The British Association of Retinal Screening

"Working to Support Professionals Involved in Retinal Screening for People with Diabetes"

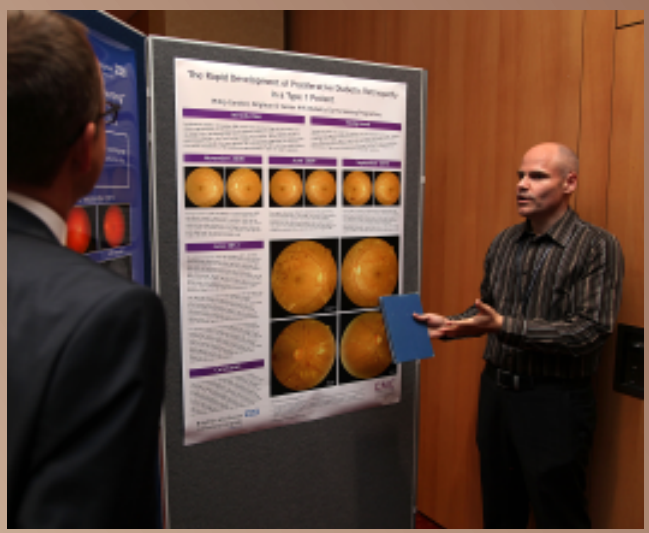
Since 2001, the British Association of Retinal Screening (BARS) has been the UK's professional organisation for those who provide retinal screening services for people with diabetes. We offer education, representation and support to a wide range of professionals involved in diabetic retinopathy screening, and our members include retinal screeners, graders, administrative and failsafe staff, programme managers, optometrists and ophthalmologists – in fact anyone with a professional interest or involvement in diabetic eye screening.

Founded by Professor Roy Taylor and Lillian Lovelock from the Newcastle-upon-Tyne diabetic retinopathy screening programme, BARS is a not-for-profit organisation, run by an elected council of volunteers who are drawn from a range of roles within eye screening programmes across the UK, and we aim to support our members via regular conferences, meetings, training days and educational activities. The association has assisted those studying for the City & Guilds Diploma in Diabetic Retinopathy Screening by offering tutorial days for individual units, while administrative staff have benefitted from our popular Failsafe Discussion days. Programme managers and clinical leads can access our online support forum, and we organise regular programme managers' meetings, often with input from the national team. BARS has a representative on the National Grading Resources Advisory Group, giving a voice to BARS members on important national issues such as the Grading College and online Test & Training system.

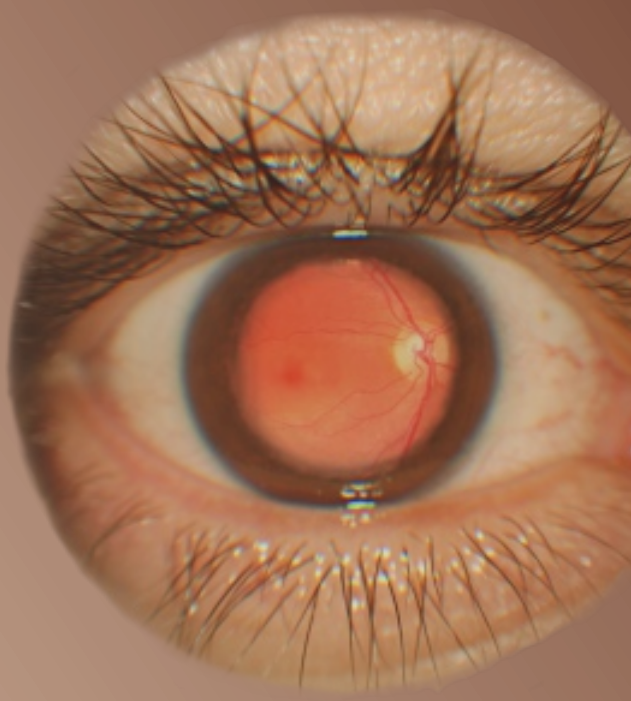
Since 2014, BARS has been responsible for publishing the Diabetic Eye Journal, which is produced twice a year, and distributed to all diabetic eye screening programmes and major hospital eye services across the country, providing a much needed platform for practitioners to share their experience, expertise and research with fellow professionals.

