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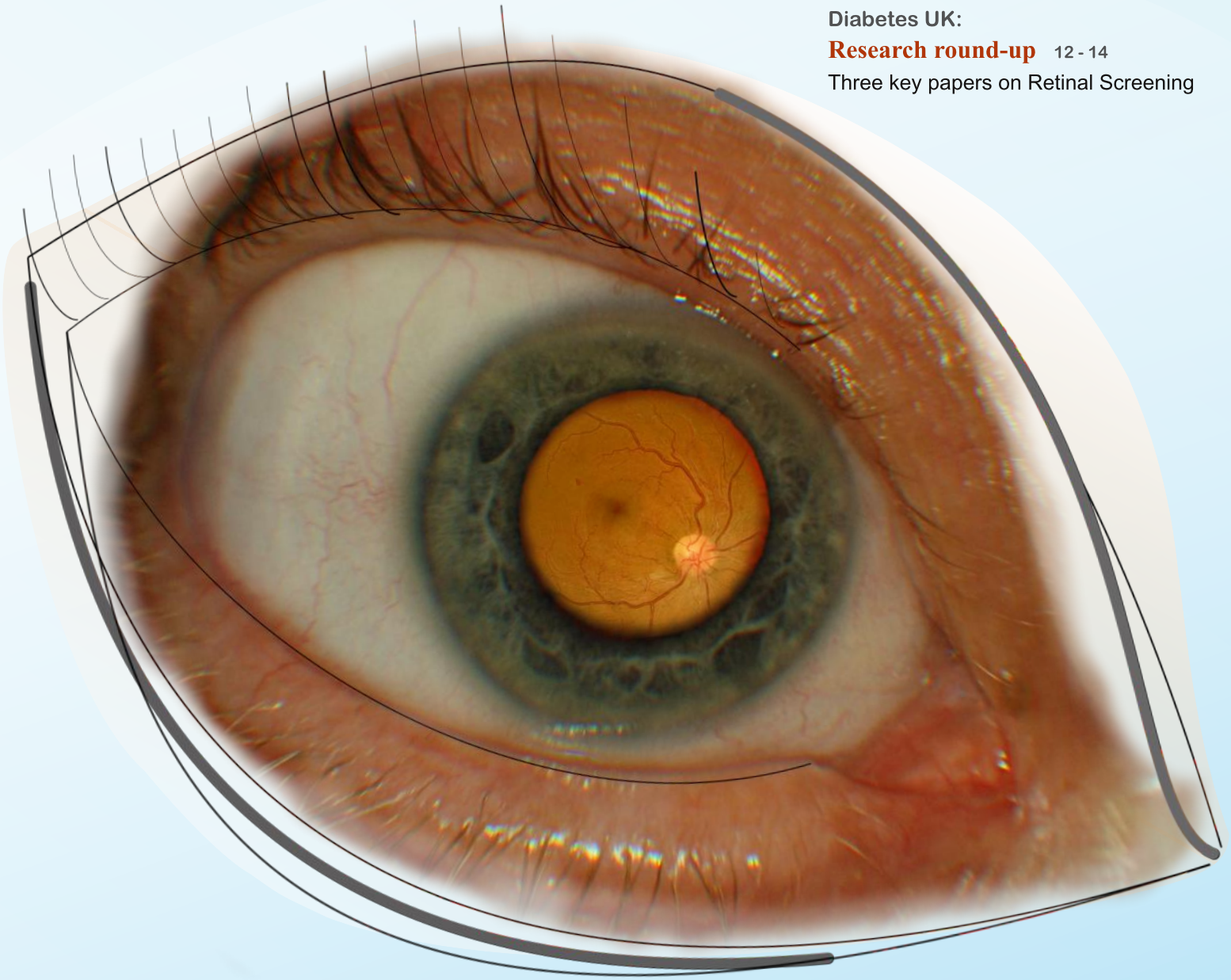

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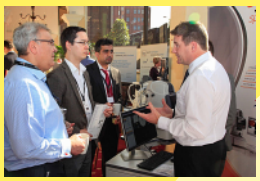


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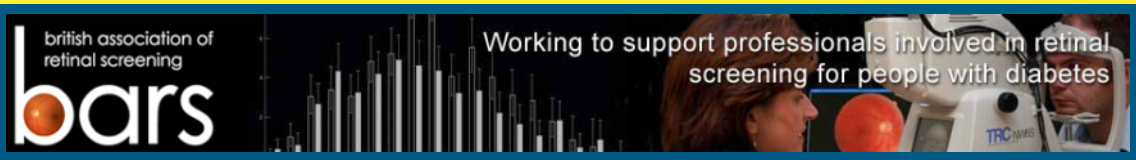

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DiabeticEyeJournal

FROM THE EDITOR

Are the treatments for Diabetic Retinopathy as effective as they could be? Or is there more that could be done within the National Health Service to minimise the deterioration and progression of this debilitating eye disease?

