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جمعية أطباء العيون العراقية

The Higher Council for Scientific Societies

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Editor's Note

Before you is the first issue of the Uyoon (Eyes) bulletin, published after a hiatus of more than a quarter of a century. Its revival has been driven by distinguished Iraqi determination and resolve, to make it a scientific and professional outlet for ophthalmologists and a source for keeping abreast of the latest research, trials, innovations, and scientific studies in ophthalmology, both in Iraq and around the world. The bulletin will also provide access to a range of professional news and educational publications directed at the general public and at other medical and public health specialties.

The bulletin's pages are open to contributions from all fellow ophthalmologists, both within Iraq and abroad. The editorial board will select the material most suitable and appropriate for publication, in keeping with the bulletin's core editorial direction.

We always look forward to receiving your contributions in service of ophthalmology, as both a science and a profession.

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المجلس الأعلى للجمعيات العلمية

جمعية علمية مؤسسة بموجب قانون الجمعيات العلمية رقم 55 لسنة 1981 المعدَّل، بموجب الأمر الوزاري المرقم ب ت 2/5084 الصادر عن وزارة التعليم العالي والبحث العلمي، وتتمتع بشخصية معنوية مستقلة.

كلمة العدد

بين أيديكم العدد الأول من نشرة (عيون) التي تصدر بعد توقُّف دام أكثر من ربع قرن، وبعد أن تم إحياء صدورها بهمة وإصرار عراقي مميز، لتكون متنفَّساً علمياً ومهنياً لطبيب العيون، ورافداً للاطلاع على أحدث ما وصل إليه طب العيون من بحوث وتجارب وابتكارات ودراسات علمية تخص طب العيون في العراق والعالم أجمع، كما ستتيح الاطلاع على الأخبار المهنية المختلفة والنشرات التثقيفية الموجهة لعموم المجتمع وباقي تخصصات مهنة الطب والصحة العامة.

أبواب النشرة مفتوحة لاستقبال ما يردها من مشاركات من كافة الزملاء أطباء العيون في داخل العراق وخارجه، حيث ستقوم هيئة التحرير باختيار المناسب والملائم للنشر، ووفق توجهات النشرة الأساسية.

نتطلع دائماً إلى استلام مساهماتكم بما يخدم طب العيون علماً ومهنة.

د. حمزة الماجدي

From the past to the future

Dr. Nada Al-Jasem, MDS · Jordan

IOS member in Ur, Sumar, Mesopotamia/ Nasiriyah, Iraq

Mesopotamia, Sumar, 3600 BCE

Sumar is the cradle of civilization, it's the first known civilization on earth

One of the discoveries was the earliest recorded ocular biomarkers of internal diseases found on cuneiform tablets representing diagnostic medical texts. They considered the eye is a mirror for inner health. For example, Sumerian recognized yellowing of the eyes to be secondary to something reside in the liver and put prescription of herbs and animal parts to heal the body and soul.

Oculomics

Is an emerging scientific field that uses eye imaging with the help of artificial intelligence to detect diseases elsewhere in the body. Like analysing fundus photos for microscopic changes in the retina, to diagnose cardiovascular disease, diabetes, Alzheimer's, and Parkinson's long before traditional symptoms appear.

Through the Digital Lens: Artificial Intelligence in Ophthalmology — A Practical Path Forward for the Middle East

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Ophthalmology is at the forefront of artificial intelligence (AI) in medicine. As an imaging-intensive specialty with well-defined clinical endpoints, it has become the proving ground for deep learning algorithms that can match and sometimes exceed expert human performance in pattern recognition tasks.[1] The volume and standardization of ophthalmic data make the specialty uniquely suited for AI integration, making it an ideal lens for examining AI's clinical value.

For ophthalmologists practicing in the Middle East, this technological revolution could potentially change the practice of ophthalmology. The region bears one of the highest burdens of diabetes worldwide, with age-standardized prevalence rates exceeding 10% in eleven countries. Iraq has the highest age-standardized diabetes prevalence in the region at 15.3% (95% uncertainty interval [UI] 14.3–16.2), followed closely by Kuwait (15.2%), Qatar (15.1%), and Bahrain (15.0%). Moreover, the projected increase in type 2 diabetes prevalence in North Africa and the Middle East, an estimated 82.7% rise by 2050, is the highest of any global super-region,[2] and the International Diabetes Federation (IDF) Diabetes Atlas confirms the Middle East and North Africa (MENA) region has the highest regional diabetes prevalence at 17.6%, with the number of people affected projected to rise by 92% by 2050.[3] In Iraq specifically, the age-standardized incidence of diabetes and kidney diseases increased by 42.9% between 2003 and 2021, the largest increase among all non-communicable disease categories in the country.[4] Compounding this, a nationally representative survey found that 8.1% of Iraqi adults have undiagnosed type 2 diabetes and almost 8.9% have diagnosed disease, meaning almost half of all diabetes in Iraq is undetected.[5]

Diabetic retinopathy (DR) prevalence in the Eastern Mediterranean Region is approximately 31%.[6] Middle Eastern individuals with diabetes carry 2.4-fold higher odds of DR compared with Asian populations.[7] In Arab countries, the prevalence of blindness and severe visual impairment also exceeds global averages.[8] Taken together, these figures demand scalable, efficient screening solutions, precisely the kind AI is designed to deliver.

AI in Clinical Patient Care: The Promise

The most mature clinical application of AI in ophthalmology is autonomous DR screening. Three AI platforms have received U.S. Food and Drug Administration (FDA) authorization: AEYE-DS (AEYE Health), EyeArt (Eyenuk), and Luminetics Core (formerly IDx-DR, Digital Diagnostics), each supported by prospective multicenter clinical trials. In addition, the American Diabetes

Association now recognizes these AI systems as an alternative to traditional screening for detecting more than mild DR and diabetic macular edema (DME).[9] Real-world deployment has demonstrated robust performance, with one study reporting an area under the curve of 96.5%, sensitivity of 88.9%, and specificity of 98.7% for detecting referable DR.[10] AI-based screening has also been shown to increase patient compliance with ophthalmic follow-up from 18.7% to 55.4% in primary care settings.[11] The Eyenai AI DR screening program has been indigenously developed in Saudi Arabia and holds promise for deployment in the Middle East.[12]

Beyond DR, deep learning systems have achieved strong classification performance in detecting glaucoma, age-related macular degeneration (AMD), retinopathy of prematurity (ROP), and cardiovascular risk factors from retinal imaging.[1] In parallel, optical coherence tomography (OCT)-based AI algorithms are increasingly used to monitor progression and assess treatment response in neovascular AMD and DME. FDA-authorized home OCT platforms are now enabling remote monitoring of retinal fluid in patients with AMD.[13]

The integration of AI with teleophthalmology is especially relevant for the Middle East, where geographic distances and specialist shortages in rural areas create barriers to care.[14] AI-powered screening deployed in primary care clinics, compatible with non-mydriatic cameras and smartphone-based devices, can extend ophthalmic expertise to underserved communities.

AI in Clinical Patient Care: The Limitations

Despite these advances, major challenges temper enthusiasm. The “black-box” problem is the inability to fully explain how a deep learning algorithm arrives at its output, and it remains a fundamental barrier to clinical trust. Data bias is a major concern: most AI algorithms have been trained predominantly on North American, European, and East Asian populations, and the lack of Middle Eastern populations calls into question generalizability and equity. Moreover, AI-generated inaccuracies create risks when systems are used without adequate human monitoring. Medicolegal liability for AI-driven diagnostic errors remains poorly defined in most jurisdictions, including those in the Middle East.[1]

Practical barriers also persist, including reliable internet connectivity, integration with electronic health records, data privacy protections, and implementation costs.[14] In addition, the workforce must be prepared to critically interpret and contextualize AI outputs.

AI in Ophthalmic Research

AI is transforming ophthalmic research across the translational spectrum. In clinical trials, machine learning algorithms improve patient recruitment, automate information management, and standardize outcome assessment. In drug discovery, AI accelerates target identification, lead compound optimization, and prediction of pharmacokinetics and toxicity. At the same time, foundation models developed on large-scale retinal imaging datasets are supporting scalable phenotyping and biomarker discovery.[13]

For Middle Eastern researchers, including those in Iraq, AI offers an opportunity to leverage the region's large diabetic populations and rich imaging datasets to contribute meaningfully to global ophthalmic science. Iraq's exceptionally high diabetes prevalence and large population of unscreened individuals represent a unique research resource[2][3], though data-sharing regulations may prevent global collaboration.[14]

AI in Ophthalmic Education and Training

AI is changing ophthalmology training. Deep learning models can deliver personalized, case-based learning by classifying incoming clinical cases and assigning them to the resident who would benefit most from them. In addition, AI-based teaching systems have been shown to significantly improve resident progress compared with traditional lectures alone.[15] In surgical training, computer vision and sensor-based technologies provide objective feedback on microsurgical skills, while AI-enabled virtual reality simulators support standardized operative habits. Large language models are being investigated for knowledge assessment, educational content generation, and patient education.[15]

However, documented risks include "deskilling" or the erosion of clinical competencies when trainees rely excessively on automated platforms and automation bias, where clinicians uncritically accept AI outputs. In this context, ophthalmology-specific competency frameworks that account for AI are still underdeveloped.[15]

When to Use AI: A Practical Model

AI is most accurately described as a decision-support tool rather than a replacement for clinical judgment, and current evidence supports its use most strongly in four settings. It is most valuable for screening, where autonomous AI can perform DR screening in primary care and community settings in which specialist access is limited and patient volume is high.[9] It is similarly useful for triage, helping to rank urgent referrals from OCT and fundus images. In monitoring, AI-powered analysis of serial OCT images can track disease progression or treatment response, increasingly through home-based platforms.[13] Finally, it strengthens quality assurance by serving as a "second reader" that reduces missed diagnoses in high-volume settings.[11]

AI should not currently be used as the sole basis for management decisions. Human review is still essential, and every AI-generated output should be interpreted in the full clinical context.[1]

Regional Considerations for the Middle East

The Middle East's unique position allows it to benefit from and shape the future of AI in ophthalmology. The region's high diabetes burden creates both an urgent need and a large-scale testing ground for AI-driven screening programs.[2][3] In addition, several Gulf states have invested heavily in digital health, creating an environment conducive to rapid adoption.

