brolucizumab in Adult Patients with Suboptimal Anatomically Controlled Neovascular Age-related Macular Degeneration (SWIFT)- started in December 2020 and will be over by September 2022. Intravitreal brolucizumab therapy is effective in both treatment-naïve patients and patients who receive the drug as switch therapy. There is a small but definite risk associated with the drug (1.9% overall in our series; 0.95% as far as vascular occlusion is concerned). Notwithstanding the small risk of untoward events, intravitreal brolucizumab therapy is a useful addition to the retinal surgeon's armamentarium and should establish itself as an effective form of primary therapy that can do well with infrequent administration. A high index of suspicion maintained both by the physician and the patient can help avert disastrous complications.[19] In a real-world scenario, brolucizumab therapy is efficacious and safe in the management of nAMD over the short term. Further long-term studies are warranted to validate these findings. Additionally, lack of ocular inflammation after 126 brolucizumab injections in our Indian data is peculiar and underlines the necessity to explore the role of race and genetics in predisposing to or safeguarding against brolucizumab-related IOIs.[20]

**CONCLUSION -** PCV is more common in Asian populations than in white populations. Based on various epidemiological, histological and genetic studies, there are similarities and differences in the pathogenesis of PCV and neovascular AMD. PCV patients are generally younger than typical neovascular AMD and PCV patients can have history of CSC, suggesting that pachychoroid changes can lead to the development of PCV. Multimodal ocular imaging like high resolution SD-OCT and OCTA imaging has increased sensitivity and specificity in diagnosing PCV without the use of ICGA. Various clinical trials have demonstrated significant visual gains and reduction in disease activity, with either using anti-VEGF monotherapy or combination therapy of anti-VEGF with vPDT with variable results due to differences in baseline ocular characteristics like choroidal thickness and choroidal vascular hyperpermeability. Loading phase treatment with intravitreal brolucizumab appeared to be effective for improving visual acuity and reducing exudative changes in eyes with nAMD associated with type 1 CNV. Moreover, polypoidal lesions appeared to frequently show regression after this treatment. However, it is essential to carefully monitor patients for brolucizumab-related IOI in order to avoid delaying the necessary steroid therapy.

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# CASE REPORT

## AFLIBERCEPT AS EFFECTIVE THERAPY IN POLYPOIDAL CHOROIDAL VASCULOPATHY (PCV)

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Introduction –

Polypoidal choroidal vasculopathy (PCV) is a clinical condition that is generally classified as a subtype of type 1 neovascular age-related macular degeneration (nAMD). Hallmarks of the disease include a characteristic branching vascular network and polypoidal choroidal vascular lesions.[1] The prevalence of PCV in newly diagnosed nAMD has been reported as approximately 23%-55% in Asian patients, which is higher than in white patients.

Aflibercept is a soluble, decoy receptor fusion protein; it consists of the binding domains of VEGF receptors 1 and 2 fused to the Fc portion of human immunoglobulin G1. This structure allows the drug to bind all isoforms of VEGF-A, VEGF-B, and placental growth factor (PlGF).[2,3] Intravitreal aflibercept injections dosed monthly or every 2 months after 3 initial monthly doses demonstrated similar therapeutic effect compared with monthly intravitreal ranibizumab injections.[4]

This case report studies the effect of aflibercept as compared to ranibizumab in a case of PCV in a real world practice.

Case Report –

A 68 year old female presented with diminution of vision in both eyes since 2 months. The best corrected visual acuity (BCVA) in right eye was 6/60 while in left eye was 6/18. On ocular examination, anterior segment findings were within normal limits while posterior segment revealed hard exudates with macular neovascularization. There was history of uneventful cataract surgery done in both eyes. Multimodal investigations were done. The patient was diagnosed as a case of PCV on the basis of characteristic spectral domain optical coherence tomography (SD OCT) and fundus photography features which revealed multiple large pigment epithelial detachment, double layer sign, exudative changes with subretinal and intraretinal fluid (figure 1). Follow-up examinations, including BCVA measurement, fundus photography, and SD OCT, were done at every monthly visit.

The patient was given loading dose of anti-vascular endothelial growth factor (VEGF) injection. Though patient was advised for intravitreal injection aflibercept to start with, patient opted for injection ranibizumab. After initial first 2 doses of injection ranibizumab, there was gradual reduction in intra retinal fluid (IRF) and sub retinal fluid (SRF) in right eye but left eye had massive sub retinal bleed (figure 2).

The BCVA in right eye improved to 6/36 but deteriorated to 1/60 in left eye. The patient then opted for intravitreal aflibercept in both eyes. There was marked reduction in SRF and IRF fluid in right eye along with gradual resolution of sub retinal hemorrhage with central scarring in left eye (figure 3). The patient was followed for the next 2 months following injection aflibercept after which further treatment with intravitreal aflibercept was advised. The BCVA also improved to 6/18 in right eye and 6/60 in left eye.

