OUT OF SIGHT

A REPORT INTO DIABETIC EYE DISEASE IN AUSTRALIA

Baker IDI
HEART & DIABETES INSTITUTE

Centre for Eye Research Australia

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Aboriginal and Torres Strait Islander people should be aware that this document may contain images or names of people who have since passed away.

THE AUTHORING ORGANISATIONS

Baker IDI Heart and Diabetes Institute

Baker IDI Heart and Diabetes Institute (Baker IDI) is an independent, internationally renowned medical research facility, with a history spanning more than 87 years. The Institute's work extends from the laboratory to wide-scale community studies with a focus on the diagnosis, prevention and treatment of cardiovascular disease, diabetes and their complications.

Australia faces an ageing population and rapidly growing rates of chronic disease that threaten to significantly impair quality of life for millions of Australians. Cardiovascular disease, diabetes and obesity are the biggest health challenges facing our society today. Cardiovascular disease remains the leading cause of death in Australia while type 2 diabetes is projected to become the leading cause of disease burden for men and the second leading cause for women by 2023, mainly due to the expected growth in the prevalence of obesity. Baker IDI is well positioned to address these challenges, with multidisciplinary teams comprising medical specialists, scientists and public health experts all focussed on translating laboratory findings into new approaches to prevention, treatment and care.

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The Centre for Eye Research Australia

Centre for Eye Research Australia

The Centre for Eye Research Australia (CERA) is at the forefront of ophthalmic research in Australia. Our mission is to eliminate vision loss and blindness. CERA is designated as a World Health Organization Collaborating Centre for the Prevention of Blindness, the only such centre in Australia.

We are strongly positioned to rise to the challenge of an ageing society and rising rates of diabetes. It is an unfortunate reality that more than a third of people with diabetes will develop some form of diabetic eye disease (retinopathy) in their lifetime. In 2010, it was estimated 93 million people worldwide had some form of diabetic retinopathy.

CERA is ranked fifth globally by scientific output in ophthalmology. Our integrated approach to research brings together different disciplines, from basic science and genetics to clinical and health services perspectives, to tackle complex conditions in a holistic way.

Established in 1996 as a not-for-profit company, CERA grew out of the research activities of the University of Melbourne Department of Ophthalmology, the oldest specialist department of its kind at an Australian University, founded in 1963.

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EXECUTIVE SUMMARY

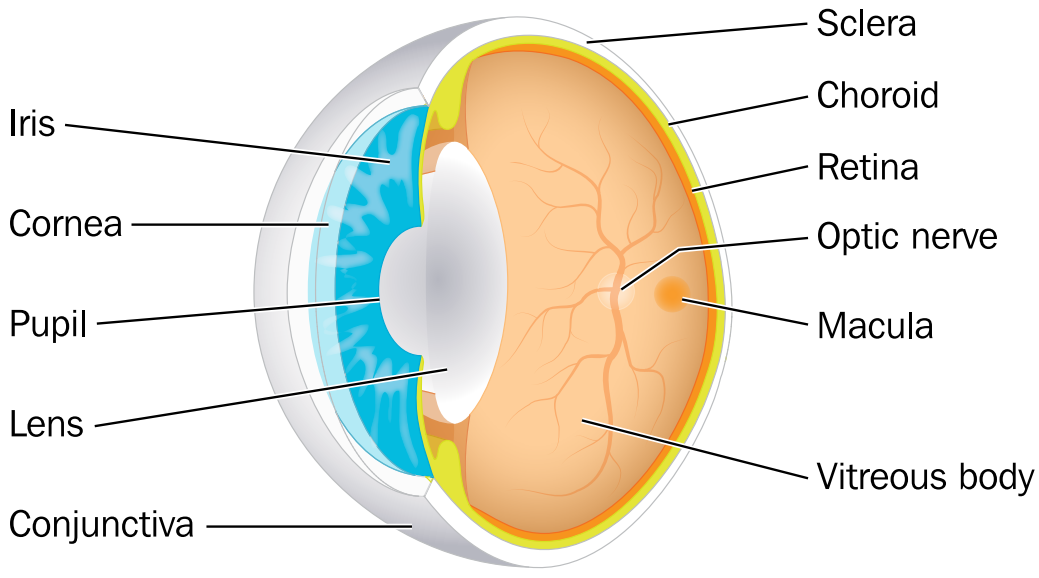
Diabetes and blindness

Diabetes affects approximately one million Australian adults. The number is expected to double by the year 2025, posing major public health and economic concerns. Diabetes may be associated with a number of serious complications, including heart disease, kidney failure, limb amputations and diabetic eye disease. Almost all those with type 1 diabetes and more than 60% of those with type 2 diabetes will develop diabetic eye disease within 20 years of diagnosis. Rising diabetes prevalence is expected to substantially increase the number of Australians impacted by diabetic eye disease and resultant vision loss.