We will attempt to answer these questions in this September issue of DEJ in the article by Razia Amin who is the Diabetes Advanced Nurse Practitioner at Moorfields Eye Hospital in London. She has been working closely with their Medical Retina department for over a year, supporting patients with diabetes who are undergoing eye treatments for retinopathy. Could integration between departments increase the success rate in treating and stabilising diabetic retinopathy and become a model for all Hospital Eye Service departments? More data is needed, but the work done so far is very promising.

Hyperlipidemia and High Blood Pressure, possible exacerbating factors in Diabetic Retinopathy, are also contributing factors to the occurrence of Retinal Vein Occlusions. In a second contribution from Moorfields Eye Hospital, and by our new BARS president Dr Tunde Peto, we are exploring RVO types, their management and current treatments in the section on Other Lesions.

Dr Andrew Brown who is the Clinical lead for Staffordshire DESP shares with us part of his PHD study about Characteristics and Outcomes of Referable Diabetic Maculopathy, the topic that many programmes and HES departments are very familiar with partly due to the increased pressure of rising numbers in referrals.

And there is much more to explore in this September issue including our new section about 'Screeners in Diabetic Eye Careers', which might inspire you to share your journey within DES careers with our readers - so do get in touch.

We hope this varied mixture of articles will not only be informative but also inspiring, and don't forget that we are very interested in your valuable feedback. Have a nice read!

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Diabetic Retinopathy Eye Disease

Main author: **Razia Amin** Diabetes Advanced Nurse Practitioner, and Co-author: **Rahila Bashir**, Senior Grader at the Reading Centre, both at Moorfields Eye Hospital London

Introduction

Diabetic retinopathy is a common and serious microvascular complication of diabetes. Nearly all patients with Type 1 diabetes and greater than 60 per cent (%) of patients with Type 2 diabetes will have some form of retinopathy a decade after developing diabetes (1,2).

The financial cost of diabetes annually is £9.8 billion, which is around 10% of the National Health Service budget and 80% of these costs are spent on largely preventable complications (3). With the increasing prevalence of diabetes, combined with an ageing population and increased life expectancy, it is anticipated that these costs will soar in the future.

In addition, the cost of complications to the individual with diabetes is immeasurable. Diabetic retinopathy is a major cause of severe visual impairment and may affect various aspects of life such as having to spend lots of time at medical appointments, losing the ability to drive or work and the loss of independence, all of which can greatly compromise quality of life. People with diabetes are also more likely to suffer from anxiety and depression compared to people without diabetes (4).

Development and Progression of Diabetic Retinopathy

The Diabetes Control and Complications Trial (DCCT) in people with Type 1 diabetes (5) and the United Kingdom Prospective Diabetes Study (UKPDS) in Type 2 diabetes (6) clearly demonstrated the benefits of improving glycaemic control. Each 1% reduction in mean glycated haemoglobin (HbA1c) was associated with a 37% reduction in microvascular complications, including retinopathy. Achieving an HbA1c of 7.0% (53 mmol/mol) greatly reduced the risk of development and progression of these complications. The UKPDS trial provided further evidence that tight control of blood pressure, mean measurement of 144/82 mmHg compared to 154/87 mmHg, was associated with a 34% reduction in the rate of progression of diabetic retinopathy (7).

Education and Diabetes Self-Care

People with diabetes spend on average three hours a year with a healthcare professional (8). They carry the responsibility for the management of their condition the remainder of the time and have to endure the demands of multiple self-care behaviour on a daily basis. This may include testing blood glucose levels and injecting insulin several times a day, adhering to drug regimens, and balancing their diabetes treatment, dietary intake and physical activity to maintain blood glucose levels within an acceptable range. Therefore education and support are essential, to help individuals to increase their knowledge and understanding and develop the skills and confidence necessary to enable them to self-manage this complex and challenging condition effectively.