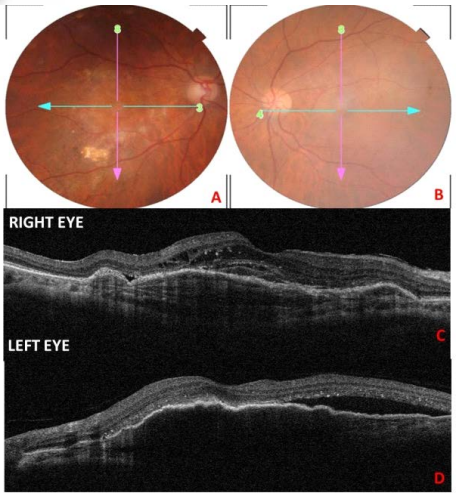


Figure 1

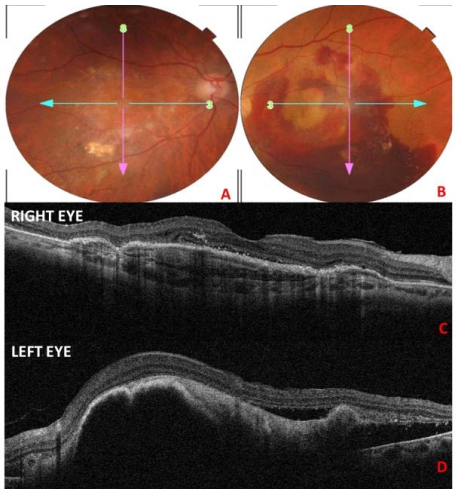


Figure 2

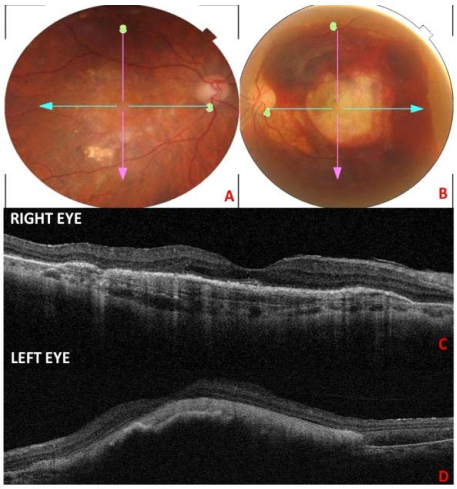


Figure 3

Figure 1 – Colour fundus photography and spectral domain optical coherence tomography (SD OCT) of right eye (A and C) and left eye (B and D) revealed multiple large pigment epithelial detachment, double layer sign, exudative changes with subretinal and intraretinal fluid.
Figure 2 - Colour fundus photography and spectral domain optical coherence tomography (SD OCT) of right eye (A and C) and left eye (B and D) revealed gradual reduction in intra retinal fluid (IRF) and sub retinal fluid (SRF) in right eye while massive sub retinal bleed in left eye after initial first 2 doses of intravitreal ranibizumab.
Figure 3 - Colour fundus photography and spectral domain optical coherence tomography (SD OCT) of right eye (A and C) and left eye (B and D) revealed marked reduction in SRF and IRF fluid in right and left eye along with gradual resolution of sub retinal hemorrhage and central scarring in left eye after intravitreal aflibercept.

## Discussion –

In the present case report, the patient with PCV developed massive sub retinal hemorrhage in left eye while on treatment with intravitreal ranibizumab. Also, the reduction in IRF and SRF in right eye was suboptimal. There was marked reduction in fluid following intravitreal aflibercept as compared to intravitreal ranibizumab in right eye along with sub retinal hemorrhage clearance in left eye in addition to improvement in visual acuity. Polypoidal lesions are one of the clinical characteristics that distinguish PCV from typical nAMD. They are thought to be the main source of exudative change, pigment epithelial detachment (PED) development, and hemorrhagic complications in PCV.[5,6] In addition, polypoidal lesions of PCV are associated with the expansion of the branching vascular network. The reason for the higher rate of polyp regression when using aflibercept is unclear. Recent reports have suggested it may be associated with the ability of aflibercept to bind not only VEGF-A, but also VEGF-B and placental growth factor (PlGF).[7,8] Regarding other differences in therapeutic effects, a recent study in nAMD patients found that choroidal thickness was more decreased after aflibercept treatment than after ranibizumab treatment.[9] In real world setting, where patients with PCV are reluctant to start with intravitreal aflibercept to start with due to lack of awareness and financial constraints and are less compliant to follow up, the chances of complications such as exudative change, PED development, and hemorrhagic complications are much more. The timely use of intravitreal aflibercept along with regular treatment can avoid these complications.

References –

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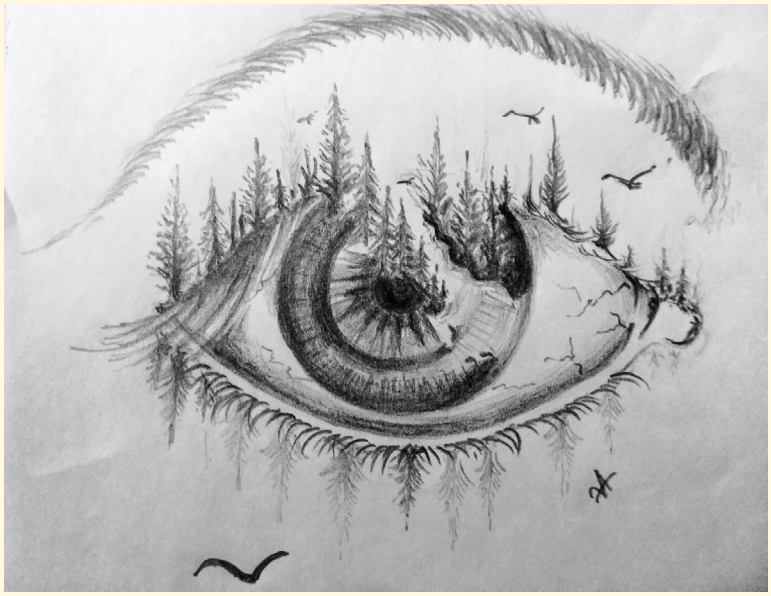
# BEYOND OPHTHALMOLOGY