For the first fourteen years, the work of the association was funded in part by an annual subscription paid by all members, but the world of diabetic eye screening has changed considerably over that time, and in 2015, BARS took the important step of changing the association's constitution in order to abolish the membership fee. A wide range of roles - and accompanying variations in salary - now exist within the profession, and BARS aims to be representative of all those working in the field, regardless of personal circumstances. It was therefore decided that BARS membership should be freely available to all, enabling the association to be truly representative of all those involved in retinal screening.

BARS members have the chance to attend a variety of events throughout the year, providing an opportunity to network with others in similar roles, share good practice, and receive the education and support they need to improve or expand their skills. Last year's annual conference in Birmingham was a huge success, and featured talks from leading experts in their fields on topics ranging from retinal vein occlusions and intravitreal therapies, to sleep apnoea, new treatments and pregnancy in diabetes. Other speakers tackled diverse subjects such as improving uptake, getting the most from your intergrader reports and effective communication with deaf patients, and the conference also featured case studies, poster presentations and a photo competition.



This year's BARS conference will take place in Bristol on 24th and 25th September 2015, with a number of high profile speakers being lined up to share their knowledge and experience. These include consultant ophthalmologist, Rehna Khan, who will be speaking about diabetic macular oedema, and Paul Galsworthy from the Birmingham Heartlands DESP, who will be sharing his experiences with the LEOPARD Project to establish a diabetic retinopathy screening programme in Ethiopia.

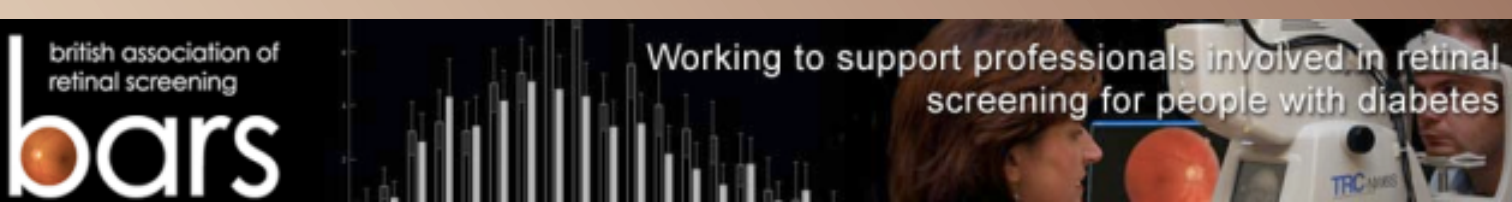


In addition to attending conferences, being a BARS member gives you the chance to have your say about all the services we offer. BARS exists to represent its members, and we do our best to deliver whatever support and education you need. Joining the association gives you that opportunity to directly influence our actions, and request the services that will help you most within your role. If members ask for something, we do our best to provide it!

Members are entitled to attend the association's AGM which is held each year at our annual conference, and can vote on a range of proposals to help shape our future. As vacancies arise, members have the opportunity to stand for election to the BARS council and take a hands-on role in running the association, while those not wishing to stand can vote for those who do, using our web-based online voting system.

If BARS isn't currently offering what you want, then make your voice heard by becoming a member and telling us what we can do for you. Our future plans include expanding our range of meetings and training days to include staff groups and topics not previously covered, but we need your input to tailor these events to members' needs.

To find out more about the British Association of Retinal Screening and to become a member, please visit our website at *www.eyescreening.org.uk* or connect with us via our Facebook page at *www.facebook.com/eyescreening*



Retinitis Pigmentosa

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Inherited retinal disorders are a heterogeneous group of conditions, many of which present in childhood. They now represent the commonest cause of visual impairment registration in the working-age population and the second commonest cause in childhood in the UK. Most occur as an isolated condition affecting the retina, however they can rarely be associated with other systemic abnormalities. An approach to studying these conditions is to group them on the basis of the predominant photoreceptor class first affected (rod or cone), and whether the disorder is stationary or progressive. A stationary disorder is known as a dysfunction syndrome and a dystrophy would refer to a progressive disorder.

The rod-cone dystrophies are characterised by greater and earlier rod system involvement compared to cone system, with Retinitis Pigmentosa (RP) being the commonest rod-cone dystrophy. There is progressive loss of rod photoreceptor function followed by loss of cone function with resulting severe visual impairment. Retinitis pigmentosa is clinically and genetically diverse, affecting approximately 1 in 3000 people, with significant variation in disease presentation and progression both within and between families.

Symptoms

The onset of symptoms is variable but patients often present by late childhood or early adulthood. Typical visual problems experienced are difficulty seeing in the dark (nyctalopia) and constriction of the peripheral field of vision. These may result in unintended consequences such as falls or collision with objects.