In the author's experience many people with diabetes who attend medical retina clinics are unaware of basic information such as what HbA1c is, their last HbA1c test result, and general targets for HbA1c, capillary blood glucose, blood pressure and cholesterol. Structured education is recommended for people with Type 1 (9) and Type 2 (10) diabetes. However, there are major gaps in the training and support available for people with diabetes. A recent report found that only 15.9% of people newly diagnosed with diabetes were offered access to a structured patient education course and of those only 3.4% actually attended one (8). Structured diabetes education tends to be delivered to groups of patients. Whilst the benefits of group education are many, it may be less suitable for some patients in areas where there are diverse populations with high cultural and language variations.

Medical Retina Clinics

A high number of patients who attend medical retina clinics have diabetes. The aim of the ophthalmology team is to reduce the risk of progression of diabetic retinopathy and improve patient outcomes. To achieve this, patients require support to manage systemic risk factors, primarily blood glucose, blood pressure, and also cholesterol which is important to reduce the risk of cardiovascular disease.

Due to busy clinic lists and limited time, it is difficult for ophthalmic clinicians to address the additional care needs of diabetes patients and deal with the diabetes management issues that may have influenced the development of retinopathy. The need for diabetes input for patients was recognised by the medical retina service at Moorfields Eye Hospital (MEH) NHS Trust and this resulted in the creation of a new diabetes advanced nurse practitioner (ANP) post, which was taken up by the author in February 2014.

The Diabetes Advanced Nurse Practitioner Role

At present, the diabetes ANP at MEH covers medical retina clinics at the main hospital site in London and at satellite clinics in Northwick Park and Ealing.

Due to the pressure on health services, appointments for review following referral to both general practitioners and specialist diabetes services may take some time. Therefore, the diabetes ANP role allows patients an opportunity to access education and support to enhance their diabetes management skills while they attend their eye clinic appointments. This service is provided in addition to their usual diabetes care. It also allows for opportunistic diabetes care as some patients who attend the medical retina clinics have been lost to diabetes follow-up and some may not even be in any system of health care. This may represent an opportunity to reconnect patients with their local diabetes team and establish the important link between primary and secondary care.

Helping patients to manage their diabetes requires a truly holistic approach. The barriers preventing them from achieving control of their diabetes may be due to a variety of physical, psychological or social factors rather than a lack of knowledge and understanding of their diabetes.

Reviewing Diabetes Care

Diabetes ANP consultations with patients are on a one-to-one basis and involve family members or carers where possible. Due to the multitude of nationalities and language variations in the area, language translators to aid communication are often required.

The main focus initially is information gathering and getting to know the patient and this may take some time. **As well as identifying medical history, the following are some examples of information obtained during assessment:**

- Social – family, relationships, support networks
- Psychological – any concerns, issues the patient wishes to address regarding diabetes management, their understanding of the situation and the development of diabetes complications, motivation to improve diabetes control, gaps in knowledge and skills, learning ability
- Lifestyle – dietary intake, activity levels, weight, employment and work schedule, driving, smoking, alcohol intake, whether the patient experiences any hypoglycaemia, how hypoglycaemia is managed, whether home blood glucose monitoring is carried out, blood glucose patterns, the times of day blood glucose levels are too high or too low
- Medication and insulin – understanding of how treatments work, any side effects experienced, adherence, practical aspects of administering insulin, suitability of equipment used, ability to administer correct doses if vision is impaired, injection technique, whether injection sites are lumpy

Capillary HbA1c testing is likely to be carried out to assess glycaemic control, blood pressure is measured, urinalysis may be performed, and other blood tests or investigations may be requested.

Following assessment, any education and interventions are tailored to the individual needs of the patient, and realistic goals are set jointly involving the patient in the decision-making process. This may involve lifestyle changes and adjustments to medication. Lifestyle modification and changing unhealthy behaviour to improve health can be difficult and a real challenge for patients. Importantly, access to the diabetes ANP at MEH is available when some patients may be at a stage of being motivated to change their behaviour due to the diagnosis of their eye disease (11).

Following the consultation, it is essential to liaise with the patient's primary care and specialist diabetes team, and any other health care professionals involved in their care to share information and plans of care. Patients may also be referred to other services such as podiatry or for psychological care if the need is identified. Follow-up to review the patient and their progress is most often arranged to coincide with their next eye clinic appointment. However, depending on the timescale of the next appointment the patient is given the choice of returning earlier for review of their diabetes.