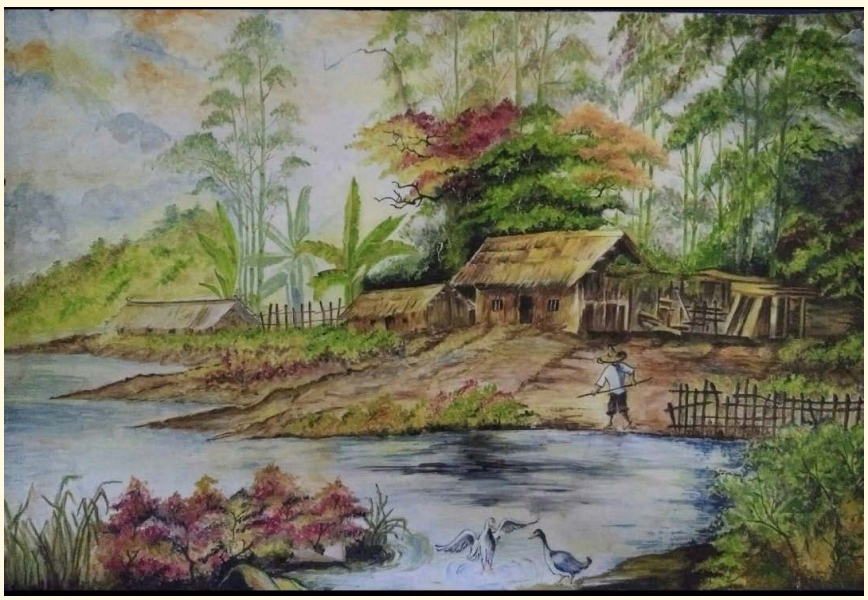
## PAINTING IS BLISSFUL

**Dr. Varsha Vaishnav**

I am Dr. Varsha Vaishnav, a practicing Ophthalmologist at Bhopal. Art and painting has been my hobby since childhood. My father, an engineer by profession and a wonderful sketcher at heart, has been my sole inspiration for nurturing my passion for painting, along with my profession. As a doctor, I am always on the clock with the appointments of my patients. However, I still try to make some free time and portray the way I see the world, through the medium of my paintings. This also helps me to relax my mind and sometimes to take some time off ,of my hectic professional schedule! Wish I continue my passion for ever...



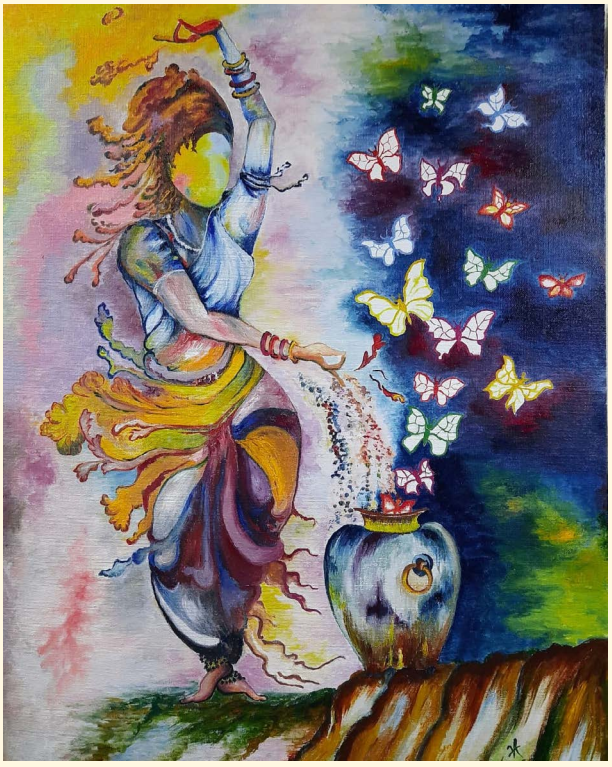
1. Eyes are an ocean in which pleasant dreams are reflected...those are seen more clear than the imagination awake...



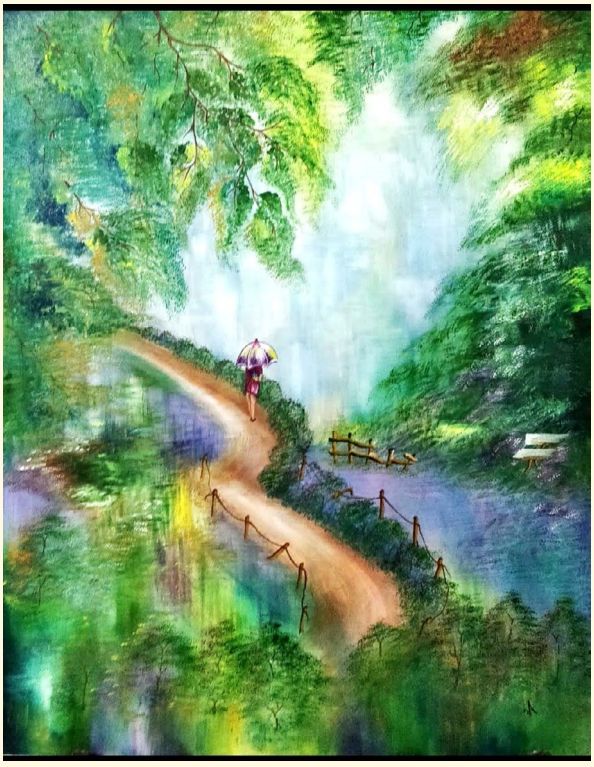
2. The country life...

3. HOPE...the essence of life...

4. Roses are my favorite to paint & if it's a first try for a knife painting, then nothing happier than that...

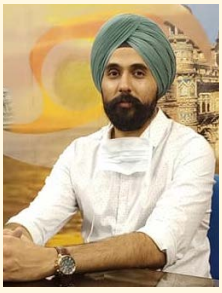


5. A colourful & cheerful life awaits, beyond the pandemic...



6. The monsoon...

# BEYOND OPHTHALMOLOGY



## CIRCLE OF LIFE

**Dr. Manbir Singh**

Nights and days, darkness and light
Joys and sorrows, are all part of life..
We all experience our share of plight,
It's how we overcome it defines our might..