Data sovereignty and privacy regulations vary across Middle Eastern countries and must be harmonized to enable cross-border collaboration and algorithm validation.[14] In turn, training datasets must be diversified to include Middle Eastern populations to ensure the algorithm performs equitably. Ethical models should incorporate regional values, including Islamic bioethical considerations on patient autonomy and data stewardship.[1]

A collaborative, multi-stakeholder approach involving ophthalmologists, AI developers, regulators, ethicists, and decision-makers will be essential to realizing the complete potential of AI while preventing its risks.

Conclusion

AI in ophthalmology is no longer a future prospect; it is an existing reality. FDA-approved screening systems are in clinical use, AI-powered monitoring platforms are entering patients' homes, and machine learning is accelerating research and redefining education. For ophthalmologists in the Middle East, particularly in Iraq, where the burden of diabetes is the highest in the region, AI delivers a powerful tool to extend the reach and quality of eye care, strengthening the need for regional adoption.

Yet the technology is not free of peril. Bias, opacity, medicolegal uncertainty, and the risk of deskilling demand vigilance. The way forward calls for not blind adoption but thoughtful integration, guided by robust evidence, ethical reflection, and a lasting commitment to the patients we serve. For the Middle East, the central question is not whether AI will shape ophthalmology, but how to shape it responsibly. The digital lens can sharpen our vision, but it must never replace the clinical eye.

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Therapeutic Algorithms for Glaucoma in the Twenty-First Century: From a Single Drop to a Lifelong Strategy

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Glaucoma remains the leading cause of irreversible blindness worldwide, and the scale of the problem is growing. An estimated 76 million people were affected in 2020, a figure projected to reach 112 million by 2040, with primary open-angle glaucoma accounting for roughly three-quarters of cases.1 As our populations age, every ophthalmology service including those across Iraq and the wider region will manage a steadily rising burden of this silent, progressive optic neuropathy. The central question for the clinician is therefore not merely whether to treat, but how to treat well. Are we approaching our patients adequately, or are we over-treating some, under-treating others, and reaching too quickly for interventions that do not fit the eye in front of us?

Reducing intraocular pressure (IOP) remains the only intervention proven by randomised controlled trials to slow glaucomatous progression, and the relationship is robust across the disease continuum described by Weinreb and colleagues, from undetectable retinal nerve fibre layer change to established field loss.2,3 The landmark trials, the AGIS, CNTGS, EMGT and related studies converge on a consistent message: lower pressure preserves visual function, and the magnitude and stability of that reduction matter.3 This evidence base underpins the concept of a target IOP, a pressure judged low enough to halt progression for a given eye, set individually according to the stage of damage, the rate of change, life expectancy and risk factors such as pseudoexfoliation, advanced age and a positive family history.4 The target is not a fixed number but a working hypothesis to be revised as the disease declares itself.

If the goal is clear, the path to it should be equally disciplined. The therapeutic algorithm of the twenty-first century is best understood as a stepwise escalation in which each rung is chosen for efficacy, safety and the preservation of ocular tissue. The first rung is conventionally topical medical therapy, and here the European Glaucoma Society guidelines remain a sound framework for choosing an agent, prioritising monotherapy and respecting quality of life and cost alongside efficacy.4 Yet the limitations of drops deserve far more candour than they usually receive. Non-adherence is the rule rather than the exception: roughly half of patients fail to comply even with a single medication, and adherence falls further with each additional bottle.5 Persistence over two years is disappointing, and the practical act of instillation defeats a substantial minority of patients, who miss the eye, contaminate the tip, or instil a drop onto the cheek or nose.6,7 Pharmacological detail compounds the problem; an inadequate interval between successive drops produces a washout effect that blunts efficacy, and the time between administration and pressure reduction is real and measurable.8,9 The lesson is uncomfortable but important:

a prescription is not a treatment. The full pharmacology of our medications, and patient education in how to use them, are as decisive as the choice of molecule itself.

These shortcomings have moved selective laser trabeculoplasty (SLT) from a late salvage option to a legitimate first-line intervention. Head-to-head data show comparable pressure reduction between laser and medication, but with fewer subsequent treatment changes in the laser arm, and SLT can be performed safely and effectively even by trainees, with the strongest predictor of success being a high baseline pressure.10,11 Offering laser early sidesteps the adherence problem entirely for a meaningful period and spares the ocular surface the cumulative insult of preservatives, an argument for placing SLT firmly at the foot of the algorithm rather than reserving it for failure.

When pressure remains inadequate, or when fluctuation and other risk factors drive progression despite apparently acceptable readings, surgery enters the algorithm. The most important conceptual shift of the past two decades is that surgery is no longer a single decision between trabeculectomy and a drainage tube. It is a graded continuum. Angular, ab interno procedures that target the trabecular meshwork and Schlemm's canal, among them goniotomy with dual-blade devices, trabecular micro-bypass stents, gonioscopy-assisted transluminal trabeculotomy (GATT) and related techniques, often combined with phacoemulsification, share a consistent profile: an IOP reduction in the order of 30–40%, a roughly 75% reduction in medication burden, and durable control in approximately 70% of patients at three to five years.12 For early-to-moderate disease, these tissue-sparing operations can defer or avoid bleb-based surgery altogether. Beyond the angle lie the subconjunctival microstent procedures and non-penetrating options such as deep sclerectomy, and beyond these the traditional filtering operations and aqueous drainage devices.

For advanced disease, or when angular and minimally invasive approaches are exhausted, trabeculectomy and tubes retain their central role, and the comparison between them is now well characterised. Long-term data show that drainage tubes carry a substantially lower five-year reintervention rate than trabeculectomy, an important consideration when planning a strategy that may span decades.13 Cyclodestructive procedures transscleral and micropulse cyclophotocoagulation, endoscopic cyclophotocoagulation and ultrasound cycloplasty, complete the armamentarium for refractory eyes. The clinician's task is to match the rung to the eye, not to apply a favourite operation universally.

Three principles emerge from this algorithm and deserve emphasis for everyday practice. First, the prevailing tendency is to err on the side of caution by over-treating, escalating medication when the more rational step is to question adherence, technique and the true target pressure. Second, correct instruction in the use of drops and a full command of glaucoma pharmacology are not optional refinements but the foundation of medical therapy; without them, even the best molecule fails. Third, and most consequential for surgical planning, glaucoma is a lifelong

disease, and most patients will require more than one procedure over their lifetime. Every intervention should therefore preserve tissue, conjunctiva, sclera and the angle as far as possible, keeping future options open. There is no single operation that suits all cases, and the search for one is misguided.

For the Iraqi ophthalmologist, these messages translate into a practical, resource-aware strategy: set an individualised target IOP, treat the patient and not only the pressure number, consider laser and tissue-sparing angular surgery early, and plan each step with the next one in mind. The algorithms of the twenty-first century are less about novel hardware than about sequencing our existing tools wisely, preserving what we cannot replace, and remembering that the most sophisticated device cannot compensate for a drop that never reaches the eye.

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Guiding points to incorporate Selective Laser Trabeculoplasty (SLT) into your practice

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SLT is a quick, non-destructive, safe, office-based laser therapy for open-angle glaucoma (OAG), it got the FDA approval in 2001, gained popularity during the last decay, European glaucoma society guideline 6th edition recommends using SLT as initial glaucoma treatment, as an add on to glaucoma medications or replacement treatment,[1] and the latest SLT clinical trial LiGHT had been added to their landmark trails, that guides glaucoma management.[2]

Reported success rate might reach to 90%, with high survival rate for many years, and due to high safety profile, we can repeat the procedure as needed.[3]

SLT is effective in POAG, Pseudo exfoliation glaucoma (PXFG), Pigment dispersion syndrome, Primary angle closure glaucoma with open angle in at least 180° following successful peripheral iridotomy, as well as in steroid induced glaucoma, and even following previously failed trabeculectomy. [4,5]

SLT is not suitable for Neovascular and Congenital glaucoma treatment, where IOP cannot be reduced by trabecular meshwork (TM) outflow modification, although successful cases have been reported in paediatric cases of OAG with normal angles.[6] same for Juvenil open angle glaucoma, SLT is effective only in cases with no signs of angle dysgenesis on gonioscopic examination.[7]

SLT machine utilizes a Q-switched Nd:YAG laser that operates at a wavelength of 532 nm. It delivers very low, specific energy bursts (typically 3-nanosecond pulses) to the pigmented cells in the TM, changing its composition through mild inflammatory reaction, making it more water permeable, thus clearing more water from AC (anterior chamber) and reducing IOP.

Your first patient to practice SLT, better to have widely open angle, so may be choose myopic with POAG, early PXFG, or pseudophakic eyes. Before proceeding for SLT, always perform a meticulous gonioscopic evaluation of the angle to confirm TM visibility, check for synechiae, check patients' tolerance to the procedure & your abilities to identify angle structures easily.

Better to have mildly pigmented angle for easier identification of angle landmarks, but do not choose heavily pigmented angle for your first cases, as you might mistake Sampaolesi's line for pigmented TM, as in PXFG & pigment dispersion.

If you want SLT as replacement therapy, you can washout drops prior; asking the patient to stop drops for an appropriate period before SLT, or you can stop medications after performing SLT, both protocols will give the same end result, it depends only if you want to keep patient on his

glaucoma drops for few weeks after SLT because patient cannot come for close monitoring, especially with advanced cupping and or very high IOP.