In the early stages, affected individuals have normal central vision with scotomata in the periphery. These peripheral defects gradually coalesce resulting in a peripheral ring scotoma. As the condition advances, the affected individual is left with a constricted tunnel of central vision, often with a degree of sparing of a small peripheral island of preserved field temporally. Posterior subcapsular cataracts or macular oedema can occur causing further impairment of central vision. In sectoral RP, a mild form of RP with a relatively good prognosis, the lower nasal quadrants are commonly involved resulting in bilateral upper temporal field loss.

Fundus signs

Fundus appearance varies with the stage of RP. Typically there is increasing peripheral retinal 'bone spicule' pigmentation, optic disc pallor and retinal arteriolar attenuation over time **(Figure 1)**. The intra-retinal pigment deposition is due to the migration of RPE cells into overlying neural retinal tissue. Other findings may include vitreous cells, posterior subcapsular cataract, disc drusen, macular oedema and epiretinal membrane formation. Infrequently peripheral retinovascular changes similar to Coats disease are seen. Other less common findings are multiple white deposits scattered throughout the retina (retinitis punctata albescens).

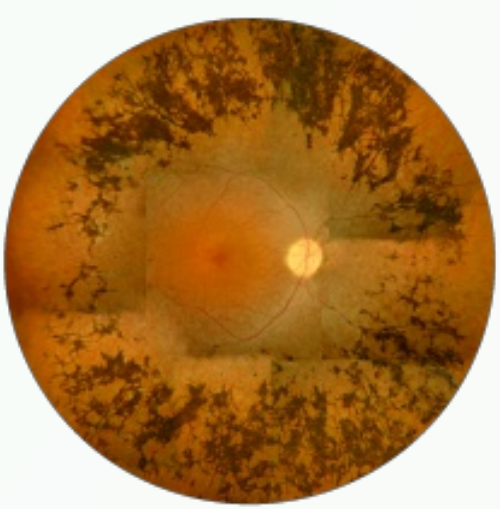
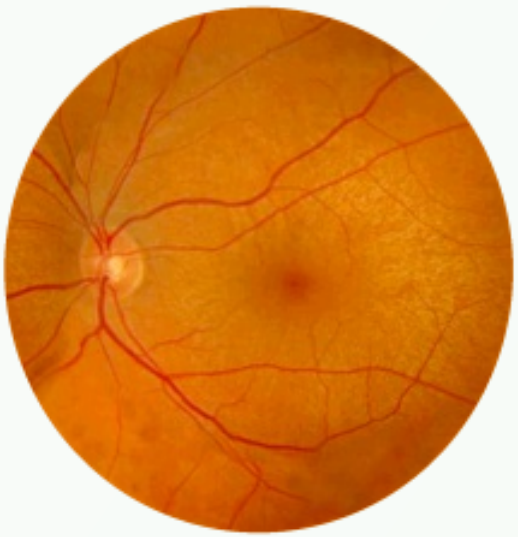


Figure 1 - Montaged colour fundus image of a patient with RP demonstrating the classic signs of peripheral retinal 'bone spicule' pigmentation, optic disc pallor and retinal arteriolar attenuation.

Figure 2 -
Montaged colour fundus image
of a female carrier
of XL RP demonstrating
a tapetal reflex
at the posterior pole.



The retinal phenotype for most forms of RP is arguably surprisingly similar given the genetic heterogeneity. There are however limited specific phenotypes commonly associated with various genotypes. For example sectoral RP with an autosomal dominant inheritance pattern is usually associated with rhodopsin gene mutations. Preserved para-arteriolar retinal pigment epithelium is seen in an uncommon autosomal recessive form of RP (RP12) and has been associated with CRB1 gene mutations.

Genetics

Retinitis pigmentosa can be inherited in an autosomal dominant (AD), autosomal recessive (AR) or X-linked (XL) manner.

Autosomal dominant RP (ADRP) is due to a mutation present on one allele. ADRP affects both sexes equally. A person with ADRP has a one in two chance of passing on the condition to their offspring. ADRP is milder and of later onset compared to AR and XLRP. Affected individuals may maintain reasonable central vision until the fifth or sixth decade despite having extremely constricted visual fields.

The commonest genes associated with ADRP are Rhodopsin (RHO), RP1 and PRPF31. There are more than 100 different mutations in the gene for Rhodopsin that can cause RP. Mutations in genes currently identified as causing ADRP are believed to account for 60-70% of ADRP.