Holding my baby girl for the first time was the best feeling ever,
And losing my grandpa the very next week  was something I had thought of never..
He was someone who taught me the rights and wrongs,
Somewhere inside my heart he still belongs..

On his bed he lay half awake, when I broke the news to him.
Dadaji I said, you have become a great grand father, I just had a daughter..
I showed him her picture on my phone, the happiness he felt was tangible in his slurry  tone..

Daughters are god's best gift,
As he said this I saw his face lit..
I wish he could stay with us a little more,
The only regret I have is he could not hold her close..

I sometimes see a part of him in her,
even in gurbani Sehaj and Santokh often come together..

Nothing is permanent, we all have to realise.
Birth and death, well that's the circle of life..

Manbir
21/05/2020

# BEYOND OPHTHALMOLOGY

## LIFE THROUGH MY EYES

**Dr. P. S. Bindra**

### जिदंगी यू ही गुजर गई

कुछ करने की तैयारी में, जिन्दगी गुजर गई
चांदनी रात में सपनों में खोया रहा ।

सुबह देर से उठने का मलाल करता रहा
सारे कार्यो को कल के लिये लंबित करता रहा

सोचता रहा क्या है जल्दी बहुत जीवन तो अभी बाकी है रहा
कभी आदर्श थे टैगोर, भगतसिंह और विवेकानंद ।

कभी आदर्श डाक्टर बन गावों में सेवा का मन करता रहा
कभी यह शरीर और मन धन की अंधी दौड़ में शामिल रहा ।

बचपन खेंल ,जवानी और मदहोशी और अब बुढ़ापा है कट रहा
एक टीस सी चुभती है , करना तो बहुत कुछ अभी बाकी रहा ।

कुछ करने की तैयारी में, जिंदगी गुजर गई
यही मलाल करता रहा ..... करता रहा
कुछ नया करने की तैयारी में, जिंदगी गुजर गई..... ।

### मॉ–तुम ईश्वरीय प्रतिबिंब हो

मेरी नित्य वंदना में तुम रहती हो मॉ ,
मेरी हर श्वास तुम से उधार है मॉ ।

ईश्वर को देखना सम्भव नहीं है मॉ ,
तुम्है देखकर ही छवि उसकी बनती है मॉ ।

मेरा रोम–रोम आपके पवित्र लहू से सिंचित है मॉ ,
असम्भव है, तेरे उपकारों का ऋण चुकाना मॉ ।

गीले में सो कर ,गरम बिछौना देती आई हो मॉ ,
बच्चों के पहले उद्बोधन में तुम रहती हो मॉ ।

बच्चों के बाद , अपने आप को भूला देती हो मॉ ,
निश्चल प्रेम और करूणा की मूरत हो मॉ ।

अपने सारे शौक हम पर वारती आई हो मेरी मॉ ,
तू त्याग, साहस और दैवीय शक्ति हो मॉ ।

तू मेरा दर्पण, मेरी प्रेरणा और प्रथम पाठशाला हो मॉ ,
तू नहीं आज मेरे साथ, , तेरी दुआओं के सदके जी रहा हूँ मॉ ।

मेरी वंदना , प्रार्थना और श्वासों में बसती हो मॉ ,
तुम ईश्वरीय प्रतिबिंब हो, प्रतिबिंब हो मॉ..... ।

# अपने को राहगीर समझें

आनंदमय जीवन जीने का मंत्र सभी जानना चाहते हैं।

खुशी संतुष्टता एवं शांति ही जीवन के हर कर्म का उद्वेश्य होता है।

अपने आप को जाने.....।

हमें संसार में रहना है, संसार हमारे अंदर नहीं रहना चाहिए। हर समय

सिर्फ सांसारिक ;मायावी बातों में न उलझे रहें। अपने में रहना सीखें,

अपने आप को जाने ,इस जीवन यात्रा का उद्वेश्य एवं लक्ष्य को पहचानें और प्राप्त करें।

अपने आप को गृहस्थी न समझ कर न्यासी या ट्स्टी समझें, और निवृत; होकर रहें। दुनिया के सारे दुःखों का कारण मोह ही है। मनोविकारों ,परनिंदा एवं क्रोध से निवृत; होकर रहें। अपने को मुसाफिर ;राहगीर मानें ।

जब हम किसी के अंतिम संस्कार के लिये शमशान जाते है तो अल्पकालिक वैराग्य का भाव मन में आता है जिसे शमशानी वैराग्य कहते हैं फिर उसी उहापोह ,मोह –माया ,तृष्णा में लिप्त हो जाते हैं।

सत्संग में, मंदिर में हम जब तक रहते हैं कहते हैं कि–

मेरा मुझ में किछु नही, जो किछु है सो तेरा

तेरा तुझको अर्पण , क्या लागे मेरा ।

इससे बाहर आते हैं सब मेरा –मेरा है, दूसरों का भी मेरा कैसे हो सकता है।यह शांतिर , चंचल ओर मायावी मन की सोच होती है।

जीवन क्षणभंगुर है, पानी का बुलबुला है। अपने आप को साक्षी मानो,

कर्ता नहीं। करन करावन हार की इच्छा सर्वोपरि एवं अटल है। मैं इस देह से न्यारा हूँ में न्यासी या ट्स्टी की नाई कार्यरत हूँ और रहूंगा।

अपने को रंगमंच का एक कलाकार मान कर जीवन जीयें। अपने श्रेष्टतम अभिनय को अपने जीवन का लक्ष्य माने । उसमें लीन हो जायें और जीवंत करे–यहीं एक राहगीर की भांति जीना होगा।