Complex Diabetic Retinopathy Case Study

This patient is a 26-year-old female with a 10-year history of Type 1 diabetes. Her last annual retinal screening appointment was in January 2015. She is on Levemir insulin once daily, Novorapid insulin at mealtimes, Ramipril for high blood pressure and Simvastatin for high cholesterol.

Initial presentation was at accident and emergency near the beginning of December 2015 (**Figures 1a** and **1b**). Visual acuities were bilaterally 6/12 (all visual acuities are measured with pinhole). The intra ocular pressure was 16 mmHg for the right eye and 18 mmHg for the left eye and has remained within the normal range throughout. The diagnosis was early proliferative retinopathy in the right eye with a query of active neovascularisation and stable maculopathy (National Screening Committee (NSC) grade R3A, M1S). For the left eye, the diagnosis was high-risk proliferative retinopathy with pre-retinal macular haemorrhage and clinically significant maculopathy (NSC R3A, M1A). Pre-retinal haemorrhages may clear spontaneously, but if not surgery may be required.

The patient required a baseline fundus fluorescein angiography (FFA) with urgent laser sessions for her left eye and possibly her right eye. A follow-up medical retina clinic appointment was booked for two weeks.

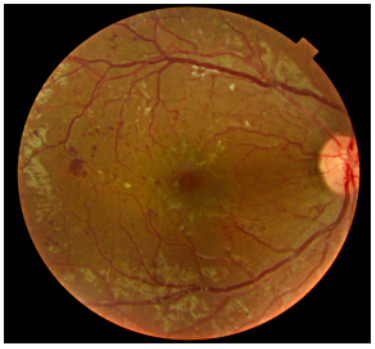

Figure 1a. (RE)

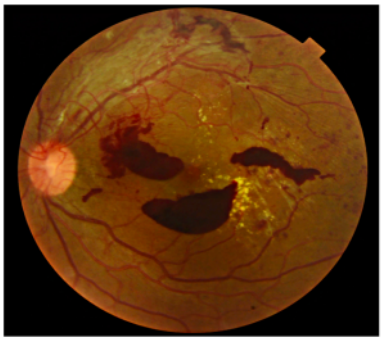

Figure 1b. (LE)

The patient attended her first appointment at the medical retina clinic near the end of December 2015 (**Figures 2a** and **2b**). Her bilateral visual acuity remained stable at 6/12. Each follow-up appointment involved a full slit lamp examination and optical coherence tomography imaging to monitor the stage of eye disease and any changes.

Outcome results stated no rubeosis but FFA confirmed bilateral proliferative changes. Grades showed bilateral high-risk proliferative retinopathy with no macular oedema (NSC R3A, M0). Pan retinal photocoagulation (PRP) was performed on the day for the left eye and booked at a future date for the right eye. Due to concerns in regard to the rapid progression of diabetic retinopathy, a carotid Doppler scan for further assessment was requested and venous blood samples for baseline blood tests for full blood count, erythrocyte sedimentation rate, C-reactive protein and urea and electrolytes were taken.

Blood pressure was 116/80 mmHg and capillary HbA1c test result was high at 99mmol/mol (11.2%) so the patient was referred to the diabetes ANP.

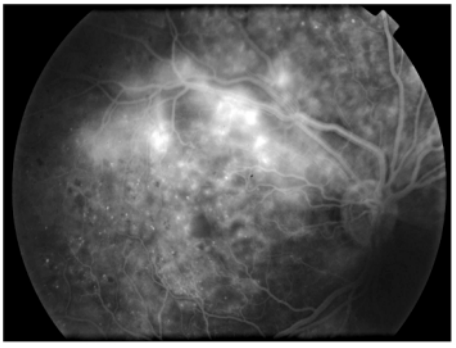

Figure 2a. (RE)

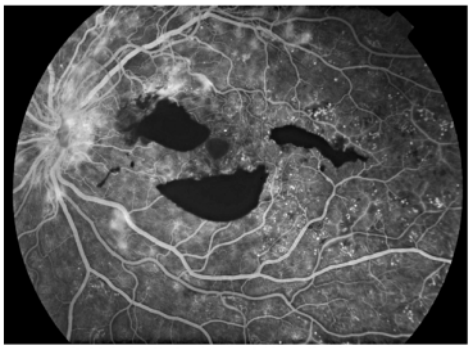

Figure 2b. (LE)

The second medical retina clinic appointment was two weeks later near the beginning of January 2016. This was a routine follow up visit. Patient presented with fallen visual acuity of 6/18 in the right eye and considerable deterioration to 6/60 in the left eye, likely due to the pre-retinal haemorrhage. Further PRP was performed to both eyes and an appointment arranged for review in a further two weeks. The patient attended for a third appointment near the end of January 2016 (**Figures 3a** and **3b**). Visual acuities were unchanged at 6/18 in the right eye and 6/60 in the left eye. At this visit she met with the diabetes ANP for support and a detailed review of her diabetes. The priorities of the patient at that time were to address the frequent hypoglycaemia she was experiencing and the challenges of managing her diet and exercise regime. Adjustment of insulin doses was discussed as well as strategies to manage the other issues.

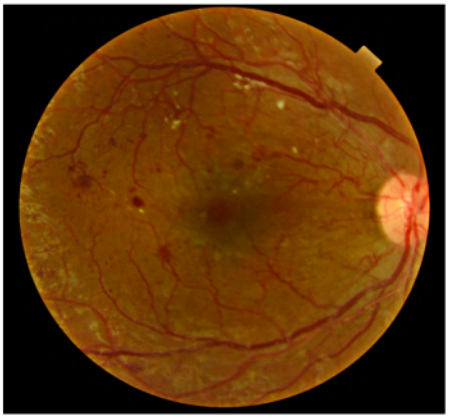

Figure 3a. (RE)

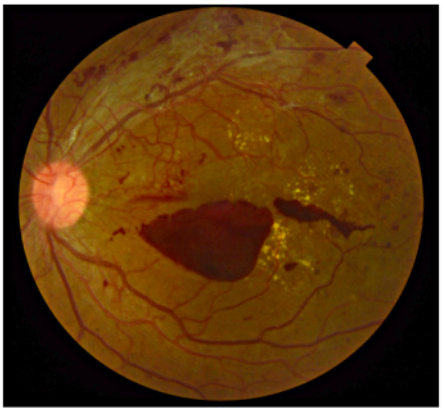

Figure 3b. (LE)

The fourth appointment was at the beginning of March 2016. Visual acuity was stable at 6/18 in the right eye and left eye had also improved to 6/18. She still had active proliferative disease and additional fill in PRP to the right eye was carried out on the day. An appointment was scheduled for additional fill in laser to the left eye in 2 weeks. Review by the diabetes ANP identified that the patient was making good progress with her diabetes control and home blood glucose test results were improving.

The patient visited for her fifth medical retina appointment mid-March 2016 (**Figures 4a** and **4b**). Visual acuities remained stable at 6/18 in both eyes. As planned, she received fill in PRP to the left eye and this time was booked for follow-up in 2 months to assess the response to the laser therapy and the status of diabetic retinopathy.

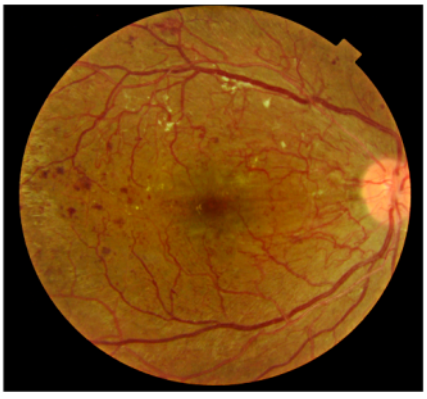

Figure 4a. (RE)

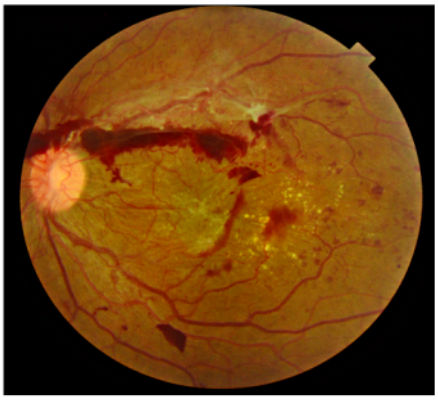

Figure 4b. (LE)

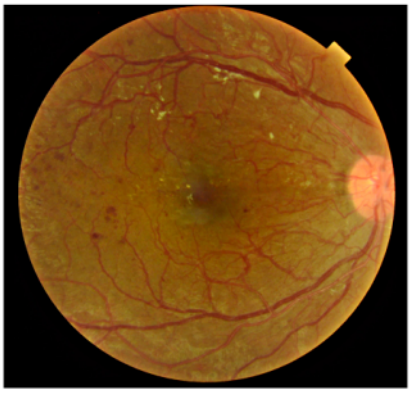

Figure 5a. (RE)

The sixth appointment was at the end of May 2016. Visual acuities remained stable at 6/18 in both eyes. The diabetic retinopathy grades for both eyes were high-risk proliferative retinopathy and not clinically significant diabetic macular oedema (NSC R3A, M1S). Further PRP laser was performed on both eyes and the diabetes ANP met with the patient again. She was still tweaking her insulin doses around her dietary intake and activities. Capillary HbA1c test result on the day had improved significantly to 74mmol/mol (8.9%). The patient was listed for a further review in 2 months.

The patient attended her seventh appointment in mid-July 2016 (**Figures 5a** and **5b**). Bilateral visual acuities remained stable at 6/18 and the grading results were the same as the previous visit (NSC R3A and M1S). Following the laser treatment, there appeared to be signs of regressing new blood vessels but continuation of some active vessels along the arcade, which required laser performance. Diabetic macular oedema was improving and the patient was placed on a 6-week review to decide whether indirect laser treatment would be required.

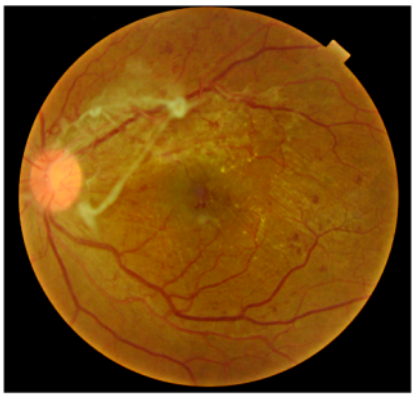

Figure 5b. (LE)

Further review by the diabetes ANP established that patient had been commenced on Metformin by her specialist diabetes team to improve insulin sensitivity. Hypoglycaemia was less frequent and she felt more confident in dealing with any episodes that did occur.

The eighth appointment was near the end of August 2016. Visual acuities had improved to 6/12 in both eyes. Diagnosis grade levels remain at high-risk proliferative retinopathy for both eyes (NSC R3A) with no macular oedema in the right eye (NSC M0) but with clinically significant macular oedema in the left eye (NSC M1A). The pre-retinal macular haemorrhage had cleared so surgery was not necessary. The patient was booked for the PRP laser clinic in 4 weeks. She was reviewed by the diabetes ANP and her HbA1c had improved to 72mmol/mol (8.7%). The advantages and disadvantages of using an insulin pump were discussed.

Conclusion

This case study is one of many examples that illustrate the seriousness of progressive diabetic retinopathy. It highlights the important role all members of the medical retina team play by providing the necessary care and treatment to help restore and maintain vision. This includes early diagnosis, appropriate investigations, timely treatments including laser therapy, regular review of progress, diabetes support and guidance to help achieve optimal control of systemic risk factors and manage lifestyle changes, all of which are essential in the management of patients with diabetic retinopathy.

The engagement of the patient with their care is crucial and much credit must be given to the patient for her cooperation and her commitment to attend frequent appointments for intensive treatment, her determination to work with the healthcare professionals and her exceptional efforts to improve her blood glucose control.

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Richard Poynter from the Medical Imaging Department at MEH for his help in providing the images.

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Research round-up

As the British Association of Retinal Screening (BARS) conference approaches, attention turns to the latest research in this area and how it can inform practice in the future. Each issue of Diabetes Update contains a digest of selected papers from Diabetic Medicine, which is Diabetes UK's academic journal. This autumn sees the publication of three key papers on retinal screening which Update's Editor, Dr Susan Aldridge, shares with us here.

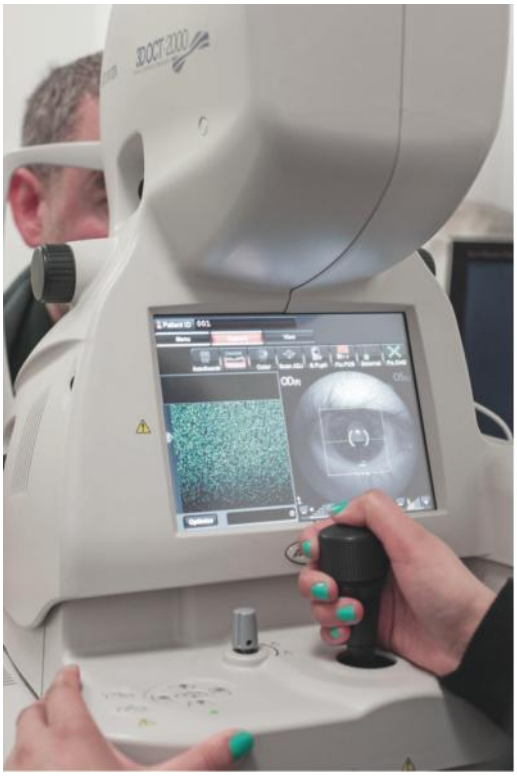

Image: NHS DESP

Timing of retinal screening, grading accuracy and the implications of extending screening intervals are all issues of interest to the screening community and will doubtless be hot topics at the BARS meeting. So it's particularly relevant to see *Diabetic Medicine* looking at all three in a recent issue. One paper shows that longer time intervals between diagnosis and screening increases the risk of retinopathy, the second looks at the cost effectiveness of extending the screening interval and the third reports on the accuracy of grading.

The danger of delay

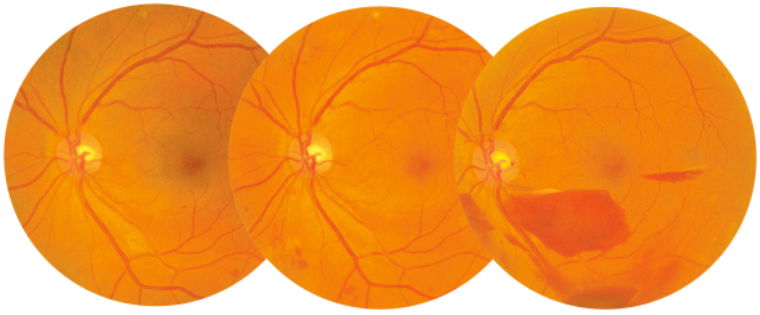

Image: NCL DESP NMUH NHS Trust

The first study, from Professor Peter Scanlon of the Gloucester Retinal Research Group and colleagues, looks at how age and time to first screening affect the risk of retinopathy. The analyses in this new study look at the relationship between time from diagnosis to first screen and the presence of retinopathy at that first screen. They also look at time from registration to screening by age group. The study data comes from national screening programmes in Wales, Scotland and Northern Ireland and from four local English programmes (Brighton, Derbyshire, Leeds and Staffordshire).

For those screened for the first time in 2011, of those who had a type and time of diagnosis recorded, the proportion of those with any retinopathy and with referable (including 'fast track') retinopathy increased with time from diagnosis to screening. For people diagnosed in 2010 or 2011, the proportion with any kind of retinopathy at screening was 18 per cent, while for those diagnosed before 1990 it was 67 per cent. The figures for 'fast track' referable retinopathy were 0.1 per cent and 8.7 per cent, respectively. Those diagnosed before 1990 and not screened until 2010 or 2011 were 19 times more likely to have referable retinopathy and 69 times more likely to have 'fast track' referable retinopathy.

Age, programme factors

The researchers also carried out an analysis of the influence of age of the individual upon the interval between registration and attendance at first retinal screening. This showed that those in the 18–34 years age group were the least likely to attend for screening in the first three years after registration. At two years, one in seven of those aged below 18 years or above 35 years had not attended screening. For the 18–34 year age group, the figure was one in four.

This study is the first to reveal that the young adult age group is more likely than other age groups to have a longer interval between registration and attendance at first screening, with a consequent greater risk of referable diabetic retinopathy being present at that first screen. This finding likely reflects the known propensity for non-attendance in this age group and that younger people are more likely to have Type 1 diabetes.

Image: NHS DESP

Another significant finding is that the risk of referable, including 'fast track', retinopathy increases among those who are not screened promptly following registration, independent of the duration of diabetes. Delaying screening for three years or more after registration increases the risk of proliferative retinopathy four-fold. The authors believe this indicates that there is a difference between those who delay and those who attend promptly. Further research is needed to understand the reasons for delay and whether screening programmes might be adapted to address these.

The findings suggest that the screening programmes should collect data on those who do and who do not attend over a 1, 2, 3, 4 and 5-year period. In addition to the date of registration, the date of diagnosis should also be routinely recorded. Without these data, the high-risk group who have never attended cannot be identified for follow-up. Finally, it was noted that some screening programmes seem better at attracting young people than others. Programmes have different approaches to delivery. It could be that those programmes with lower attendance could learn from those with higher attendance and make some changes.

Cost-effectiveness of extended screening

The NHS National Screening Committee has recently recommended extending the screening interval to two years for those who fall into a low-risk group. However, before such an approach is adopted, it is important to balance the financial gains to the health service against the potential risk of missing referable disease by extending the screening interval. Previous research on this issue has produced mixed results. Therefore, researchers in Scotland have carried out a study of the cost-effectiveness of adopting a risk-stratified approach to extended screen.

Modelling extended intervals

In this study, researchers used data from screening outcomes from the Scottish Care Information Diabetes Collaboration (SCI-DC), which captures more than 99 per cent of the diabetes population.

From this, they derived transition probabilities between non-referable and referable retinopathy. They used this to simulate the progression of a synthetic cohort through the screening pathway. Risks of visual loss associated with referable disease, health and social care costs associated with treatment and visual loss were incorporated into the model. The SCI-DC provided data for screening visits for 255,712 individuals who had had at least one screening exam between October 2005 and November 2011. This revealed 11,201 cases of referable background retinopathy (R3) or proliferative retinopathy (R4) and 25,333 cases of referable maculopathy (M2).

The study suggests that two-yearly screening would have little impact upon those with no diabetic retinopathy. For those who had no retinopathy on two consecutive screening occasions, there would be around 36 additional cases of moderate to severe loss of vision per 100,000 population over 30 years. Many of these would improve with treatment. The cost saving was estimated at £8.1m per year. The findings broadly support a move to biennial screening.

How accurate is screening?

Precision and accuracy of the grading of retinal screening photographs is key to the effectiveness of screening programmes. However, a direct estimation of misclassification rates has never been done before; screening accuracy is usually reported in terms of referable disease. Thus, Jason Oke and co-workers at the University of Oxford carried out a study to quantify the level of misclassification in a screening programme and what impact this might have upon the proposed plan to extend screening intervals.

Modelling misclassification

The researchers used longitudinal data on retinal photographs from 2005 to 2012 from the Gloucestershire Diabetic Eye Screening Programme and also risk factor data, such as HbA1c and duration of diabetes. The photos were all graded centrally by trained assessors. Where retinopathy of any level was detected, they were graded by a second assessor. There is no gold standard to represent the true state of retinopathy on each screening occasion, so statistical models were used to estimate this, using risk factor data and observed sequences of screening grade. The model relied on considering data across the whole cohort over the whole time period. The more inconsistencies – for instance, high retinopathy at one visit, none at the next – the higher the estimated misclassification rate. The model defined five levels of retinopathy/maculopathy ranging in severity from none observed to proliferative disease. These were treated as states in a hidden Markov model – an approach that has previously been used extensively to model disease progression and applied to cancer screening strategies. A hidden Markov model can account for the fact that the true state of disease might not always be reflected by the test – in other words, it accounts for misclassification.

Erring on the safe side

This study showed that misclassification is not uncommon, at 21.6 per cent of screening episodes, but occurs most often between no detectable retinopathy and background retinopathy in one or both eyes. The screening programme tended to err on the side of caution – over-grading and over-referring rather than under-grading and under-referring. Of course, under-grading could mean that individuals get their screening interval extended. A few of those who are misclassified as having no detectable retinopathy when they in fact have background retinopathy will go on to develop referable disease within two or three years. The findings of this study show that extending the interval for screening from one to two years will result in very few delays in referral.

This modelling approach could be applied to any screening programme and would save the costs of re-grading images.

[i] This is a digested version of Scanlon PH, Stratton IM, Leese GP et al (2016). Screening attendance, age group and diabetic retinopathy level at first screen. *Diabetic Medicine* 33: 904–911; Scotland G, McKeigue P, Philip S et al (2016). Modelling the cost-effectiveness of adopting risk-stratified approaches to extended screening intervals in the national diabetic retinopathy screening programme in Scotland. *Diabetic Medicine* 33: 886–895 and Oke JL, Stratton IM, Aldington SJ et al (2016). The use of statistical methodology to determine the accuracy of grading within a diabetic retinopathy screening programme. Diabetic Medicine 33: 896–903.

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