Autosomal recessive RP (ARRP) also affects men and women equally. The mutation is present on both alleles of the disease-causing gene in ARRP. An affected person inherits one disease-causing allele from each carrier parent who themselves have normal vision. Parents who are carriers have a one in four chance of having an affected child with ARRP and a three in four chance of having an unaffected child. There is a one in two (or two in four) chance of the child being a carrier. All offspring of an individual affected with ARRP will be carriers. An affected individual is unlikely to have affected children (approximately 1% risk), unless their partner is a relative which significantly increases the risk. The clinical course is often severe with early onset of disease such that affected individuals may have marked constriction of visual field by their early adulthood and central visual loss by the third to fourth decades. However accurate prognosis is challenging given the marked heterogeneity both within and between families.

Mutations in more than 30 genes have been identified, accounting for 40-50% of ARRP. The commonest gene, USH2A, accounts for 10-15% of cases. Syndromic RP, including Usher Syndrome (RP with hearing impairment) is commonly inherited in an autosomal recessive manner.

X-Linked RP (XLRP) is caused by a mutation carried on the X chromosome. This is a severe form of RP with nyctalopia occurring in childhood, extensive field loss during teenage years, central visual loss in the twenties to thirties with progression to severe sight impairment often by the third or fourth decade. Males are primarily affected, although females as carriers can be mildly affected. A tapetal reflex at the posterior pole and / or mild retinal pigmentation can be seen in female carriers **(Figure 2)**. Infrequently female carriers may be severely affected in cases of skewed X inactivation. A female carrier has a 1 in 2 chance of having an affected son, and the same chance of having a daughter who is a carrier. An affected male cannot transmit XLRP to his sons, but all his daughters will be carriers.

Mutations in three genes have been identified in XLRP, RPGR, RP2 and OFD1. Sequence variants in RPGR are believed to cause approximately 75% of all XLRP, with more than 150 different mutations in the RPGR gene reported. RPGR mutations are usually associated with typical rod-cone degeneration. Deafness and respiratory cilia abnormalities have been noted in a small proportion of patients.

Clinical examination of family members, together with genetic testing and electrophysiological assessment can be useful in helping to determine the mode of inheritance for some patients with no clear family history. The genetic mutation could also occur de novo in a minority of cases.

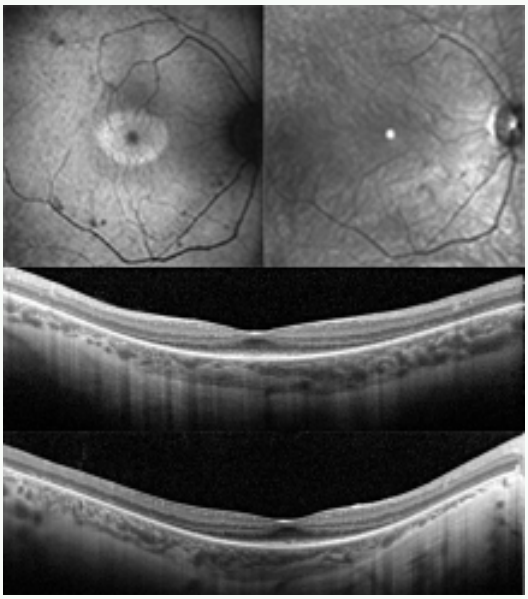
Electrophysiological Testing

These tests are a measure of retinal function by determining the electrical responses derived from the photoreceptors, retinal pigment epithelium, and inner retinal neurones. A measure of isolated macular or generalised retinal function can be obtained. They include the full-field electroretinogram (ERG) and the pattern electroretinogram (PERG). These can be performed in light and dark conditions – helping to compare cone and rod-driven responses respectively.

The full-field ERG detects electrical activity across the entire retina. In RP, the ERG shows a rod-cone pattern of dysfunction, in that rod-derived responses are more severely affected than cone-derived responses. There is marked variation in the severity of RP between individuals. The ERG may often be undetectable in the later stages of RP, or small residual cone responses may only be present. In mild or early RP, rod derived responses are reduced in amplitude and delayed; with the 30Hz cone flicker ERG also being delayed and reduced in keeping with generalised cone system dysfunction.

The PERG assesses macular function. The patient is required to look at an alternating checkerboard pattern. In early stages of RP, there may be minimal macular involvement (normal or minimally reduced PERG) despite an almost complete loss of the full-field ERG.