ऐसा कहा जाता है कि खाली दिमाग शैतान का घर, इस लिये व्यस्त रहें। रचनात्मक एवं सकारात्मक कर्म करें। मान–अभिमान ,हानि–लाभ ,निंदा –स्तुति से परे रहो। अपना उच्च स्थान ध्रुव की तरह ग्रहण करें। आप सारी पूजा, अर्चना ,सतकर्मो का परिणाम क्या चाहते हैं–? मोक्ष ही न.....।

जब आप मोह से परे होकर ,निमित्त बनकर ,साक्षी बनकर जीते है तो जीते –जी मोक्ष प्राप्त करने का आंनद उठा सकते हैं।

याद रखें आप राहगीर हैं.....इस से ज्यादा कुछ भी नही..... ।

# BDOS SCIENTIFIC ACTIVITIES

1st November 2020


WEBINAR ON NEUROPHTHALMOLOGY

1st November 2020

WEBINAR ON NEUROPHTHALMOLOGY

22nd November 2020


INTERNATIONAL MEN'S DAY CELEBRATION

22nd November 2020

## JUDGES (UMPIRES)

DR LALIT VERMA
DR HARBANSH LAL
DR SUBASH DADEYA
DR SALIL KUMAR
DR PRAMOD CHANDRA
DR YK VINAYAK
DR GM LALE







## COMMENTATOR

Dr Lalit Shrivastava (President BDOS )
Dr Vinita Ramnani (Secretary BDOS)
Dr Chahveer Singh Bindra (Clinical Secretary BDOS)