Diabetic eye disease

Diabetic retinopathy is typically divided into two stages. Key features in the early, usually asymptomatic stage, known as non-proliferative diabetic retinopathy, include haemorrhages within the retina and the leakage of fluid into the retina. The later stage of diabetic retinopathy involves the growth of new, abnormal blood vessels on the retinal surface that may lead to severe vision threatening eye complications. Diabetic macular oedema occurs when the leakage of fluid from small retinal blood vessels affects the macula. Diabetic macular oedema is the leading cause of vision loss in diabetes.

A number of risk factors have been shown to contribute to the development of diabetic eye disease, and these involve a combination of environmental factors, such as lifestyle choices and blood sugar control and the influence of our genes.



How common is diabetic eye disease?

On average one in three people with diabetes will develop some form of diabetic eye disease. The Australian Diabetes, Obesity and Lifestyle study (AusDiab) showed that in people with diabetes, 19.3% had non-proliferative diabetic retinopathy, 2.1% had proliferative retinopathy and 3.3% had diabetic macular oedema.

Two earlier studies in Australia have also reported on the rates of diabetic eye disease in Australians. The Melbourne Vision Impairment Project showed that almost one-third (29.1%) of Australians with diabetes, over the age of 40 years had diabetic retinopathy, with most having non-proliferative diabetic retinopathy. One in 24 (4.2%) had proliferative retinopathy and 5.6% had clinically significant macular oedema. The Blue Mountains Eye Study from NSW found similar disease rates and found that one in three (32.4%) people aged 49 and over with diabetes had diabetic retinopathy and one in 23 (4.3%) had clinically significant macular oedema.

The public health impact and treatment of diabetic eye disease

The chances of suffering vision loss from diabetic eye disease can be significantly reduced by good control of diabetes, having regular eye examinations, and obtaining timely treatment. Currently, up to 50% of Australians with diabetes do not undergo eye examinations at the recommended frequency of every 2 years. Despite these results, Australia still lacks a nationwide diabetic eye screening system.

Besides the traditional treatment options for vision-threatening diabetic eye disease, namely laser therapy and surgery, new treatments have emerged. Injections of medications directly into the back of the eye have been shown to be effective in the treatment of advanced diabetic eye disease.

Conclusions

Diabetic eye disease is a leading cause of irreversible blindness in Australian adults. With the number of Australians affected by diabetes expected to double in the next decade, diabetic eye disease in Australia will continue to pose public health and economic challenges. Considering that prevention is key, we must develop and implement an effective diabetic eye screening program that is accessible to all Australians with diabetes. It is also essential that high-quality treatment of diabetes, including lifestyle advice, and appropriate medication for control of blood glucose and blood pressure, is provided.

DIABETES AND BLINDNESS

60 - 100%
WITH DIABETES

Almost everyone with type 1 diabetes and more than 60% of those with type 2 diabetes will develop some form of diabetic eye disease within 20 years of diagnosis.

DIABETES AND ITS CHRONIC COMPLICATIONS – A QUICK SNAPSHOT

Diabetes mellitus (commonly referred to as diabetes) is a disease characterised by elevated blood sugar (otherwise known as blood glucose) levels, caused either by a primary deficiency of insulin, a hormone that regulates blood sugar levels, or a resistance of the body to the effects of insulin. Approximately one in 10 people with the disease have type 1 diabetes. Type 1 diabetes typically develops in childhood or in early adulthood (although it can start at any age), and people with this disease require treatment with insulin (usually administered by injection) for life. The more common form of the disease, affecting nine out of every 10 people with diabetes, is type 2 diabetes. Type 2 diabetes is usually diagnosed in adulthood and managed with healthy lifestyle changes, typically in combination with tablets and/or insulin injections.

Diabetes is a chronic condition that may be associated with a number of serious health problems that are often referred to as diabetic complications. Some of the more common complications include:

- heart disease and stroke
- reduced kidney function (nephropathy) and kidney failure
- blood vessel disease affecting the limbs (peripheral vascular disease) that may lead to limb amputation
- nerve damage that typically involves the feet (peripheral neuropathy) and can lead to amputation or damage to the nerves that regulate blood pressure, heart rhythm and gut function (autonomic neuropathy)
- diabetic eye disease characterised by damage to the small blood vessels that supply the retina – the nerve tissue within the eye that is responsible for vision (diabetic retinopathy).

The risk of developing diabetic complications increases with the duration of diabetes and is also influenced by long term blood glucose and blood pressure levels. Diabetic eye disease is one of the most common complications of diabetes. It is reported that almost everyone with type 1 diabetes and more than 60% of those with type 2 diabetes will develop some form of diabetic eye disease within 20 years of diagnosis with diabetes[1].