Figure 3 - Composite image of a male patient with XL RP. Top left shows a fundus autofluorescence (FAF) image with a parafoveal ring of increased autofluorescence – typically seen in patients with RP. Top right shows a fundus scanning laser ophthalmoscope image of the same individual. Middle and bottom images show vertical and horizontal optical coherence tomography scans respectively of the same patient taken through the fovea. The inner segment ellipsoid zone (ISe) is relatively intact at the central macula, with loss of the ISe in the peripheral macula. The outer nuclear layer thickness is also seen to progressively reduce from the fovea outwards. This region is collectively known as the transition zone and corresponds to the region of increased autofluorescence on FAF.



Management

Most forms of RP are not amenable to specific treatment. However in some rare disorders such as Refsum disease and, abetalipoproteinaemia where the biochemical basis is known, specific dietary restriction and treatment may slow the deterioration in retinal function.

There is currently no cure for RP. Management revolves around accurate diagnosis, specialised genetic counselling, provision of information on prognosis, and strategies to improve the use of residual vision. Educational and social support are also very important. Management is best provided as part of a specialised multidisciplinary service, though the availability of such services vary throughout the UK, with some areas having no access at all.

Treatment options are limited and are focused on visual rehabilitation including the use of low vision aids, specialised computer software and, orientation and mobility training. The provision of support for schooling and in the workplace is also very important. In some centres, eye clinic liaison officers (ECLOs) are an important source of support and provide advice on accessing services.

One randomised trial undertaken in the USA demonstrated a marginal effect of high dose vitamin A on the rate of decline of cone flicker ERG however no beneficial effect was found on visual acuity or field loss. This form of treatment has not gained widespread acceptance and the majority of retinal specialists do not routinely recommend Vitamin A supplements to their patients.

A healthy balanced diet rich in fruit and green vegetables (rich in lutein) is likely to be beneficial. It is also possible that oily fish rich in omega-3 may be beneficial. Smoking and smoky environments should be avoided. Excessive exposure to bright sunlight should be avoided. High quality UV-A and UV-B blocking sunglasses and a hat with a broad rim should be considered in bright conditions.

There are supportive measures that can be provided to aid visual difficulties faced by patients. Tinted lenses may help to improve visual contrast and to reduce glare. Significant refractive errors should be corrected. Access to appropriate magnification aids, including specialist low visual aid assessment is helpful. A bright light source to illuminate reading material and computer software for enlarging print and to convert print into spoken word is also available.

Macula oedema may develop as a complication of RP. Treatment with topical dorzolamide, oral acetazolamide, orbital floor or intravitreal steroids, or intravitreal anti-VEGF agents can be considered in a step-wise manner. Cataract formation can cause additional visual loss, which can be successfully addressed with cataract surgery.

Despite the current lack of effective treatment for RP, the ophthalmology team has an important role to play in the management of both the affected individual and the family. Upon establishing the diagnosis it is important that the individual, or parents and the child are given a full and sympathetic explanation. They can be reassured that most affected children can successfully complete their education at a normal school as central vision is often preserved until later on in the course of the disease. Parents are often concerned that other offspring may be at risk of developing the disease, thus genetic counselling should be offered with appropriate examination of other family members. Genetic counselling allows the individual with RP and their relatives to understand the type of RP in the family and the risk of passing on the condition to their offspring.

Future treatment options

Research is being conducted to investigate multiple treatment avenues for RP and other inherited retinal conditions, including gene therapy, stem cell therapy, neuroprotective approaches and artificial vision – with clinical trials on-going or planned in all of these areas. Some of the research is aimed at treating specific genetic mutations, whilst other research efforts are studying potential therapies that can be used in a broader range or potentially all RP types. It is possible that these potential therapies may be more valuable in combination for example by combining gene therapy or stem cell therapy with neuroprotective growth factors. These interventions may be applied sequentially, for example pharmacological approaches may be beneficial at the early stages of the disease and stem cell therapies at later stages. Further detailed information on these research avenues can be obtained from the websites of Retinitis Pigmentosa Fighting Blindness or the Foundation Fighting Blindness.

Conclusion

Inherited retinal disorders, of which RP is the commonest, are now the most common cause of certifiable severe sight impairment among working age adults in England and Wales. Given its prevalence, affected individuals may present to diabetic retinopathy screening services. Screeners should thereby be familiar with retinitis pigmentosa and the associated symptoms and signs.