## Cheerleaders – audience participation

## YELLOW TEAM - CORNEA

- DR V K NICHLANI
- DR AMIT SRIVASTAVA
- DR PRATEEK GUJAR
- DR PAWAN CHAURASIA
- DR FAROOK AMAN
- DR SANDEEP PACHOLE

CAPTAIN YELLOW TEAM- CORNEA
DR V K NICHLANI

TEAM MEMBERS YELLOW TEAM

## GREEN OR CATARACT TEAM

DR R K GUPTA
DR SURAJ KUBREY
DR ASHISH ATHALEY
DR GANESH PILLAY
DR JITENDRA MANGHNANI
DR FAZIL KHURRUM

CAPTAIN GREEN TEAM- CATARACT
DR R K GUPTA

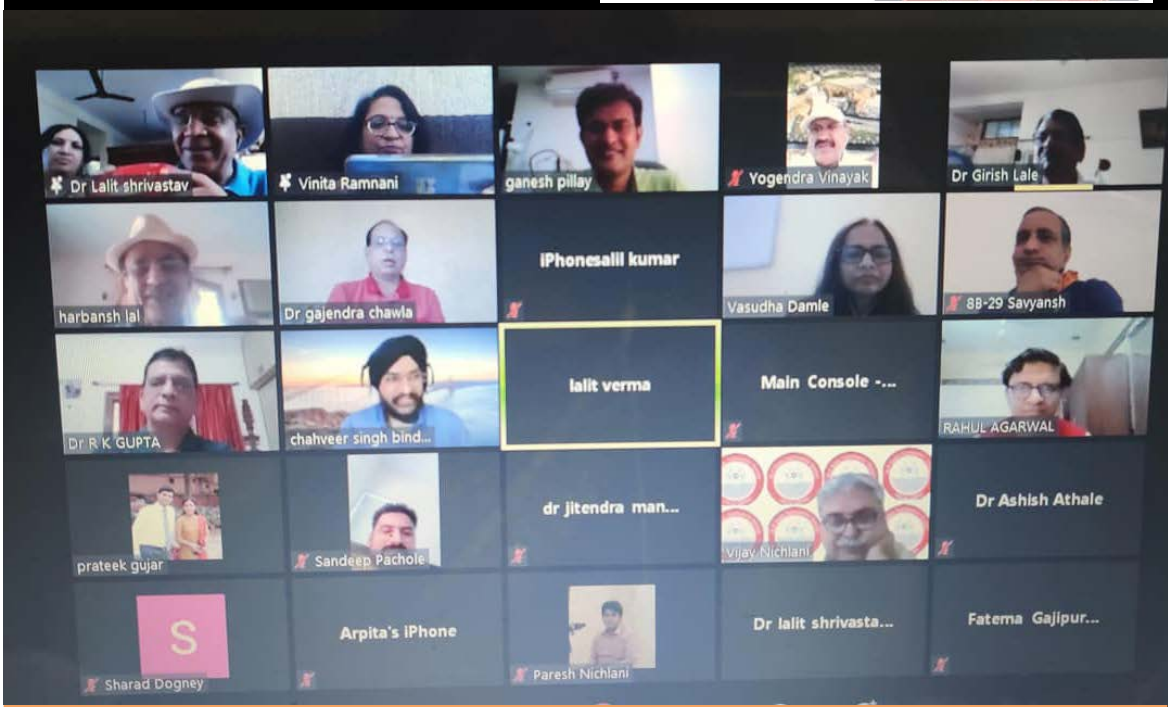
TEAM MEMBERS GREEN COLOUR

## RED OR RETINA TEAM

DR GAJENDRA CHAWLA
DR VINEET GAUR
DR RAHUL AGRAWAL
DR SHARAD DOGNEY
DR SARFARAZ KHAN
DR PARESH NICHLANI

CAPTAIN RED TEAM
DR GAJENDRA CHAWLA

TEAM MEMBERS RED TEAM



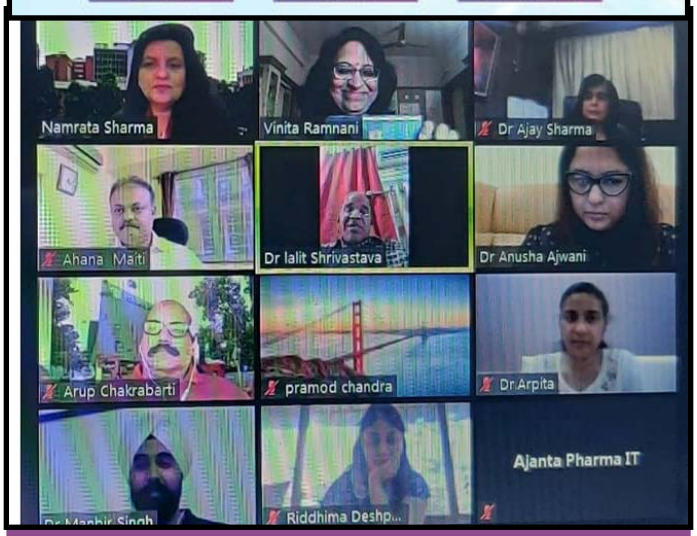

INTERNATIONAL MEN'S DAY CELEBRATION

## 10th January 2021



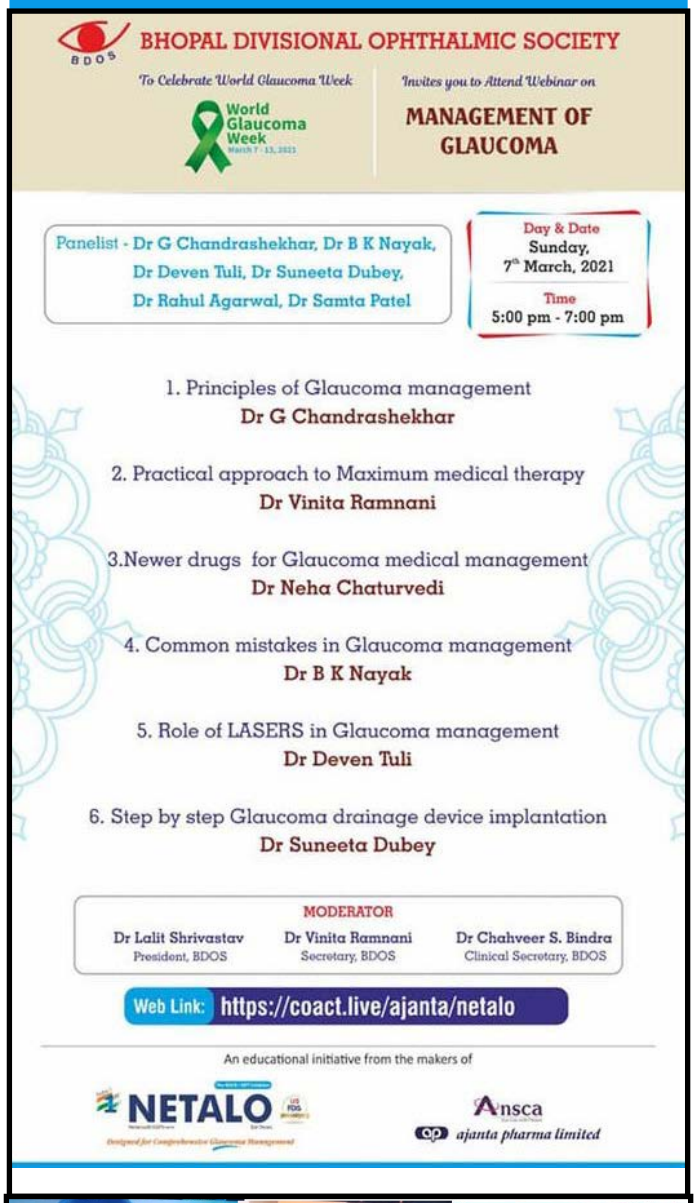

WEBINAR ON PEADIATRIC OPHTHALMOLOGY

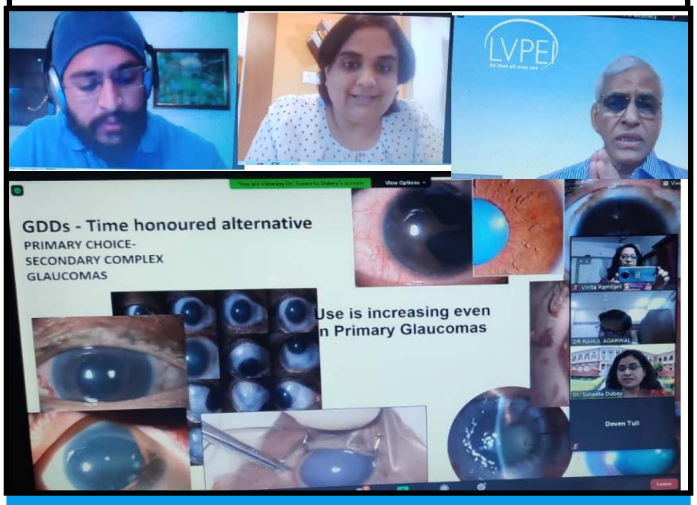
## 21st February 2021


WEBINAR ON NEWER DRUGS IN OPHTHALMOLOGY

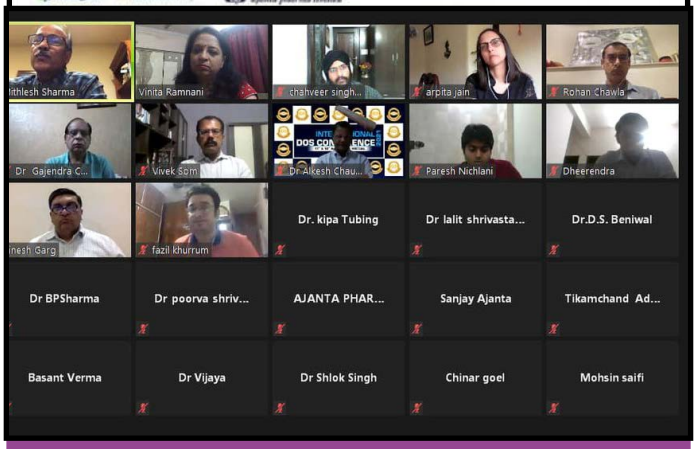
## 7th March 2021



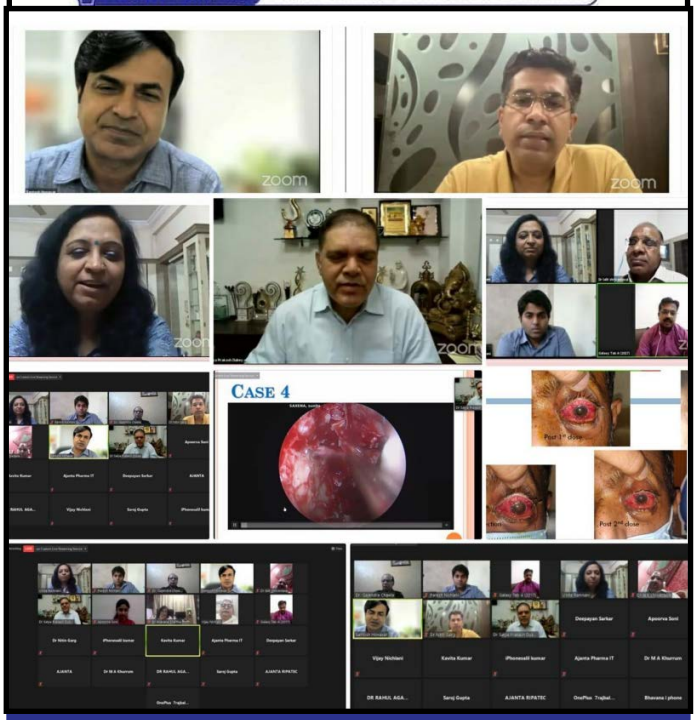

WEBINAR ON MANAGEMENT OF GLAUCOMA

## 18th April 2021

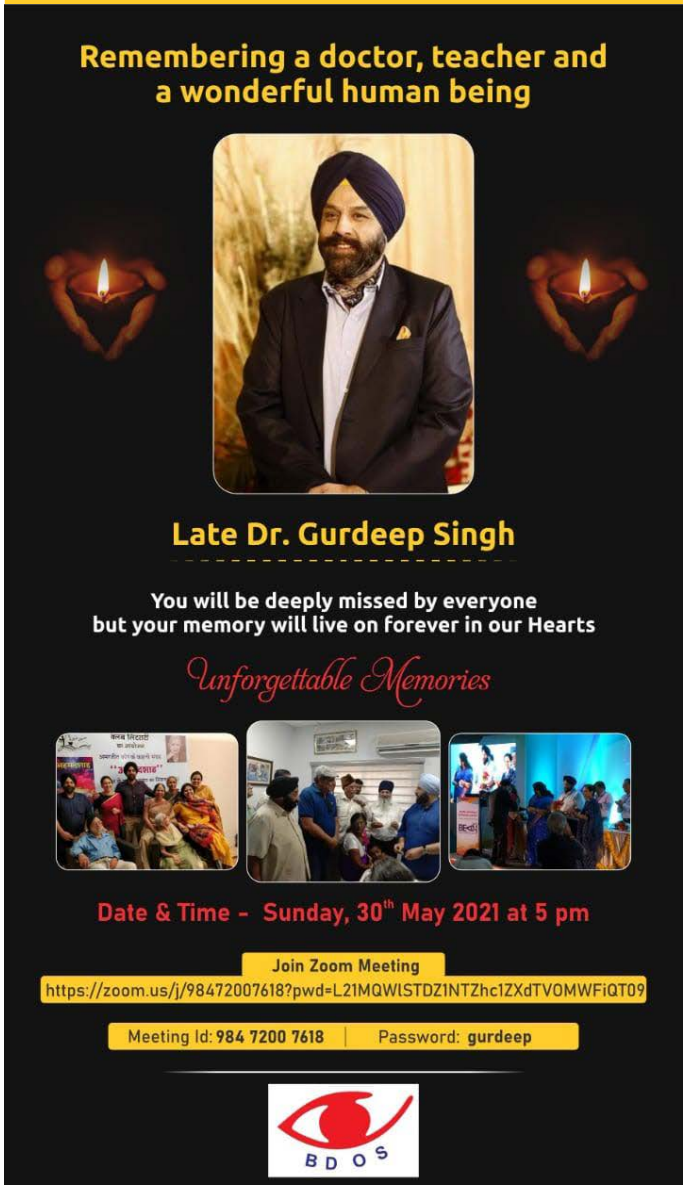

WEBINAR ON RETINA FOR GENERAL OPHTHALMOLOGIST'S

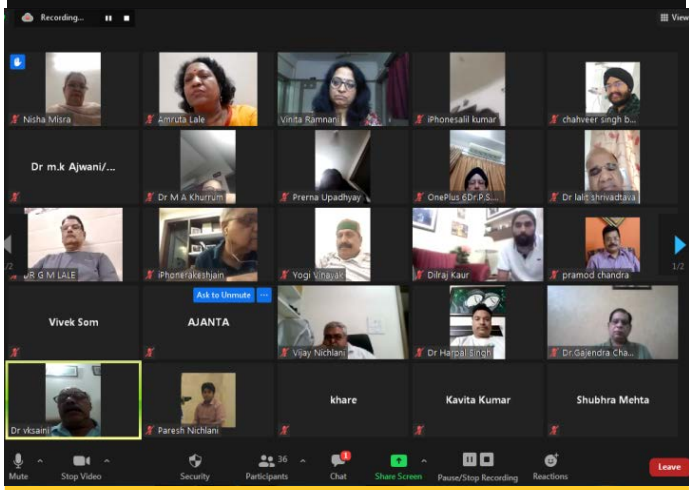
## 16th May 2021


WEBINAR ON MUCOR MYCOSIS

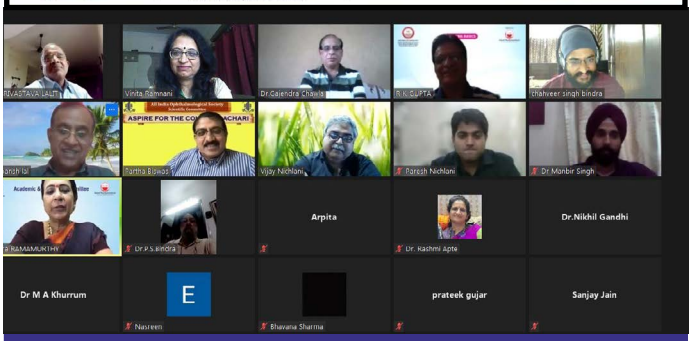
## 30th May 2021




CONDOLENCES MEETING FOR LATE DR. GURDEEP SINGH

## 25th July 2021


WEBINAR ON CATARACT

## 21st October 2021

COVID PPE KIT DISTRIBUTION AT GMC

## BDOS EXECUTIVE BODY MEETINGS

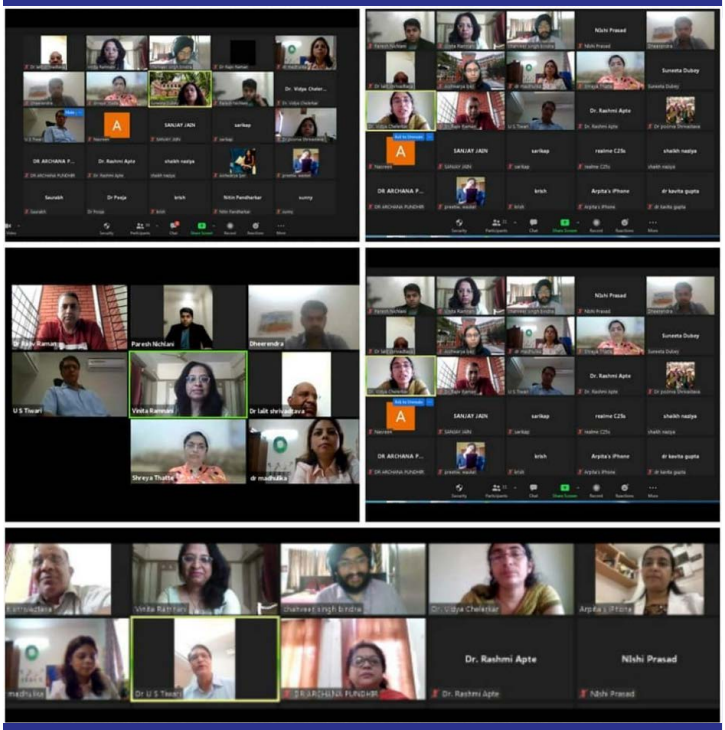
| | |
|---|---|
| 4th Virtual Meeting | 29th Nov 2020 |
| 5th Physical Meeting | 28th Feb 2021 |
| 6th Physical Meeting | 14th Aug 2021 |
| 7th Physical Meeting | 20th Nov 2021 |

BDOS EXECUTIVE BODY MEETINGS

## 10th October 2021


WORLD SIGHT DAY 2021 WEBINAR

## 10th October 2021




WORLD SIGHT DAY 2021 WEBINAR

## CONGRATULATIONS!

**(PPP)- Poster Podium Presentation**

1. Dr Nishi Prasad  2. Dr. Rashmi Apte

**Best Slogan**

1. Dr. Pooja Maravi  2. Dr. Khalid Khan

WINNERS - WORLD SIGHT DAY


• **Dr Salil Kumar r**eceived AIOS Honorary FAICO Award in Community Medicine/ Peadiatric Ophthalmology – first in MP

• **Dr Kavita Kumar & Dr Lalit Shrivastava** were honored by the Chief Minister of Madhya Pradesh on Doctor's day.

• **Dr Prerna Upadhaya** was awarded President's Appreciation Gold Plaque in 12th Annual conference of ACOIN 2020, Best paper award on Low vision in MP-SOS 2019 and Lifetime achievement award 2020 by NSPB MP branch.

• **Dr Vinita Ramnani** - Dr JK Raizada award for cataract in MPSOS 2019.

• **Dr Bhavana Sharma** – AIOS Scientific Committee Achievement Award 2021- IJO Honor Award for Peer Review for 2020.

• **Dr Aditi Dubey-** Best teacher award in 2019 MPSOS.

# Losing great souls

**Dr. Gurdeep Singh**
Professor and Senior eye surgeon of Bhopal

**Dr. P. S. Soan**
Retd. Director Health Services and ophthalmologist

**Dr. H.K. Verma**
Ophthalmologist of Vidisha civil surgeon and CMHO

**Dr. N.P. Singh**
Teachers of teachers

**Dr. R. K. Agrawal**
Eye surgeon Biora

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*Data on File


1. Diabetic Care 2012 10.2337/dc11-1909 2. Diabetes Research & Clinical Practice 94:2011;311-321
3. Investigative Ophthalmology & Visual Science, March 2007, Vol.48 No.3 Population Reference BureauToday's Research on Aging; No 25; March 2012
4. Retina 2013 Jan; 33(1):152-9 5. Ophthalmology February 2010; 117(2):313-9.e 1.


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