On the day of procedure;

- Check IOP, give the patient stat of an alpha-2 adrenergic drops (like Apraclonidine 0.5% eye drops) half an hour prior, to prevents post SLT IOP spike
- Sit the patient and yourself comfortably on the machine.
- After applying topical anaesthesia, with Latina lens, clearly visualise the angle & TM, start with 0.7 mj/shot, aiming at the pigmented TM, if too much bubbles resulted, then get the energy down, if no bubbles, then go up, titrate until you can see only fine bubbles, and in 60% of the shots
- Aim to cover 180-360° of a normal angle with 70-100 shots, and a maximum of 270° degrees in advanced glaucoma and hyperpigmented angle, to prevent post SLT IOP spike
- Check IOP 1 hour after the procedure, before sending the patient home. If IOP was high , then add some glaucoma medications, IOP spike stabilizes in few hours to days.
- Advise the patient to use heavy lubrication for the next few hours
- Steroid and anti- inflammatory use after SLT is debatable; SALT Trial:[8] advised short-term use of NSAID or steroid drops may improve IOP reduction after SLT. Our trial resulted in the same outcome when using steroid vs only Lubrication.[9]

Post SLT protocol should depend on physician preference and patient compliance, we don't want POAG patient to continue using steroid for long period.

- Next follow up depends on; starting IOP, level of glaucoma damage, and if patient kept off glaucoma medications or not.
- IOP expected to start dropping 1 week, until 4 months after SLT, so, wait for at least 4 months before deciding to repeat SLT, if response was suboptimal.
- Keep monitoring IOP & disc function, as you do with any glaucoma patients on medications, you can repeat SLT when effect wears off.

Reported complications;

- Transient IOP spike; reported rate is around 5%. patients with pigmentary glaucoma are at higher risk
- Transient, self-limited anterior uveitis; usually occurs 2–3 days following SLT in 83% of treated eyes.
- Sporadic reports;
- 1 report of a patient with iritis developed transient choroidal effusion post SLT.
- 2 cases developed hyphema, which spontaneously resolved without sequelae.
- Few reports of mild CME or worsening of DME following SLT

- Foveal burns reported after using SLT setting for YAG capsulotomy, so be extra careful when using combo SLT/ YAG machine, and double check the mode before starting any procedure.
- Corneal endothelial changes within 1–2 hours after SLT have been noted. These changes were clinically insignificant and reversible, and there was no change in endothelial cell count or visual acuity.
- The incidence of corneal edema after SLT is 0.8%, and returned to baseline at 1 month.
- Bilateral anterior uveitis has been reported in a patient underwent unilateral SLT 3 weeks prior, this supports the theory that SLT may have a systemic response, as SLT has been reported to lower IOP in the contralateral eye [10]

Most of the complication reported are mild and resolved spontaneously, which make SLT safe procedure.

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The Enduring Tube: Why Aqueous Shunts Still Matter in a MIGS World

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Not long ago I watched a younger colleague hesitate over a neovascular eye with a pressure in the forties. He had done dozens of stents. He had never placed a tube on his own. That hesitation, more than any argument about outflow physiology, is what worries me about the moment our field is in.

MIGS deserves the attention it gets. For the patient with mild or moderate open-angle disease who is already coming in for cataract surgery, an angle procedure lowers pressure, cuts drops, and does it without the drama of a bleb.1 I do these operations and I am glad we have them. Nothing here is nostalgia for the days when trabeculectomy was the answer to a pressure of 24.

But look at where that evidence comes from. Most of it is built on eyes with decent conventional outflow, a target in the high teens, and room to fail safely. The eyes I lose sleep over are not those eyes. Neovascular glaucoma. Uveitic eyes that flare the moment you look at them. The patient back after a failed trabeculectomy with a conjunctiva like cardboard. Advanced developmental glaucoma in a young child. For these, shaving a few points off the pressure and dropping one bottle is not a success. It buys a few months before the next operation. This is where the tube has always lived, and MIGS has not changed that.

It is worth remembering how much we actually know about tubes. The Tube Versus Trabeculectomy study followed eyes with prior surgery for years and showed that tubes held up, with fewer reoperations than trabeculectomy.2 The Primary Tube Versus Trabeculectomy study asked the harder question, about eyes that had never been operated on, and tubes did well there too, even if trabeculectomy still reached the lowest pressures.3 Add the Ahmed and Baerveldt comparisons and you have something the stent literature mostly still lacks: five-year randomized data on the devices themselves.4,5 When a device is three years old and the longest follow-up is eighteen months, I read the enthusiasm around it a little differently than I read a tube outcome at five years.

The tube has not stood still either. Plates and materials have changed, flow control has improved, and the complications that once made the operation intimidating are more manageable than they used to be. Even the newer bleb-forming devices that sit somewhere between a stent and a trabeculectomy are, when you think about it, just another way of doing what a tube does, which is to move aqueous somewhere it can be absorbed. The whole field still turns on that one problem.

There is also the question of whose patients we are talking about. Read some of the literature and you would think every glaucoma patient shows up early, phakic, with a modestly raised pressure. That is not who walks into my clinic. In our region patients present late, with high pressures and advanced disease, and a large share of what we see is secondary or refractory.6 For a man losing the last of his vision to neovascular glaucoma, a stent is simply not on the table. A tube is often the operation that saves what is left. Our own results in these patients say the same thing the trials do.7

My real worry is the one I started with. As training programs hand more of their operating time to angle surgery, residents finish comfortable with stents and unsure with plates. A tube is not a hard idea, but it is a hard operation, and that skill fades when it is not used and not taught.8 A generation that cannot place a good drainage device has not moved the field forward. It has quietly left its sickest patients behind.

So I am not asking anyone to give up their stents. I use them and I will keep using them. I am asking us to stop talking about the tube as if it were on its way out. The better tool for the easy eye does not replace the necessary tool for the hard one. For the worst glaucomas we treat, the tube is still the operation the patient is counting on. The task is not to pick a side. It is to know which eye is in front of you, and to make sure the next surgeon knows it too.

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Retinopathy of Prematurity: Current Concepts in Pathogenesis, Classification, Screening, and Management

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Keywords: Retinopathy of prematurity; ICROP3; ETROP; screening; laser photocoagulation; anti-vascular endothelial growth factor.

Abstract

Retinopathy of prematurity (ROP) is a developmental vasoproliferative retinal disorder affecting incompletely vascularized retinas in premature infants and remains a leading cause of preventable childhood blindness worldwide. Advances in neonatal intensive care have substantially improved the survival of extremely premature and very-low-birth-weight infants, creating an expanding population at risk of developing ROP. Early identification through well-organized screening programs, accurate disease classification, and timely intervention remain the cornerstones of preventing irreversible visual impairment. Over the past decade, important advances have refined both the understanding and management of ROP. The updated International Classification of Retinopathy of Prematurity (ICROP3) has improved disease classification and standardized clinical documentation, while the recommendations of the Early Treatment for Retinopathy of Prematurity (ETROP) study continue to guide treatment decisions. In parallel, advances in wide-field retinal imaging, telemedicine-assisted screening, and artificial intelligence have enhanced opportunities for earlier diagnosis. This review summarizes current concepts in the epidemiology, pathophysiology, classification, screening, management, long-term outcomes, and future perspectives of ROP.

Introduction

Retinopathy of prematurity (ROP) is a developmental vasoproliferative retinal disorder affecting the incompletely vascularized retina of premature infants and remains one of the leading causes of preventable childhood blindness worldwide. Advances in neonatal intensive care have substantially improved the survival of extremely preterm and very-low-birth-weight infants, resulting in an expanding population at risk for developing ROP. Premature birth interrupts normal retinal vascularization, leaving peripheral avascular retina susceptible to oxygen dysregulation, oxidative stress, inflammation, and altered angiogenic signaling, particularly involving vascular endothelial growth factor (VEGF) and insulin-like growth factor-1 (IGF-1). Recent developments including ICROP3, ETROP recommendations, wide-field retinal imaging, telemedicine, and artificial intelligence have transformed the diagnosis and management of ROP. This review provides a contemporary evidence-based overview for ophthalmologists,

neonatologists, pediatricians, and healthcare professionals involved in the care of premature infants.

Epidemiology

ROP remains one of the leading causes of preventable childhood blindness worldwide. Approximately 15 million infants are born prematurely each year, and disease incidence varies according to gestational age, birth weight, oxygen management, neonatal care, and the availability of organized screening programs. The global epidemiology of ROP is often described in three epidemics. The first resulted from unrestricted oxygen use, the second from improved survival of extremely premature infants in high-income countries, and the current third epidemic reflects increasing neonatal survival in low- and middle-income countries without parallel expansion of screening and treatment services. Continued implementation of standardized screening programs and multidisciplinary collaboration remain essential to reduce ROP-related blindness.

Pathophysiology

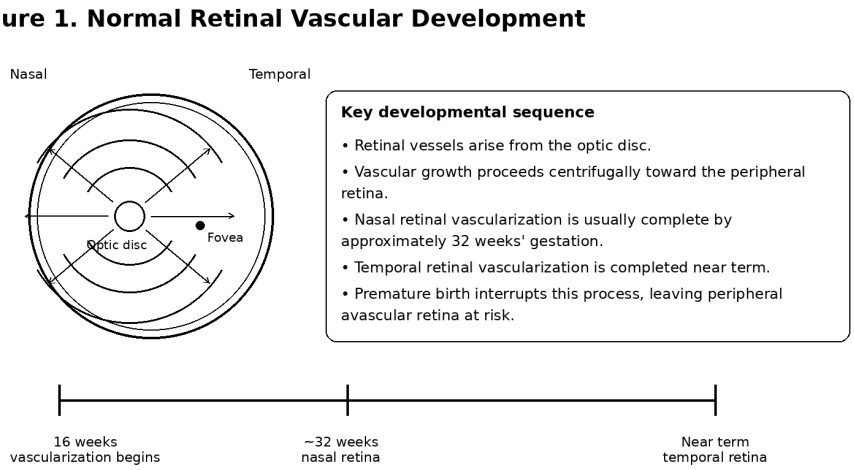
Normal Retinal Vascular Development

Retinal vascular development is a highly regulated physiological process that begins at approximately 16 weeks of gestation. Retinal vessels arise from the optic disc and extend centrifugally toward the peripheral retina in response to the metabolic demands of the developing neural retina. The nasal retina is usually vascularized earlier, reaching the nasal ora serrata at approximately 32 weeks' gestation, whereas vascularization of the temporal retina is completed near term.

This process is controlled by a complex interaction of angiogenic, metabolic, and neurotrophic signals. Vascular endothelial growth factor (VEGF) is central to physiological retinal vascular growth, while insulin-like growth factor-1 (IGF-1) supports normal endothelial cell survival and VEGF-mediated vascular development. Additional pathways, including hypoxia-inducible factor-1 alpha (HIF-1 alpha), erythropoietin, angiopoietins, oxidative stress pathways, and inflammatory mediators, also contribute to retinal vascular maturation.

Premature birth interrupts this normal developmental sequence. As a result, variable areas of peripheral retina remain avascular at birth. The immature retina is then exposed to an extrauterine environment with oxygen fluctuations, systemic illness, nutritional instability, inflammation, and oxidative stress. These postnatal factors interfere with normal vascular development and create the biological setting for retinopathy of prematurity (ROP).

Figure 1. Normal retinal vascular development.



Biphasic Pathogenesis of Retinopathy of Prematurity

The pathogenesis of ROP is classically described as a biphasic process. The first phase is characterized by interruption of normal vascular growth, whereas the second phase is characterized by hypoxia-driven pathological neovascularization.

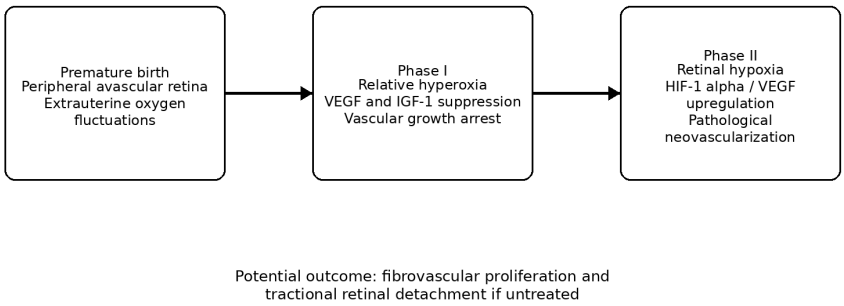
During Phase I, the premature infant is exposed to a relatively hyperoxic extrauterine environment compared with the intrauterine environment. Supplemental oxygen, oxygen fluctuations, immature antioxidant defense mechanisms, and systemic instability suppress VEGF signaling and reduce circulating IGF-1 levels. These changes lead to cessation of physiological retinal vascularization and, in some cases, vaso-obliteration of immature vessels. The consequence is persistence of peripheral avascular retina.

During Phase II, the infant grows and the metabolic demands of the developing retina increase. The avascular retina becomes progressively hypoxic, resulting in stabilization of HIF-1 alpha and upregulation of VEGF and other angiogenic mediators. This stimulates abnormal neovascularization at the junction between vascularized and avascular retina. Unlike physiological vascularization, the new vessels are disorganized, fragile, and associated with fibrovascular proliferation. Progressive vitreoretinal traction may ultimately result in partial or total tractional retinal detachment.

This biphasic model explains the rationale for current treatment strategies. Laser photocoagulation reduces angiogenic drive by ablating ischemic avascular retina, whereas intravitreal anti-VEGF therapy directly suppresses VEGF-mediated neovascularization. Understanding this mechanism is essential because anti-VEGF therapy may permit continued peripheral vascularization but also requires prolonged follow-up for reactivation or persistent avascular retina.

Figure 2. Biphasic pathogenesis of retinopathy of prematurity.

Figure 2. Biphasic Pathogenesis of Retinopathy of Prematurity



Additional Biological Mechanisms

ROP is not solely an oxygen-related disease. Although oxygen dysregulation remains central to its pathogenesis, multiple systemic and molecular mechanisms contribute to disease onset and severity. Low postnatal IGF-1 levels, poor postnatal weight gain, inflammatory cytokines, sepsis, oxidative stress, and nutritional deficiency may impair physiological angiogenesis and increase the risk of progression.

Inflammation and oxidative stress are particularly relevant in extremely premature infants because antioxidant defense systems are immature. Reactive oxygen species may damage developing retinal vessels and interact with inflammatory mediators to alter normal vascular signaling. These mechanisms help explain why infants with similar gestational age and birth weight may develop different degrees of disease severity depending on systemic condition and neonatal course.

The growing understanding of these pathways has encouraged investigation of predictive biomarkers, postnatal growth models, oxygen saturation strategies, and individualized screening approaches. However, gestational age, birth weight, retinal findings, and clinical course remain the most important determinants of screening and management in routine practice.

Risk Factors

Lower gestational age and lower birth weight are the two strongest and most consistent risk factors for ROP. The most immature infants have the largest areas of avascular retina at birth and are most vulnerable to oxygen fluctuations, systemic illness, and impaired postnatal growth.

ROP is nevertheless a multifactorial disease. Several neonatal and systemic factors have been associated with disease onset and progression, either by increasing retinal hypoxia, disrupting angiogenic signaling, increasing oxidative stress, or reflecting overall severity of prematurity.

- Extreme prematurity and very low birth weight.

- Prolonged supplemental oxygen therapy and fluctuating oxygen saturation.
- Mechanical ventilation and respiratory distress syndrome.
- Bronchopulmonary dysplasia.
- Neonatal sepsis and systemic inflammation.
- Apnea of prematurity.
- Anemia and multiple blood transfusions.
- Intraventricular hemorrhage.
- Poor postnatal weight gain and low serum IGF-1 levels.
- Necrotizing enterocolitis and severe systemic illness.
- Multiple gestation.
- Prolonged hospitalization in the neonatal intensive care unit.

Recognition of these risk factors is clinically important because screening eligibility should not rely exclusively on birth weight and gestational age in all settings. In some regions, larger and more mature premature infants may develop severe ROP, particularly when neonatal care is variable or oxygen monitoring is suboptimal. For this reason, many guidelines allow screening of selected larger infants with an unstable clinical course at the discretion of the neonatologist or ophthalmologist.

Genetic susceptibility has also been investigated, and familial or ethnic differences in disease risk have been reported. However, the precise contribution of genetic factors remains incompletely understood, and genetic testing is not part of routine ROP screening or management.

Optimizing neonatal care is therefore an essential part of ROP prevention. Careful oxygen saturation targeting, avoidance of wide oxygen fluctuations, prevention and early treatment of sepsis, improved nutrition, and close attention to postnatal growth may reduce the risk of severe disease. Nevertheless, no preventive strategy eliminates the need for organized ophthalmic screening in at-risk infants.

Clinical Pearl

ROP develops through disruption of normal retinal vascularization in susceptible premature infants. The combination of peripheral avascular retina, oxygen dysregulation, impaired IGF-1 and VEGF signaling, oxidative stress, inflammation, and systemic illness creates the conditions for pathological retinal neovascularization. Understanding these mechanisms provides the foundation for screening, treatment, and prevention of vision-threatening disease.

Classification of Retinopathy of Prematurity

Accurate classification of retinopathy of prematurity (ROP) is fundamental for clinical documentation, communication among clinicians, treatment planning, prognostication, and research. The International Classification of Retinopathy of Prematurity (ICROP) provides a standardized framework for describing disease severity according to retinal location, stage, extent, and vascular activity. Since the original classification was published in 1984, revisions have incorporated advances in clinical understanding and imaging. The third edition, ICROP3, represents the current international standard and includes refinements that are particularly relevant to contemporary practice.

ROP is described according to retinal zone, disease stage, circumferential extent in clock hours, vascular activity, and the presence or absence of aggressive ROP (A-ROP). ICROP3 also emphasizes newer concepts including posterior Zone II, regression, reactivation, and persistent avascular retina, especially in the era of anti-VEGF therapy.

Retinal Zones

Retinal zone describes the location of disease and is one of the strongest predictors of severity.

Zone I is a circular area centered on the optic disc with a radius extending to twice the distance from the optic disc to the fovea. Disease in Zone I is associated with the highest risk of rapid progression and often requires treatment.

Zone II extends centrifugally from the edge of Zone I to the nasal ora serrata. ICROP3 introduced the important concept of posterior Zone II because disease in this region may behave more aggressively than peripheral Zone II disease.

Zone III represents the residual temporal crescent of peripheral retina and is generally associated with milder disease and a lower likelihood of requiring treatment.

Disease Stages

ROP is staged according to the appearance of the vascular-avascular junction.

Stage 1 is a demarcation line separating vascularized and avascular retina.

Stage 2 is an elevated ridge with height and width at the vascular-avascular junction.

Stage 3 is extraretinal fibrovascular proliferation extending from the ridge into the vitreous.

Stage 4 is partial retinal detachment caused by traction from fibrovascular proliferation. Stage 4A spares the fovea, whereas Stage 4B involves the fovea.

Stage 5 is total retinal detachment, typically funnel-shaped, and is associated with a poor visual prognosis despite surgical intervention.

Extent of Disease

The circumferential extent of ROP is recorded in clock hours, from 1 to 12. Careful documentation of extent allows clinicians to monitor progression or regression over time and improves communication among treating teams.

Vascular Activity: Pre-plus and Plus Disease

Pre-plus disease describes posterior pole vascular abnormalities that are more prominent than normal but insufficient to meet the definition of plus disease. Recognition of pre-plus disease is clinically important because it may precede progression to treatment-requiring ROP.

Plus disease is characterized by significant venous dilatation and arteriolar tortuosity of the posterior retinal vessels in at least two quadrants. Additional anterior segment signs may include iris vascular engorgement, poor pupillary dilatation, and vitreous haze. Plus disease is a major indicator of disease activity and is central to treatment decisions.

Aggressive Retinopathy of Prematurity

Aggressive ROP (A-ROP) is a rapidly progressive form of disease that predominantly affects the posterior retina. It may demonstrate severe vascular activity, flat neovascularization, ill-defined staging, and rapid progression to retinal detachment if not treated urgently. ICROP3 recognizes that aggressive disease may occur not only in Zone I but also in posterior Zone II.

Regression, Reactivation, and Persistent Avascular Retina

ICROP3 standardized the description of regression and reactivation. Regression may occur spontaneously or after treatment and is characterized by resolution of plus disease, reduction in vascular activity, involution of fibrovascular tissue, and progression of retinal vascularization.

Reactivation refers to renewed disease activity after a period of regression. It is particularly important after intravitreal anti-VEGF therapy, because recurrence may occur weeks or months after treatment. Reactivation may present with recurrent plus disease, renewed neovascularization, or progression of peripheral vascular abnormalities.

Persistent avascular retina (PAR) refers to incomplete vascularization of the peripheral retina after spontaneous regression or treatment. PAR is especially relevant after anti-VEGF therapy. It may remain stable, slowly vascularize, or become associated with late leakage, neovascularization, or retinal complications. Ongoing surveillance is therefore required, and selected cases may require supplemental laser photocoagulation.

ETROP Classification for Treatment Decision-Making

Although ICROP3 provides the standardized language for describing disease, treatment decisions are guided primarily by the Early Treatment for Retinopathy of Prematurity (ETROP) recommendations. ETROP classified pre-threshold disease into Type 1 and Type 2 ROP, allowing

clinicians to distinguish eyes requiring prompt treatment from those suitable for close observation.

Type 1 ROP - Treatment Recommended

Type 1 ROP represents disease with a high risk of progression to unfavorable structural outcome if left untreated. Prompt treatment is recommended, usually within 48 to 72 hours of diagnosis, depending on clinical circumstances and local protocols.

- Zone I: any stage ROP with plus disease.
- Zone I: Stage 3 ROP with or without plus disease.
- Zone II: Stage 2 or Stage 3 ROP with plus disease.

Type 2 ROP - Close Observation

Type 2 ROP does not require immediate treatment but requires close follow-up because progression to Type 1 disease may occur. Follow-up intervals should be individualized according to retinal findings, zone, vascular activity, and the infant's systemic condition.

- Zone I: Stage 1 or Stage 2 ROP without plus disease.
- Zone II: Stage 3 ROP without plus disease.

Current management therefore requires integration of ICROP3 terminology with ETROP treatment thresholds. Accurate classification at each examination allows appropriate timing of intervention, prevents unnecessary treatment, and reduces the risk of retinal detachment.

Table 1. Summary of ICROP3 Classification

Component	Classification	Clinical significance
Zone I	Circle centered on optic disc with radius twice disc-fovea distance	Highest risk; often treatment-requiring
Posterior Zone II	Posterior part of Zone II recognized in ICROP3	May behave aggressively
Zone II	From edge of Zone I to nasal ora serrata	Intermediate risk
Zone III	Residual temporal crescent	Generally lower risk
Stage 1	Demarcation line	Mild disease
Stage 2	Elevated ridge	Moderate disease
Stage 3	Extraretinal fibrovascular proliferation	May require treatment depending on zone and plus disease
Stage 4A	Partial retinal detachment sparing fovea	Surgical disease; better prognosis than 4B
Stage 4B	Partial retinal detachment involving fovea	Guarded prognosis
Stage 5	Total retinal detachment	Poor prognosis
Pre-plus	Vascular abnormality less than plus disease	Close follow-up
Plus disease	Posterior vascular dilatation and tortuosity	Major treatment indicator
A-ROP	Rapidly progressive posterior disease	Urgent treatment
Regression/reactivation	Resolution or recurrence of disease activity	Important after treatment, especially anti-VEGF
PAR	Persistent avascular retina	Requires prolonged surveillance

Table 2. ETROP Classification for Treatment Decision-Making

Disease category	Clinical findings	Recommended management
Type 1 ROP	Zone I: any stage with plus disease	Prompt treatment
Type 1 ROP	Zone I: Stage 3 with or without plus disease	Prompt treatment
Type 1 ROP	Zone II: Stage 2 or 3 with plus disease	Prompt treatment
Type 2 ROP	Zone I: Stage 1 or 2 without plus disease	Close observation
Type 2 ROP	Zone II: Stage 3 without plus disease	Close observation

Clinical Pearl

ICROP3 provides the standardized language for describing ROP, while ETROP defines the practical treatment thresholds. The combination of accurate ICROP3 documentation and appropriate identification of Type 1 and Type 2 ROP is essential for safe, evidence-based management.

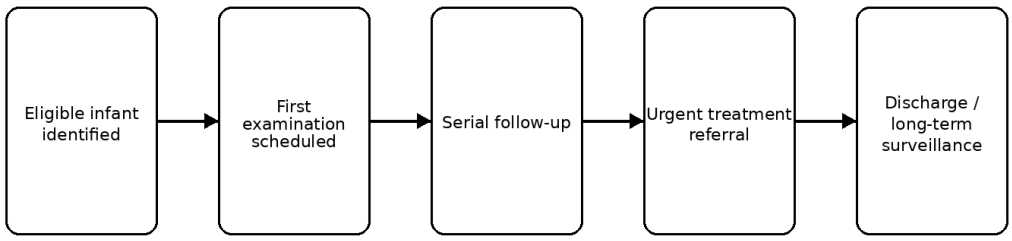
Screening

Retinopathy of prematurity (ROP) screening represents one of the most effective strategies for preventing childhood blindness. Because the disease is asymptomatic during its early stages, affected infants cannot be identified on the basis of clinical symptoms alone. Timely retinal examination of at-risk premature infants is therefore essential to detect disease before irreversible structural retinal damage develops. The success of modern ROP care depends not only on effective treatment but also on organized screening systems integrated into neonatal intensive care units (NICUs).

The primary objective of screening is to identify treatment-requiring ROP before progression to retinal detachment. Delayed examination, missed follow-up, poor communication at discharge, or failure to arrange outpatient review remain important causes of preventable visual loss. Effective screening therefore requires coordination among neonatologists, pediatricians, ophthalmologists, neonatal nurses, discharge coordinators, and parents. Screening should be considered a structured clinical pathway rather than an isolated eye examination.

Figure 4. Screening pathway for retinopathy of prematurity. identification of eligible infants in the NICU, scheduling of first examination according to gestational age and postmenstrual age, serial follow-up according to retinal findings, urgent referral for treatment-requiring disease, discharge planning, and long-term ophthalmic surveillance.

Figure 4. Screening pathway for retinopathy of prematurity



Screening Eligibility

Screening eligibility is generally determined by gestational age (GA), birth weight (BW), and the clinical course of the infant. Although criteria vary slightly across countries and professional societies, most guidelines aim to capture infants at greatest risk while allowing clinician discretion for larger or more mature premature infants with unstable neonatal courses.

Infants who should undergo routine ROP screening generally include:

- Birth weight of 1500 g or less.
- Gestational age of 30 weeks or less, or 30 to 31 weeks according to local recommendations.
- Selected infants with birth weight between 1500 and 2000 g or gestational age greater than 30 weeks who have an unstable clinical course and are judged by the neonatologist or ophthalmologist to be at increased risk.

Clinical circumstances that may justify screening despite exceeding standard BW or GA thresholds include prolonged supplemental oxygen therapy, significant oxygen saturation fluctuations, mechanical ventilation, bronchopulmonary dysplasia, severe neonatal sepsis, necrotizing enterocolitis, multiple blood transfusions, anemia, poor postnatal weight gain, intraventricular hemorrhage, severe cardiorespiratory instability, and prolonged NICU hospitalization.

The need for local adaptation is particularly important in middle-income countries, where larger and more mature premature infants may develop severe ROP because of variations in neonatal care, oxygen monitoring, staffing, access to ophthalmic screening, and follow-up infrastructure. For this reason, screening programs in countries such as India, China, and several Latin American settings often use broader eligibility criteria than those used in North America or Western Europe. Local guidelines should maintain high sensitivity for treatment-requiring disease while avoiding unnecessary examinations when possible.

Table 1 summarizes selected international ROP screening eligibility recommendations and illustrates why protocols should be adapted to local epidemiology and neonatal care resources.

Region / guideline	Birth weight criterion	Gestational age criterion	Additional infant groups	Comments
United States AAP/AAO/AAPOS	<=1500 g	<=30 weeks	Selected infants 1500-2000 g or >30 weeks with unstable clinical course	Commonly used benchmark criteria; clinician discretion is emphasized.
United Kingdom / RCPCH style criteria	<=1500 g	<=31 weeks	Infants outside criteria if considered high risk locally	Slightly broader GA threshold than many US protocols.
Canada	<=1500 g	<=30 weeks	Selected larger infants with complicated clinical course	Similar risk-based framework with local neonatal input.
India	<=2000 g or <1750 g depending on program	<=34 weeks or <35 weeks in some protocols	Infants with oxygen therapy, sepsis, transfusion, respiratory support, or unstable course	Broader criteria reflect severe ROP occurring in larger infants in some settings.
Latin America / middle-income settings	Often <=1500-2000 g	Often <=32-34 weeks	High-risk infants beyond thresholds depending on neonatal course	Criteria should be tailored to local disease patterns and resources.
Local institutional protocol	Defined by national or hospital policy	Defined by national or hospital policy	Any infant judged at risk by neonatologist or ophthalmologist	Local audit data should guide refinement of criteria.

Table 3. Selected international screening recommendations for retinopathy of prematurity. Exact thresholds vary among national guidelines and should be interpreted according to local policy, neonatal survival patterns, and resource availability.

Timing of the First Examination

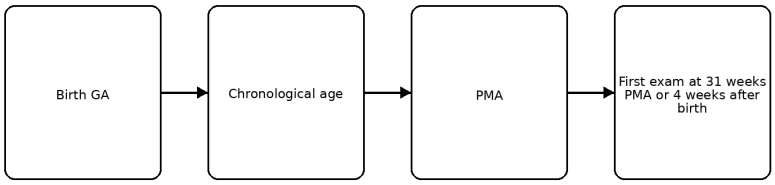
The timing of the first retinal examination is critical. An examination performed too early may fail to identify clinically meaningful disease, whereas delayed examination increases the risk of missing rapidly progressive ROP. Because retinal vascular maturation correlates more closely with postmenstrual age (PMA) than chronological age alone, the first examination should be scheduled according to PMA and postnatal age.

In most infants, the first examination is performed at 31 weeks PMA or 4 weeks after birth, whichever is later. Extremely premature infants, particularly those born at 22 to 27 weeks of gestation, may require earlier scheduling according to detailed local tables, but screening should generally begin around 30 to 31 weeks PMA. Infants who remain medically unstable should still be scheduled for screening when clinically feasible because systemic instability itself may increase ROP risk.

A practical approach is to ensure that every eligible infant is identified at NICU admission, entered into a screening register, and assigned a due date for the first examination. The due date should be visible to the neonatal team and should remain active even if the infant is transferred to another facility. Missed screening after transfer or discharge is a preventable systems failure and should be avoided through clear written communication.

Figure 5. Timing of the first ROP examination. timeline showing birth gestational age, chronological age, postmenstrual age, first examination at 31 weeks PMA or 4 weeks postnatal age whichever is later, and modified timing for extremely premature infants.

Figure 5. Timing of the first ROP examination



Examination Technique and Infant Preparation

The standard screening examination remains binocular indirect ophthalmoscopy after pharmacologic pupil dilation, with careful assessment of the posterior pole and peripheral retina. Scleral indentation is often required to visualize the peripheral avascular retina and to determine zone, stage, extent of disease, and the presence or absence of plus or pre-plus disease. Wide-field digital imaging may complement or, in organized telemedicine programs, support

remote screening, but it should be interpreted within the limits of image quality, field of view, and grader expertise.

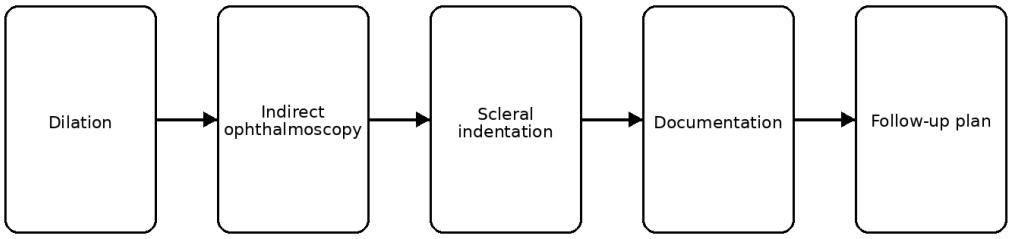
Infant preparation should prioritize safety and physiological stability. The NICU team should confirm that the infant is medically stable enough for examination. Topical anesthetic may be used before placement of an eyelid speculum, and nonpharmacological comfort measures such as swaddling, facilitated tucking, oral sucrose when permitted, and appropriate cardiorespiratory monitoring may reduce distress. Examination should be performed efficiently but carefully, with attention to oxygen saturation, heart rate, and apnea or bradycardia episodes.

Pupil dilation protocols vary, but low-concentration mydriatic regimens are commonly preferred in premature infants to reduce systemic adverse effects. Combination drops such as cyclopentolate and phenylephrine may be used according to local policy, with careful avoidance of excessive dosing. Infants should be monitored for cardiorespiratory changes, feeding intolerance, temperature instability, and other systemic effects after dilation and examination.

Infection control is essential because screening is performed in vulnerable NICU patients. The examiner should follow institutional hand hygiene and equipment disinfection protocols. Specula, depressors, imaging contact lenses, and camera components that contact the infant should be sterilized or disinfected according to manufacturer and hospital infection-control guidance. Separate sterile or appropriately disinfected instruments should be used for each infant.

Figure 6. Essential components of the ROP screening examination. dilated examination, indirect ophthalmoscopy, scleral indentation, wide-field imaging, documentation of zone, stage, extent, plus disease, and follow-up plan.

Figure 6. Essential components of the ROP screening examination



Documentation and Communication

Accurate documentation is a central component of ROP screening. The examination note should record the date of examination, PMA, birth weight, gestational age at birth, current systemic status when relevant, retinal zone, stage, extent in clock hours, plus or pre-plus disease, presence of aggressive ROP, regression or reactivation, image findings if obtained, and the recommended follow-up interval. The plan should clearly state whether the infant requires routine follow-up, urgent review, treatment within a specified time frame, or transfer to a center capable of treatment.

Communication must be explicit. The ophthalmologist should communicate treatment-requiring or high-risk findings directly to the neonatology team, and the plan should be documented in the medical record. Parents should be informed that ROP screening is not optional once the infant is eligible and that examinations may need to continue after discharge. Written discharge instructions should include the date, time, and location of the next eye appointment, the responsible ophthalmology service, and a clear warning that missed follow-up can result in permanent blindness.

Follow-up Intervals

Follow-up intervals are determined by the most posterior zone of vascularization, disease stage, presence of plus or pre-plus disease, and evidence of progression or regression. Infants with immature vascularization in posterior retina require closer follow-up than infants with more peripheral vascularization and no ROP. Follow-up should be shortened if there is worsening stage, increasing extent, posterior disease, plus disease, aggressive ROP, poor-quality examination, or uncertainty regarding findings.

Table 2 provides a practical follow-up framework that can be adapted to local screening guidelines.

Retinal finding	Suggested follow-up interval	Clinical rationale
Immature vascularization in zone I, no ROP	Within 1 week	Posterior avascular retina carries high risk and may progress rapidly.
Immature vascularization in posterior zone II, no ROP	1-2 weeks	Requires close observation until vascularization progresses or disease declares itself.
Stage 1 or 2 ROP in zone I	Within 1 week or less	Posterior disease may progress and requires careful surveillance.
Stage 3 ROP in zone I or any plus disease	Urgent treatment evaluation	May meet Type 1 ROP criteria; treatment is usually required promptly.
Stage 1 or 2 ROP in zone II without plus	1-2 weeks	Often regresses but requires monitoring for progression.
Stage 3 ROP in zone II without plus	1 week or less	May progress to Type 1 disease; close monitoring is needed.
Immature vascularization in zone III, no previous zone I or II ROP	2-3 weeks or per local policy	Lower risk when vascularization has reached zone III.
Regressing ROP	1-3 weeks depending on prior severity and treatment status	Regression should be documented until safe termination criteria are met.
After anti-VEGF therapy	Close and prolonged follow-up, often weekly initially, then individualized	Late reactivation and persistent avascular retina may occur.

Table 4. Practical follow-up intervals for ROP screening. Intervals should be individualized according to retinal findings, image quality, systemic status, local protocol, and examiner judgment.

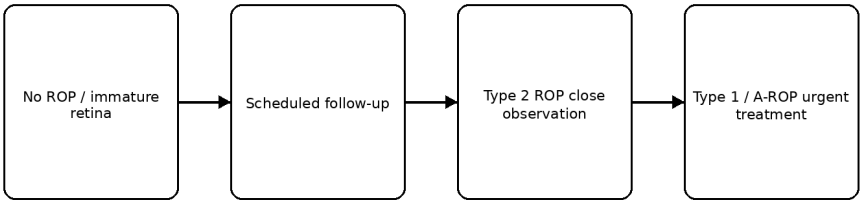
Treatment-Requiring Disease and Urgency of Referral

The screening pathway must rapidly identify infants with treatment-requiring disease. Type 1 ROP generally requires prompt treatment, typically within 48 hours when feasible, because delay increases the risk of progression to tractional retinal detachment. Treatment-requiring findings include zone I ROP with plus disease, zone I stage 3 ROP with or without plus disease, and zone II stage 2 or 3 ROP with plus disease. Aggressive ROP is particularly urgent because it may progress quickly and may not pass through classic sequential stages.

Type 2 ROP is generally observed closely rather than treated immediately, but it requires careful follow-up because progression to Type 1 disease can occur. Type 2 disease includes zone I stage 1 or 2 ROP without plus disease and zone II stage 3 ROP without plus disease. The distinction between Type 1 and Type 2 disease should be clearly documented because it directly determines urgency and management.

Figure 7. Screening-to-treatment decision pathway. no ROP or immature vascularization leading to scheduled follow-up; Type 2 ROP leading to close observation; Type 1 ROP and aggressive ROP leading to urgent treatment; post-treatment follow-up leading to monitoring for regression, recurrence, and persistent avascular retina.

Figure 7. Screening-to-treatment decision pathway



Criteria for Termination of Acute Screening

ROP screening should continue until the risk of developing treatment-requiring disease has passed. Termination criteria vary across guidelines but generally include complete or near-complete retinal vascularization, vascularization into zone III without previous significant ROP, sufficient PMA with no active disease, or definite regression of ROP. Screening should not be stopped prematurely in infants with posterior disease, prior severe ROP, uncertain regression, poor examination quality, or after anti-VEGF therapy without a clear long-term follow-up plan.

Common criteria supporting termination of acute screening include vascularization reaching zone III without previous zone I or zone II ROP, full retinal vascularization, PMA of approximately 45 weeks with no prethreshold or worse disease and no evidence of active progression, or documented regression of ROP judged unlikely to reactivate. After laser treatment, follow-up continues until regression is stable. After anti-VEGF therapy, longer follow-up is required because recurrence may occur later than after laser and peripheral avascular retina may persist.

Termination of acute screening does not necessarily mean termination of ophthalmic care. Premature infants, especially those with any history of ROP, remain at increased risk for refractive error, anisometropia, strabismus, amblyopia, cataract, glaucoma, and late vitreoretinal complications. Therefore, the screening program should include a plan for pediatric ophthalmology follow-up beyond the acute neonatal period.

Discharge Planning and Parent Counseling

Discharge before completion of ROP screening is a high-risk transition point. The NICU team should not discharge or transfer an eligible infant without a documented eye examination status and a scheduled follow-up appointment. The discharge summary should include the most recent

retinal findings, the next required examination date, the urgency of follow-up, and contact details for the receiving ophthalmology service. When infants are transferred between hospitals, responsibility for continuing screening must be explicitly handed over.

Parent counseling should be clear and direct. Families should understand that ROP can progress silently, that the infant may appear visually normal even when sight-threatening disease is developing, and that missed appointments can lead to irreversible blindness. Counseling should be repeated before discharge and supported by written instructions in language the family understands. For families with social, geographic, or transport barriers, the care team should arrange support early rather than waiting for missed follow-up.

Telemedicine and Wide-Field Digital Imaging

Telemedicine has become an important strategy for expanding access to ROP screening, particularly in regions with limited availability of pediatric retinal specialists. Wide-field digital retinal imaging allows trained personnel to acquire retinal photographs in the NICU and transmit them to remote experts for grading. This model can improve screening coverage, reduce delays, support quality assurance, and facilitate triage of infants requiring urgent ophthalmic examination or treatment.

Successful telemedicine programs require standardized imaging protocols, trained imagers, secure image transfer, defined grading criteria, rapid reporting systems, backup pathways for poor-quality images, and clear referral mechanisms. Telemedicine should not be viewed simply as image capture; it is a complete clinical service that requires governance, audit, equipment maintenance, data security, and medicolegal accountability.

Wide-field imaging has several advantages, including objective documentation, easier longitudinal comparison, remote expert review, education of trainees and parents, and potential integration with artificial intelligence (AI). However, limitations remain. Peripheral image quality may be reduced, scleral indentation cannot be fully replicated by standard imaging, media opacity may limit visualization, and image-based grading may miss subtle peripheral findings if the image set is incomplete. Therefore, indirect ophthalmoscopy remains essential when images are inadequate, disease is severe, treatment decisions are uncertain, or local policy requires direct examination.

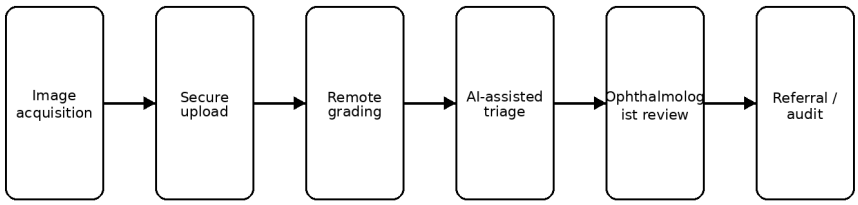
Artificial Intelligence in ROP Screening

AI-assisted ROP screening is an active area of research and clinical development. Deep learning systems trained on wide-field retinal images can identify plus disease, pre-plus disease, disease severity, and referral-warranted ROP with high diagnostic performance in selected datasets. Systems such as i-ROP deep learning and other automated grading approaches may reduce interobserver variability, support triage, and improve access to screening where expert graders are limited.

Despite this promise, AI should currently be considered an adjunct rather than a replacement for clinical responsibility. Important limitations include dataset bias, variable image quality, differences in camera systems, medicolegal accountability, integration into clinical workflow, performance in diverse populations, and the need for prospective validation. AI tools must be embedded within a supervised screening program with clear thresholds for referral, human review, quality control, and safety monitoring.

Figure 8. Telemedicine and AI-assisted ROP screening model. bedside image acquisition, image quality check, secure upload, remote grading, AI-assisted triage, ophthalmologist review, urgent referral pathway, documentation, audit, and parent communication.

Figure 8. Telemedicine and AI-assisted ROP screening model



Quality Assurance and Program-Level Considerations

A reliable ROP screening program requires more than clinical expertise. Program-level quality assurance should include a registry of all eligible infants, automated reminders for due examinations, documentation of completed examinations, tracking of missed or delayed follow-up, audit of treatment outcomes, and periodic review of local screening criteria. Units should monitor whether any infant developed treatment-requiring ROP outside the existing eligibility criteria and should revise protocols if needed.

Training is also essential. Ophthalmologists require experience in neonatal retinal examination and ICROP classification, while NICU staff should understand eligibility criteria, timing, preparation, and discharge responsibilities. In telemedicine programs, imagers and graders require certification, ongoing feedback, and periodic intergrader agreement assessment. Standardized terminology based on ICROP3 improves communication and reduces ambiguity.

Clinical Pearl

ROP screening is a time-sensitive safety pathway. Every eligible infant should be identified early, examined at the correct PMA, followed until safe termination criteria are met, and discharged only with a documented follow-up plan. The most dangerous screening failures are not usually

diagnostic uncertainty but missed eligibility, delayed first examination, loss to follow-up after discharge or transfer, and failure to communicate urgent findings. Organized systems, not isolated examinations, prevent blindness.

Management of ROP aims to prevent progression to tractional retinal detachment while preserving retinal structure and visual function. Treatment decisions are guided by disease severity according to the International Classification of Retinopathy of Prematurity (ICROP3) and Early Treatment for Retinopathy of Prematurity (ETROP) recommendations discussed previously.

Laser photocoagulation remains the standard treatment for most infants with treatment-requiring Type 1 ROP. By ablating the peripheral avascular retina, laser reduces vascular endothelial growth factor (VEGF) production, promoting regression of pathological neovascularization. It provides excellent long-term anatomical outcomes with a relatively low recurrence rate, although it permanently destroys peripheral avascular retina and is associated with greater myopic refractive error than anti-VEGF therapy. Landmark CRYO-ROP and ETROP studies established the benefit of timely ablative treatment and remain the foundation of current practice.

Intravitreal anti-VEGF therapy has become an important alternative, particularly for Zone I disease and aggressive posterior ROP (AP-ROP). Bevacizumab, ranibizumab, and aflibercept have demonstrated favorable anatomical outcomes, especially in posterior disease where laser treatment may be technically difficult. Advantages include preservation of peripheral retinal vascularization and reduced myopia; however, prolonged follow-up is mandatory because of late disease reactivation, and questions remain regarding systemic VEGF suppression in premature infants.

Surgical management is reserved for Stage 4 and Stage 5 ROP with tractional retinal detachment. Lens-sparing vitrectomy is preferred for selected Stage 4 disease, whereas advanced Stage 5 disease may require vitrectomy with or without lensectomy. Visual prognosis declines with increasing disease severity, emphasizing the importance of early screening and timely treatment.

Table 5. Comparison of Laser Photocoagulation and Anti-VEGF Therapy

Feature	Laser	Anti-VEGF
Main indication	Most Type 1 ROP	Zone I and AP-ROP; selected Type 1 ROP
Mechanism	Ablates avascular retina, reducing VEGF	Neutralizes VEGF
Advantages	Established long-term evidence; low recurrence	Preserves peripheral retina; less myopia
Limitations	Peripheral retinal destruction	Late recurrence; prolonged follow-up
Systemic concerns	None related to VEGF	Potential systemic VEGF suppression

Conclusion

Retinopathy of prematurity (ROP) remains a leading cause of preventable childhood blindness despite major advances in neonatal care. Improvements in understanding retinal vascular development, the adoption of the ICROP3 classification, evidence-based screening protocols, and timely treatment with laser photocoagulation or intravitreal anti-VEGF agents have substantially improved anatomical and visual outcomes. Nevertheless, delayed diagnosis, inconsistent screening, and disparities in neonatal care continue to contribute to avoidable vision loss, particularly in low- and middle-income settings.

Optimal ROP care requires close collaboration between neonatologists, ophthalmologists, nurses, and families. Screening programs should be integrated into neonatal services, and infants who receive anti-VEGF therapy require prolonged follow-up because of the risk of late reactivation and persistent avascular retina. Emerging technologies, including wide-field imaging, telemedicine, and artificial intelligence, have the potential to improve access to expert screening while complementing—not replacing—clinical judgement.

Future research should focus on optimizing treatment selection, clarifying the long-term systemic and ocular safety of anti-VEGF therapy, refining individualized screening strategies, and expanding equitable access to high-quality neonatal and ophthalmic care worldwide. Continued multidisciplinary collaboration remains the cornerstone for reducing the global burden of ROP-related visual impairment.

Declarations

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- Data Availability: Not applicable for this narrative review.

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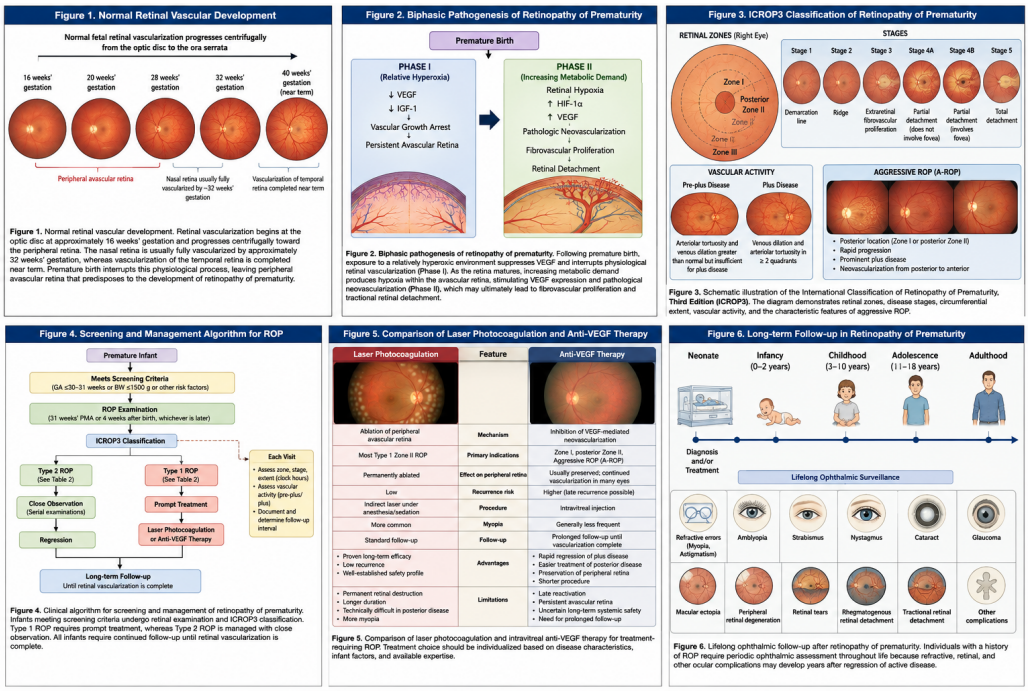
Composite Figures

Local journal draft: the six approved figures are provided as a single composite figure page. This composite replaces the separate draft figure placeholders for this submission version.



Composite Figure. Figures 1–6: Normal retinal vascular development; biphasic pathogenesis; ICROP3 classification; screening and management algorithm; comparison of laser photocoagulation versus anti-VEGF therapy; long-term follow-up in retinopathy of prematurity.

The "Setting Sun" Sign: A Proposed Grading Scale

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The "Setting Sun" sign is a neuro-ophthalmic finding observed in infants with hydrocephalus, characterized by conjugate downgaze due to pressure effects on the posterior third ventricle and midbrain. This sign can be perceived in about third of infants with obstructive hydrocephalus, and could serve as an early clinical indicator for the progression in intracranial pressure. Despite its significance, there is a paucity of standardization to quantify the hydrocephalus severity, limiting objective assessment and monitoring. Here, we propose a novel, simple and sensitive grading system based on the degree of iris and pupil coverage by the lower eyelid. This system aims to enhance early detection, facilitate disease monitoring, and improve treatment decision making in the management of infantile hydrocephalus.

KEYWORDS: Setting-Sun sign, infantile obstructive hydrocephalus.

Abbreviations: MRI: Magnetic Resonance Imaging.

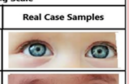
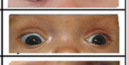
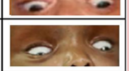
INTRODUCTION: Clinical measurement scales play a crucial role in evaluating patient status and tracking disease progression. Standardized tools such as the Glasgow Coma Scale(1), Karnofsky impaired upward gaze. It is commonly associated with hydrocephalus but can also appear in conditions such as Parinaud's syndrome(5), kernicterus(6), and transiently in some healthy infants(7). It is encountered in infants and young children with raised intracranial pressure (seen in up to 40% of children with obstructive hydrocephalus and 13% of children with shunt dysfunction)(8).Given the dynamic nature of the "Setting Sun" sign, a standardized grading system is necessary to improve early diagnosis, track progression, and guide timely interventions. In the normal infant, the upper lid covers the upper part of iris, while in hydrocephalus, the lower eyelid covers the iris at various degrees depending on the severity. Given the dynamic nature of the "Setting Sun" sign, where severity fluctuates with hydrocephalus progression or improvement following interventions such as a ventriculoperitoneal shunt, an objective grading system is necessary. Such a system would: 1. Improve Early Detection – Allow clinicians to document subtle changes in ocular findings before hydrocephalus worsens. Scale(2), Rankin Exophthalmos Scale(3) Scale enable and Thyroid quantitative assessments, improving clinical decision-making. However, no formal grading system exists for the "Setting Sun" sign, a key neuro-ophthalmic marker of hydrocephalus first described by Cernerud in 1975(4). This phenomenon, characterized by downward eye deviation and superior scleral exposure, occurs due to pressure effects on the midbrain, leading to 2. Facilitate Monitoring – Enable consistent tracking of disease progression and response to treatment. 3. Enhance Decision-Making – Assist neurosurgeons and paediatricians in determining when surgical intervention (e.g., shunt placement or revision) is required. 4. Promote Research and Clinical Communication – Establish a universal reference point that can

be used in studies and clinical reports to describe the severity of the “Setting Sun” sign more precisely

The proposed “Setting Sun” sign grading system:

In a normal anatomical state, the upper eyelid typically covers the upper part of the iris, leaving only a portion of the sclera visible inferiorly. This position is maintained by the coordinated function of the levator palpebrae superioris muscle and Müller's muscle, which regulate upper eyelid positioning. Additionally, normal eye movements allow for smooth conjugate gaze in all directions, including unrestricted upward gaze. In contrast, the 'Setting Sun' sign is characterized by downward deviation of the eyes, exposing an abnormally large portion of the superior sclera. This occurs due to upper lid retraction and impaired upward gaze, a hallmark of midbrain dysfunction commonly seen in hydrocephalus. The lower eyelid progressively covers more of the pupil and iris as the severity of the condition increases. Understanding the normal eye position is essential in recognizing and grading this pathological deviation. To standardize the assessment of the “Setting Sun” sign, we introduce a five-grade classification system based on the degree of iris and pupil coverage by the lower eyelid. This scale can serve as a quantitative tool for monitoring patients, particularly in cases of shunt failure or progressive hydrocephalus. Grade 0 (Normal Eye Position): The upper eyelid covers the upper portion of the iris, and the eye maintains normal upward gaze ability. Grade I The lower eyelid covers only the lower part of the iris (mild increase in intracranial pressure).. Grade II The lower eyelid reaches the lower edge of the pupil. Grade III The lower eyelid covers the lower half of the pupil. Grade IVOnly the upper part of the pupil is visible. (Moderate-to-severe hydrocephalus). Grade VOnly the upper tip of the iris is visible (severe hydrocephalus requiring urgent intervention). Where grade I is the early increase in the intracranial pressure and the higher the grade may indicate worsening hydrocephalus.

Table 1: The “Setting Sun” sign grading system with illustrative depiction and real case examples.

“Setting Sun” Sign Grading Scale			
Grade	**Description**	**Depiction**	**Real Case Samples**
Grade 0	(Normal) Upper lid covers upper iris		
Grade I	Lower lid covers lower part of iris		
Grade II	Lower lid touches lower edge of pupil		
Grade III	Lower lid covers half of pupil		
Grade IV	Only upper part of pupil is showing		
Grade V	Only upper tip of iris is showing		

This grading system provides a structured approach to evaluating the severity of the “Setting Sun” sign, making it a potential tool for identifying early signs of hydrocephalus decompensation. Future studies should assess its inter-rater reliability and compare its findings with neuroimaging results, such as ventricular index measurements or optic nerve sheath diameter changes on MRI. By integrating this scale into routine clinical evaluations, clinicians may achieve earlier detection

of hydrocephalus worsening, improving patient outcomes. Limitations: This grading scale is based on clinical observations that may vary between patients due to individual differences in eyelid position and ocular muscle tone. It is not intended to replace radiological assessment but rather to complement existing diagnostic tools. Further prospective studies are needed to evaluate its inter-rater reliability, correlation with imaging findings, and potential role in predicting hydrocephalus progression or shunt failure.

CONCLUSION: With over three decades of experience managing pediatric hydrocephalus, we propose a novel grading system for the "Setting Sun" sign. This standardized classification enables more precise monitoring of hydrocephalus progression and treatment response. Future research may address the accuracy, and the reliability of this grading system, and could investigate the potential correlation with neuroimaging and clinical assessment. Once validated, this system could enhance early diagnosis, improve clinical communication, and optimize treatment strategies for infants with hydrocephalus.

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More Than an Eye Surgeon: The Teacher Who Restored Perspectives

Dr. Anees Akram Sadiq, MBChB · Iraqi Board of Medical Specialisations, Anaesthesia

First glimpse of my memory as a child was Liverpool1971 when I was 3, my father was working there as a senior house officer when he took me and my mother there to accompany him helping him achieve his dream of being FRCS in ophthalmology.

I remember him holding that strange white structure staring at it reading notes to understand later it was a human skull

3 years later in Salisbury where we lived I remember him taking notes from that huge volume and a book from a collection I remember as Duke Elder in name using his lifelong grey Parker fountain pen.

Then going to the royal college itself in London with my pregnant mum witnessing him taking his degree.

We came back to Iraq as he told me people there slept on the roof of the house something I couldn't comprehend as a kid because English homes are not flat.

1975 he took me to his workplace the old Ramad hospital now obsolete when it was the first time, I went to the operation theatre watching astonishingly how someone put a rubber tube into a sleeping man's mouth that is Anasthesia he told me never knowing on that day I will be an Anaesthetist myself.

Years go by he comes home smelling of halothane carrying his old brown bag with a canister of refrigeration gas used as a cryo probe in intracapsular cataract extraction.

I can't forget the many times he took me at night to Yarmook hospital when I was a teenager to perform an operation on an injured eye

I was proud of him then and now

My father saves people's eyes

My pride was maximum when sat in the lecture hall with 200 other undergraduate students listening to his lectures

He was unique when lectured

Talk and chalk he said

He pulled you to the world of ophthalmology made easy something I learned when I lectured anaesthesia in the same Mustansiriya medical school

Life completes a cycle

I made his dream come true by being a doctor myself

Let's make a team he said you are my anaesthetist he said

I will be always proud of him as a doctor a teacher and most of all as a father

God bless his soul for if not for him I wouldn't be the man I am now

Photo gallery


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