> “Diabetic eye disease is one of the most common complications of diabetes.”

THE RISE AND RISE OF DIABETES – A LOOMING PUBLIC HEALTH CRISIS

The rapid population growth that is expected in the coming decades means that many more Australians will be living with diabetes in 2030 than are doing so today[2,3]. In the year 2011, the International Diabetes Federation estimated that 366 million people in the world had diabetes, and this number is expected to increase to 552 million by 2030[4]. Of equal concern is that many people with diabetes do not know that they have the disease: in 2011 it was estimated that worldwide as many as half of the total number of cases of diabetes were undiagnosed[4].

While some one million Australians aged 25 years or older had diabetes in 2000[5], estimates suggest that in excess of two million Australians will be living with the disease[6] by 2025. One measure of the impact of the rise in diabetes is the cost posed to the Australian economy. The Australian Diabetes, Obesity and Lifestyle study (AusDiab) has recently estimated that the total annual costs of diabetes in 2005 was in excess of 10 billion dollars, and costs are expected to rocket to well in excess of 20 billion dollars by 2033[7]. Indeed diabetes is expected to show the greatest proportional increase in cost to the economy in the next two decades of all diseases studied[8]. The prevention and management of diabetes and its complications must become one of the key health priorities in Australia.

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1.6%
OF AUSTRALIANS OVER 40

A 2004 Access Economics report found that 1.6% of Australians aged 40 years and older had vision-impairing diabetic retinopathy.

VISION LOSS AND DIABETES

Diabetic retinopathy is the leading cause of blindness among working age adults in the world[9]. In Australia, diabetic retinopathy still remains one of the top five causes of irreversible blindness among adults[10]. Research into knowledge and attitude to blindness in Australia found that it is second only to cancer among the medical conditions that people fear most[11]. With a rapidly growing Australian population, the number of people with diabetic eye disease and associated vision impairment is expected to increase, placing pressure on the health system and economy. Australia will not be alone in tackling this growing problem. One study has estimated that in 2012, 93 million people worldwide had evidence of diabetic eye disease, and in 21 million of these the disease was already affecting their central vision[12].

In 2011, figures from the Australian National Diabetes Information Audit & Benchmarking (ANDIAB) study showed that 42 out of 4,629 patients attending specialised diabetes clinics became blind in the preceding 12 months[13]. Similarly, an Access Economics report commissioned by CERA in 2004 found that 1.6% of Australians aged 40 years and older had vision-impairing diabetic retinopathy[10]; these findings being based on the results of two landmark Australian studies, the Vision Impairment Project[14] and the Blue Mountains Eye Study[15]. The expected growth in the number of Australians living with diabetes in coming decades will lead to a corresponding rise in diabetic eye disease and vision loss – numbers are expected to at least double between 2004 and 2024[10]. The number of individuals with diabetic eye disease may be even higher given that up to half of all cases of diabetes are presently undiagnosed and that obesity, a key risk factor for type 2 diabetes, is also on the rise.

> “Individuals with diabetes are often unaware that they have retinopathy and the disease may progress to advanced stages without any effects on vision: It is essential that people with diabetes have regular eye examinations so that treatment can be delivered before irreversible vision loss occurs.”

DIABETIC EYE DISEASE

THE PROGRESSIVE NATURE OF DIABETIC EYE DISEASE – FROM BAD TO WORSE

Diabetic retinopathy, a common complication of diabetes, is an eye disease that worsens over time, and if left untreated can lead to irreversible blindness. Diabetic retinopathy can be divided into two stages: an early stage, known as non-proliferative diabetic retinopathy, and a later stage referred to as proliferative diabetic retinopathy.

Key features of non-proliferative retinopathy are bleeding (haemorrhage) within the retina and the leakage of fluid into the retina. These changes may go unnoticed, or they may cause visual impairment if they involve the macula, the region of the retina responsible for central detailed vision. Non-proliferative diabetic retinopathy is divided into three categories – mild, moderate or severe – according to the severity of retinal disease. Clinical studies of large numbers of individuals with retinopathy have provided information about the risk of vision loss for each category of retinopathy[16].

Proliferative diabetic retinopathy, the more advanced stage of the disease, is so named as it is characterised by the growth (proliferation) of new, abnormal blood vessels on the retinal surface. These new blood vessels may bleed into the jelly-like substance in front of the retina (vitreous haemorrhage) and they may be associated with the formation of fibrous scar tissue that can pull on the retina, causing it to detach from the back of the eye (tractional retinal detachment). The risks of severe vision loss from untreated proliferative diabetic retinopathy are high. Individuals with diabetes are often unaware that they have retinopathy and the disease may progress to advanced stages without any effects on vision: It is essential that people with diabetes have regular eye examinations so that treatment can be delivered before irreversible vision loss occurs.

Diabetic macular oedema occurs when the leakage of fluid from small retinal blood vessels affects the macula, the central part of the retina that is responsible for fine detail vision. **Macular oedema is the single leading cause of vision loss in diabetes[17].** When retinal swelling affects, or is very near to, the area serving central vision it is referred to as clinically significant macular oedema and it may require treatment.

It is important to note that people with diabetes are also at higher risk of developing other eye conditions, such as cataracts, which often require treatment to reverse the vision loss caused by clouding of the normally clear lens in the eye[18]. The link between diabetes and glaucoma (a group of eye conditions that cause damage to the nerve that connects the eye to the brain) is less clear, but there have been reports of people developing secondary glaucoma as a complication of proliferative diabetic retinopathy[19].

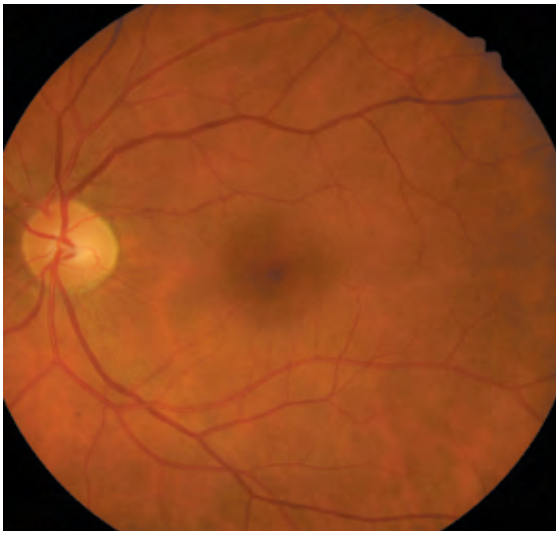
THE INFLUENCE OF GENES AND THE ENVIRONMENT ON THE DEVELOPMENT OF DIABETIC RETINOPATHY

Dedicated research teams within Australia and around the world are hard at work teasing out the causes of diabetic eye disease. We know that an individual's genetic make-up and environmental influences, such as their lifestyle choices and blood sugar control, together contribute to their risk of developing retinopathy[20]. A longer duration of diabetes, high blood pressure and high blood sugar levels are known as major risk factors for the development of diabetic eye disease. Other factors such as physical inactivity, diet and obesity also play important roles in the development and progression of diabetic eye disease.

The search for genes for diabetic retinopathy has mainly been conducted using the candidate gene approach, which only maps specific regions in the genome. So far, several dozen possible genes have been identified, with one of the most consistent being the gene for a protein called vascular endothelial growth factor, VEGF[20-24]. VEGF stimulates the growth of new blood vessels (angiogenesis). In people with diabetes, VEGF has been consistently found to be overexpressed in the retina causing advanced stages of diabetic retinopathy and diabetic macular oedema. Hence anti-VEGF agents are used as an option for treating diabetic eye disease, administered as injections directly into the eye.

At present our ability to accurately predict who will develop sight-threatening retinopathy, and when they will do so, is relatively limited. Regular eye examinations are vital for timely intervention. The frequency of eye examinations for a given individual is determined by their current stage of retinopathy and by risk factors such as their prior history of progression, blood sugar and blood pressure control, and key aspects of general health.

Fundus photographs eye professionals would assess, showing a normal eye (left) and an eye showing the presence of non-proliferative diabetic retinopathy and clinically significant macular oedema (right).



The Blue Mountains Eye Study found that one in three people with diabetes had diabetic retinopathy and one in 23 had clinically significant macular oedema.

1 IN 3 PEOPLE

HOW COMMON IS DIABETIC EYE DISEASE?

A GROWING PROBLEM

Diabetic retinopathy is a leading cause of vision loss in adulthood. A recent study of 33 countries across the globe estimates that on average one in three people with diabetes have diabetic retinopathy and approximately one in 20 have diabetic macular oedema[3]. Three key Australian population studies have provided information about the proportion of those with diabetes who have retinopathy: the AusDiab study[25], the Melbourne Vision Impairment Project[26] and the Blue Mountains Eye Study[15]. While the studies differ in their design, methods and findings, together they provide an overview of the true human impact of diabetic retinopathy in Australia.

The AusDiab study, conducted in 2000 and again in 2004, found that one in six Australians with diabetes (aged 25 years or older) had diabetic retinopathy. Of those people with type 2 diabetes, almost one in five (19.3%) had non-proliferative diabetic retinopathy, one in 50 (2.1%) had proliferative retinopathy and one in 30 (3.3%) had diabetic macular oedema. It was estimated that in 2004 a staggering 1.2% of Australian adults (133,900 individuals) had diabetic retinopathy[25].

The Melbourne Vision Impairment Project (conducted 1992–96) showed that as many as one in 3 (29.1%) Australians over the age of 40 with diabetes had diabetic retinopathy, with most having non-proliferative diabetic retinopathy. One in 24 (4.2%) had proliferative retinopathy and one in 18 (5.6%) had clinically significant macular oedema[26].

The Blue Mountains Eye Study (carried out from 1992–94, among people aged 49 and over) reported similar findings: one in three (32.4%) people with diabetes had diabetic retinopathy and one in 23 (4.3%) had clinically significant macular oedema[15]. Both the Melbourne Vision Impairment Project and the Blue Mountains Eye Study reported similar rates for diabetic retinopathy and diabetic macular oedema in men and women. In summary, these studies showed that up to a third of Australians with diabetes have some form of diabetic eye disease, with the most common form being the non-proliferative diabetic retinopathy.

FUTURE CHALLENGES

The alarming projections of the number of Australians with diabetic retinopathy in the coming decades have major implications for the health system and the economy more broadly[27]. A joint Access Economics and CERA report found that the number of Australians aged 40 years or older with vision impairment or blindness from all causes, including oedema, will almost double in the two decades between 2004 and 2024. An estimated 480,257 Australians had vision impairment in 2004, a figure predicted to increase to almost 800,000 by 2024. 50,548 Australians were blind in 2004 and the number is expected to exceed 87,000 by 2024[10]. Diabetic eye disease constitutes a major cause of vision impairment and blindness.

The economic implications of these projections are enormous: direct health system costs to accommodate for vision disorders in Australia amounted to 1.8 billion dollars in 2004, and this amount was expected to jump by another one to two billion dollars in the following 10 years[27]. Direct healthcare costs of vision impairment are dwarfed by the indirect costs posed to the economy – costs of such things as loss of capacity for work and the need for community support. Nevertheless, the take home message here is that vision impairment and blindness caused by major eye diseases, including diabetic eye disease, are placing substantial economic pressure on the Australian economy and the individual.

DIABETIC EYE DISEASE IN INDIGENOUS AUSTRALIANS

It is known that many Indigenous Australians experience poorer health than non-Indigenous Australians, and often die younger. Indigenous Australians are at least four times more likely than non-Indigenous Australians to develop diabetes[28]. This fact, coupled with barriers to eye health care delivery in Indigenous communities, places Indigenous Australians at a high risk of developing diabetic retinopathy and diabetic macular oedema[29]. The proportion of Indigenous Australians who develop retinopathy may vary depending on the population surveyed, the eye tests conducted and the number of people included in the study.

A recent study known as the National Indigenous Eye Health Survey[30], found that the proportion of Indigenous Australians who were reported to have diabetes was almost eight times higher (37.9%) than that of the general population of Australia. One in three (29.7%) Indigenous Australians with diabetes had diabetic retinopathy. The most common form of retinopathy in this group was the mild to moderate non-proliferative diabetic retinopathy (17.8%), however a high proportion of those with diabetes had clinically significant macular oedema (10%).

This survey[30] and another study[31] found that clinically significant macular oedema was present in Indigenous Australians at earlier stages of diabetes, necessitating earlier intervention than is the case for non-Indigenous Australians. The study highlighted a need for earlier screening for and treatment of diabetic retinopathy in Indigenous communities: just over half of those with clinically significant macular oedema and less than 40% of those with the early stages of diabetic retinopathy had consulted a health care provider in the preceding year. Taken together these studies identify Indigenous Australians as being at heightened risk of diabetes and vision impairment from diabetic eye disease. Specifically tailored interventions are required to tackle these significant problems.

8X

THE NATIONAL AVERAGE

The National Indigenous Eye Health Survey found that the proportion of Indigenous Australians reported to have diabetes was almost eight times higher than the general population.

GET IN EARLY TO AVOID BLINDNESS

Almost all cases of sight-threatening diabetic eye disease can be avoided by having regular eye checks, and obtaining timely treatment[32,33]. Regular eye checks are essential to monitor the early stages of the disease so that risk factors for worsening retinopathy can be tackled and treatment can be delivered at the most appropriate time. The most recent National Health and Medical Research Council guidelines for the management of diabetic retinopathy recommend a diabetic eye check when diabetes is diagnosed and at least every two years thereafter[34]. Eye examination on at least an annual basis is recommended for those who have been previously diagnosed with diabetic retinopathy, as well as for those at a higher risk of developing diabetic retinopathy, such as Indigenous Australians, individuals from a non-English speaking background, and those with longer duration of diabetes. Individuals with more advanced stages of diabetic retinopathy may require eye examinations on a much more frequent basis, as often as three-monthly[34]. Unfortunately, numerous studies have shown that between one in five and one in two (22%–50%) of Australians with diabetes do not undergo eye examinations at the recommended frequency[35-37]. Australia currently lacks a nationwide diabetic eye screening system, even though such systems have been successfully implemented in other countries with significant improvements in outcomes for those with diabetic retinopathy[38].

THE SOCIAL AND EMOTIONAL IMPACTS OF DIABETIC EYE DISEASE

Diabetic retinopathy can have devastating impacts on the lives of those people affected by the disease. Even the threat of reduced vision and the need for ongoing examinations and treatment can have negative emotional, social and economic effects. The ability to perform the daily tasks that most people take for granted can become extremely challenging, if not impossible, by diabetic eye disease, particularly proliferative retinopathy and clinically significant macular oedema[39]. It is now well recognised that advanced diabetic eye disease, may be associated with depression, loss of confidence, anger as well as strains on social and work commitments[40]. A recent study from CERA has provided valuable insights into patient perspectives on the impact of diabetic eye disease on quality of life. Patient concerns ranged from the frustrations caused by driving restrictions, to wide ranging impacts on social and work lives, emotional states, and financial situations[41]. A 2004 joint report from Access Economics and CERA estimated that vision disorders, including diabetic eye disease, comprise nearly 3% of the total disability burden of all diseases. **The disability burden of vision disorders was estimated to be greater than that of prostate cancer, melanoma and oral diseases**[10]. The 2004 report also found that only one in three people with vision disorders in the 40 to 65 year age group were employed – less than half the rate for those in the same age group in the general population. It is clear that the optimal management of diabetic eye disease extends well beyond the eyes. The importance of interventions to address the emotional, lifestyle, and medical needs of every patient affected by the disease cannot be overstated.

TANIA'S STORY

Tania was diagnosed with type 1 diabetes at 11 years of age after several weeks of ill-health culminated in an admission to hospital. She struggled to manage her diabetes during her teenage years and in early adulthood. At the age of 23, Tania was experiencing blurred vision and was referred to an eye care professional. She underwent a series of eye tests that confirmed the presence of diabetic retinopathy. Tania's concern about the diagnosis and its implications for her future were compounded by a sense of guilt – she had not attended screening eye exams in the past, despite recommendations to do so.

Despite several rounds of laser treatment and surgery, her retinopathy progressed over the following two years to the point that she became legally blind in both eyes. Tragically Tania's retinopathy was already at an advanced stage by the time it was diagnosed and the damage could not be reversed by treatment.

When asked how she coped with blindness at such a young age she responded: "being blind put a lot of strain on my relationship with my partner, and with my mother and sister. I had to make a choice of either living my life listening to TV or have a purpose, and to say at least it's been a journey towards finding a purpose". Tania has clearly found her purpose: she has a part-time job in a gymnasium and is committed to remaining fit and physically active. She lives with the regret of not taking a more active role in the management of her diabetes during her teen and early adult years and not having had regular eye exams. She is now a passionate advocate for early diabetic eye screening.

> "Being blind put a lot of strain on my relationship with my partner, and with my mother and sister. I had to make a choice of either living my life listening to TV or have a purpose, and to say at least it's been a journey towards finding a purpose."

TREATMENT OPTIONS

Before addressing treatment options for diabetic retinopathy it is important to emphasise that most of the vision loss caused by diabetic eye disease can be avoided by two key preventative measures. The first of these is achieving optimal diabetes control and maintaining a healthy lifestyle: having a healthy, balanced diet; engaging in moderate levels of physical activity; and complying with prescribed medications to achieve satisfactory blood pressure and blood sugar levels. A second important priority in the prevention of avoidable vision loss is adherence to regular eye examinations. Early detection of diabetic retinopathy is important for timely treatment. **The value of regular eye examinations cannot be overstated.**

Treatment is usually required when diabetic retinopathy has advanced to the proliferative stage, characterised by the growth of new retinal blood vessels, or when the part of the eye responsible for central vision begins to be affected by macular oedema. This stage of eye disease is commonly referred to as vision-threatening diabetic retinopathy, but vision is still usually normal at this stage. Broadly speaking there are three types of treatment for diabetic retinopathy. These include laser therapy, intravitreal injections (direct injection of medication into the vitreous, the jelly-like substance in the eye), and in more severe cases surgery, typically in the form of a vitrectomy where the vitreous is removed from the eye. These treatments may be used singly, or in combination to achieve the best outcome for each individual. The treatment offered varies depending on what stage diabetic retinopathy is present. In most instances the principal aim of the treatment is to reduce the risk of further vision loss[1,17].

The most common form of treatment for vision-threatening diabetic retinopathy is laser therapy. There are two main types of laser treatments. The first approach, used in the management of proliferative diabetic retinopathy, is known as panretinal laser therapy. Panretinal laser involves the application of typically between 1500 and 2000 laser spots to the majority of the retina, sparing the macula – the region serving central vision. A second form of laser treatment, known as macular laser therapy, involves the administration of precisely aimed and typically lower energy laser spots to the macula, the central part of the retina affected by diabetic macular oedema. Macular laser may be described as either focal or grid treatment, according to the pattern of laser spot application. Timely laser therapy is important in reducing the risk of further vision loss from worsening diabetic retinopathy: studies have shown that appropriately timed laser treatment can reduce these risks by 50%[17]. As with all invasive treatments, laser therapy may have side-effects including: reductions in peripheral vision, changes in colour vision, and in the case of panretinal laser possible worsening of macular oedema. Overall the benefits of laser treatment far outweigh the risks in patients with vision-threatening diabetic eye disease. Reports of marked improvements in vision after laser therapy alone are rare in those with vision threatening diabetic retinopathy – the aim of treatment is to reduce the risk of further vision loss.

22-50%

OF AUSTRALIANS

Numerous studies have shown that **between one in five and one in two (22%–50%) of Australians with diabetes do not undergo eye examinations** at the recommended frequency.

> "In most instances the principal aim of the treatment is to reduce the risk of further vision loss."

A relatively new treatment option for diabetic eye disease involves the injection of medications directly into the vitreous of the eye (intravitreal injection). There are two main classes of medications used in this manner: inhibitors of a growth factor known as vascular endothelial growth factor (VEGF) and steroid medications such as triamcinolone. VEGF is produced in excess by the diseased retina and it drives the development of abnormal blood vessels in the retina, as well as the leakage of fluid from established blood vessels. Accordingly, drugs that target VEGF may be effective in reducing the growth of new vessels in proliferative retinopathy and minimising fluid leakage in macular oedema. Triamcinolone is also effective in minimising fluid leakage in diabetic macular oedema. Intravitreal injection is an invasive procedure with rare, but potentially serious risks to the eye. Intravitreal injections may be required as often as monthly for extended periods in some patients. Studies are ongoing to better understand the long-term effects of intravitreal injections in different clinical populations worldwide[1].

Surgery may be required to treat advanced diabetic retinopathy. The most common reasons for surgery are for the treatment of bleeding into the vitreous (jelly-like substance within the eye) of the eye that obscures vision, or pulling on the retina exerted by fibrous scar tissue that can cause the retina to detach (tractional retinal detachment). In these cases a surgical procedure known as vitrectomy is performed, where the vitreous is removed and replaced with a saline solution, gas or silicone oil. Surgical techniques for severe cases of vision threatening diabetic retinopathy are constantly improving, however surgery remains a last-line of therapy for diabetic eye disease.

CONCLUSIONS

Diabetic eye disease is a common complication of diabetes, and remains as one of the leading causes of irreversible vision loss and blindness in Australian adults. With an ageing population, a high proportion of undiagnosed cases of diabetic eye disease, and increasing numbers of people with health conditions linked to diabetic eye disease, such as obesity, the impact of diabetic eye disease in Australia will only continue to place more pressure on our health system and economy.

As with most medical conditions, prevention is key. To substantially reduce the number of Australians unnecessarily going blind from diabetic eye disease, we must develop and implement an effective and efficient diabetic eye screening program that is accessible to all Australians with diabetes. Even though laser therapy still remains the most common treatment for advanced stages of diabetic eye disease, more recent clinical trials are also supporting the role of intravitreal injections in the treatment of diabetic eye disease, particular for macular swelling. Genetic studies into diabetic eye disease have also played a significant role in understanding the causes of diabetic eye disease and have been beneficial in paving the way for alternate treatment options, such as anti-VEGF treatments.

In summary, the essentials for people with diabetes are to be diligent with diabetes self-management in regard to medication and following a healthy lifestyle, and to be very strict about regular eye examinations, as the early stages of diabetic eye disease typically do not affect vision, and therefore go unnoticed.

REFERENCES

01. Cheung N, Mitchell P, and Wong TY, *Diabetic retinopathy*. Lancet., 2010. 376: p. 124-136.
02. Shaw, J.E., R.A. Sicree, and P.Z. Zimmet, *Global estimates of the prevalence of diabetes for 2010 and 2030.* Diabetes Res Clin Pract, 2010. 87(1): p. 4-14.
03. Ruta, L.M., et al., *Prevalence of diabetic retinopathy in Type 2 diabetes in developing and developed countries.* Diabet Med, 2013. 30(4): p. 387-98.
04. IDF, *International Diabetes Federation: Diabetes Atlas*, 2011.
05. Dunstan, D.W., et al., *The rising prevalence of diabetes and impaired glucose tolerance: the Australian Diabetes, Obesity and Lifestyle Study. Diabetes Care*, 2002. 25(5): p. 829-34.
06. Magliano, D.J., et al., *Lifetime risk and projected population prevalence of diabetes.* Diabetologia, 2008. 51(12): p. 2179-86.
07. Lee, C.M., et al., *The cost of diabetes in adults in Australia. Diabetes Res Clin Pract, 2013.* 99(3): p. 385-90.
08. Begg, S., et al., *An alternative approach to projecting health expenditure in Australia.* Aust Health Rev, 2008. 32(1): p. 148-55.
09. Klein, B.E., *Overview of epidemiologic studies of diabetic retinopathy.* Ophthalmic Epidemiol, 2007. 14(4): p. 179-83.
10. *The Economic Impact and Cost of Vision Loss in Australia*, August 2004, Access Economics: Melbourne.
11. Livingston, P.M., C.A. McCarty, and H.R. Taylor, *Knowledge, attitudes, and self care practices associated with age related eye disease in Australia.* Br J Ophthalmol, 1998. 82(7): p. 780-5.
12. Yau, J.W., et al., *Global prevalence and major risk factors of diabetic retinopathy.* Diabetes Care, 2012. 35(3): p. 556-64.
13. National Association of Diabetes Centres, *Final Report ANDIAB 2011*, 2011, Australian National Diabetes Information and Benchmarking (ANDIAB).
14. VanNewkirk, M.R., et al., *Cause-specific prevalence of bilateral visual impairment in Victoria, Australia: the Visual Impairment Project.* Ophthalmology, 2001. 108(5): p. 960-7.
15. Mitchell, P., et al., *Prevalence of diabetic retinopathy in an older community. The Blue Mountains Eye Study.* Ophthalmology, 1998. 105(3): p. 406-11.
16. *Grading diabetic retinopathy from stereoscopic color fundus photographs–an extension of the modified Airlie House classification. ETDRS report number 10. Early Treatment Diabetic Retinopathy Study Research Group. Ophthalmology*, 1991. 98(5 Suppl): p. 786-806.
17. *Mohamed Q, Gillies MC, and Wong TY, Management of diabetic retinopathy: a systematic review*. JAMA., 2007. 298: p. 902-916.
18. Tan, J.S., J.J. Wang, and P. Mitchell, *Influence of diabetes and cardiovascular disease on the long-term incidence of cataract: the Blue Mountains eye study.* Ophthalmic Epidemiol, 2008. 15(5): p. 317-27.
19. Jeganathan, V.S., J.J. Wang, and T.Y. Wong, *Ocular associations of diabetes other than diabetic retinopathy.* Diabetes Care, 2008. 31(9): p. 1905-12.
20. Schwartz, S.G., M.A. Brantley, Jr., and H.W. Flynn, Jr., *Genetics and diabetic retinopathy*. Curr Diabetes Rev, 2013. 9(1): p. 86-92.
21. Awata, T., et al., *A common polymorphism in the 5'-untranslated region of the VEGF gene is associated with diabetic retinopathy in type 2 diabetes.* Diabetes, 2002. 51(5): p. 1635-9.
22. Awata, T., et al., *Functional VEGF C-634G polymorphism is associated with development of diabetic macular oedema and correlated with macular retinal thickness in type 2 diabetes.* Biochem Biophys Res Commun, 2005. 333(3): p. 679-85.
23. Fujisawa, T., et al., *Length rather than a specific allele of dinucleotide repeat in the 5' upstream region of the aldose reductase gene is associated with diabetic retinopathy.* Diabet Med, 1999. 16(12): p. 1044-7.

24. Kang, P., C. Tian, and C. Jia, *Association of RAGE gene polymorphisms with type 2 diabetes mellitus, diabetic retinopathy and diabetic nephropathy.* Gene, 2012. 500(1): p. 1-9.
25. Tapp, R.J., et al., *The prevalence of and factors associated with diabetic retinopathy in the Australian population.* Diabetes Care, 2003. 26(6): p. 1731-7.
26. McKay, R., C.A. McCarty, and H.R. Taylor, *Diabetic retinopathy in Victoria, Australia: the Visual Impairment Project.* Br J Ophthalmol, 2000. 84(8): p. 865-70.
27. Taylor HR, Pezzullo ML, and Keeffe JE, *The economic impact and cost of visual impairment in Australia.* Br J Ophthalmol, 2006. 90: p. 272-275.
28. Gracey, M., et al., *An Aboriginal-driven program to prevent, control and manage nutrition-related "lifestyle" diseases including diabetes.* