

Retinitis pigmentosa: A brief overview

Retinitis pigmentosa (RP) is a group of hereditary disorders of the photoreceptors and retinal pigment epithelium (RPE) which gradually causes night blindness and progressive constriction of the visual field. Waxy optic disc pallor, arteriolar narrowing and hyalinization are found in almost all cases. Pigmentary changes are usually seen but may be absent or mild, invariably early in the course of the disease. The pigmentary changes seen are characteristic of bone spicules, diffuse granularity or stippling and pigment clumping; these are due to photoreceptors' degeneration, atrophy in the outer retina and pigment epithelium, and RPE cells migrating into the retina.^[1] 1 in 4,000 is the conservative prevalence estimate of RP worldwide. It is seen that prevalence increases during the first four decades of life and does not progress over the following decades. Mostly up to 25% of patients with RP become legally blind in both eyes, rarely they lose total vision. Half or even more of patients have visual acuity of 6/12 or better in at least one eye. There is no known prescription practice cure for the disease at present, except for the dramatic visual recovery in patients who have undergone gene therapy or retinal chip implantation. Patterns of inheritance in RP are autosomal dominant, autosomal recessive, X-linked recessive or isolated. The age of onset and the severity varies, depending on the inheritance pattern. Autosomal dominant RP has a milder clinical picture, with good central vision even till the sixth decade. The most severe and the least common in India is the X-linked recessive form, in which affected males have severe visual impairment by the fourth decade.

RP usually affects only the eye, but rarely it can occur with a systemic association. In Usher syndrome it is very important to counsel the patient that sensorineural deafness may not progress, as much as the visual deterioration. In Kearns-Sayre syndrome there can be associated external ophthalmoplegia and heart block. Bardet-Biedl and Laurence-Moon syndromes are associated with mental retardation, hypogonadism, polydactyly and obesity. Vision loss in RP is commonly due to the progressive retinal degeneration in such cases, cystoid macular edema and posterior subcapsular cataract.

The photoreceptor and RPE function loss in RP progresses posteriorly and can lead to loss of visual acuity from involvement of the macula and constriction of the field of vision. Macular degeneration is the most common cause of visual loss in macular disease which affects RP. Patients who have a long duration are those who have widespread peripheral degenerative changes, have macular atrophy of the RPE and mottled angiographic transmission defect.

The pathogenesis of cystoid macular edema (CME) in RP is not known; the proposed mechanisms are blood-retinal barrier breakdown and retinal edema secondary to chronic low-grade intraocular inflammation.

About 50% of the patients develop posterior subcapsular cataract (PSC), the cause of which is speculated to be low-grade inflammation.

RP patients have a higher prevalence of myopia, astigmatism and higher-order wavefront aberrations. They may also have floaters, more commonly due to vitreous degenerative changes like vitreous cells, clumps and posterior vitreous detachment. The incidence of RD in RP is the same as that of the myopic population. To note optic disc pallor in RP patients does not necessarily mean optic atrophy, as a matter of fact inner retinal layers are preserved till the late stages of the disease. Thus, optic disc atrophy cannot be considered a common cause for visual loss in RP. Examination of the optic disc for glaucomatous changes poses a challenge but incidence of open-angle glaucoma is the same as in the general population.

A large double-masked, randomized trial showed that there was no improvement in the visual field or visual acuity in patients who received long-term daily oral vitamin A (15,000 IU/day) vs. controls.^[2] But the study also revealed a slower rate of decrease in cone electroretinogram (ERG) amplitude in those who were receiving vitamin A vs. controls over a four- to six-year period. This has led to the recommendation by some professionals that vitamin A may be offered as a treatment to slow the progression of macular degeneration. However, this study has been quite a controversial one and therefore is now never a part of any recommendation.

An Omega-3-rich diet containing docosahexaenoic acid can further slow disease progression.^[3] A diet like this would call for one to two 3-ounce servings per week of oily fish such as salmon, tuna, herring, mackerel or sardines. Researchers estimated that the combination of vitamin A plus this diet could provide almost 20 additional years of useful vision for adults who start the regimen in their 30s. Again this is still a point of contention.

Some rare forms of RP have also yielded to nutritional treatment, including hereditary abetalipoproteinemia (Bassen-Kornzweig syndrome) and hereditary phytanic acid oxidase deficiency (Refsum's disease). Decrease in vision due to development

of CME in RP patients can be reversed with the use of systemic carbonic anhydrase inhibitors like acetazolamide. Daily oral acetazolamide was shown to result in decreased central macular thickness and CME on serial Optical coherence tomography (OCT) examinations.^[4] Risks associated with cataract surgery in patients with RP include progression of outer layer macular retinal atrophy, macular edema, phototoxicity, posterior capsular opacification and anterior capsular phimosis. Visual acuity, however, does improve after cataract surgery, there is more chance of posterior capsular opacification compared with the normal eyes but the incidence of macular edema is comparatively lower.^[5]

Low-vision devices can be very useful to RP patients who have so many disabilities in doing their everyday chores and activities. RP patients often develop a scanning pattern with distance vision in order to adapt to a diminishing visual field. Functional vision is greater than a visual field test would measure.

Dark-adaptation difficulties can be overcome by using a simple penlight for searching in dark cabinets or finding a keyhole at night, for reading and writing near visual aids such as lighted magnifiers and closed-circuit televisions are useful.

But considerable progress has been made in the genetics of RP, and treatment modalities are being studied in both animal models of retinal degeneration and humans, giving retina specialists and their patients reasons for hope.^[6]

Gene therapy involves replacement of defective genes with functional ones. The most promising approach would involve using vectors such as recombinant adeno-associated virus to deliver new genes to the retina, therefore it has concerns for risk of complications when a virus is injected into the eye and even the safety of vectors. With gene therapy we would protect the retina before injury occurs to the retina.^[7] Two independent groups in the UK and US have successfully treated patients with Leber congenital amaurosis. Molecular genetic technology is now able to identify many genetic mutations causally linked to RP. More than 40 genes have been identified to be causative of RP, if we would know the type of mutation we might be able to give our patients more accurate diagnosis, genetic counseling and participate in clinical gene therapy trials affecting the particular gene.

Treatment with specific growth factors may be a way to slow RP progression in people with mild or later-onset disease as suggested by animal models of retinal degenerations. Currently, research includes ciliary neurotrophic factor encapsulated cell technology but seems to be controversial.^[8]

Stem cell research is currently being undertaken for those patients who have significant vision loss, someday degenerated photoreceptors might be replaced by stem cell transplantation.

Retinal implants are being developed and implanted at various centers in the world. There are two types of implants, either epiretinal or subretinal. The basic concept is microchip implantation of electrodes on the retina or below it. They are stimulated by light, converting them to electric signals. Then these electric impulses induce biological visual signals in the remaining functional retinal cells and which are transmitted through the optic nerve to the brain. Drs. Mark Humayun and Eugene DeJuan at the Doheny Eye Institute (USC) were the original inventors of the active epiretinal prosthesis and demonstrated proof of principle in acute patient investigations at Johns Hopkins University in the early 1990s along with Dr. Robert Greenberg. In the late 1990s the company Second Sight was formed by Dr. Greenberg along with medical device entrepreneur Alfred E. Mann to develop a chronically implantable retinal prosthesis.^[9] The epiretinal approach concept is used by IMI Intelligent Medical Implants using the concept of a learning retina implant.^[10-12] One of the principal investigators is Dr. Gisbert Richard and his team with the IMI system. We as ophthalmologists should give these patients a positive ray of hope as well address their clinical situation. I always tell them that the researchers around the world are relentlessly working for them and some cure already rising on the horizon would surely land in the clinical practice arena in the near future.

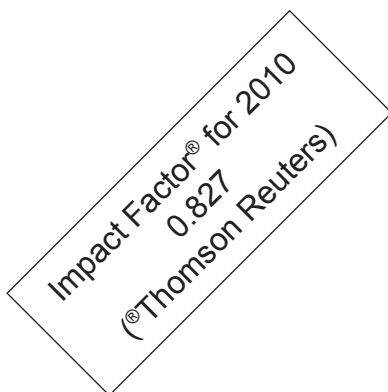
EDITORIAL PEARLS – I would like to bring forth attention to basics of two fundamental concepts in Medical Journals, i.e. Peer reviewed journals and indexed journals, what's the difference?

Peer reviewed journals are the journals reviewed by qualified individuals within the relevant field. It is a process of self-regulation, employed by physicians or surgeons to maintain standards, improve performance and provide credibility to the journal.^[13,14]

Indexed journals are the journals certified by *Index Medicus*. *Index Medicus* (IM) was initiated by John Shaw Billings, head of the Library of the Surgeon General's Office, United States Army. This library later evolved into the United States National Library of Medicine (NLM), which continues publication of the Index. From 1960 to 2004 the printed edition was published by the National Library of Medicine under the name *Index Medicus/Cumulated Index Medicus* (IM/CIM).^[15] The last issue of *Index Medicus* was published in December 2004 (Volume 45). The stated reason for discontinuing the printed publication was that online resources had supplanted it,^[16] most specially PubMed, which continues to include the *Index* as a subset of the journals it covers.^[17]

Journal impact factor is from Journal Citation Report (JCR), a product of Thomson ISI (Institute for Scientific Information). JCR provides quantitative tools for evaluating journals. The impact factor is one of these; it is a measure of the frequency with

which the "average article" in a journal has been cited in a given point of time. Our current impact factor is 0.827 for IJO.^[18,19]



Citation indexing makes links between books and articles that were written in the past and articles that make reference to ("cite") these older publications. In other words, it is a technique that allows us to trace the use of an idea (an earlier document) forward to others who have used ("cited") it. The evidence that we take as indicating this "relationship" between earlier research and subsequent research are the references or footnotes or endnotes (citations) in the more recent work.^[20] We have introduced author mapping, which would print a map of the world and actually pin down various parts of the world from where authors are contributing. In addition we have introduced authors' instructions, reference checking facility and a host of other features.

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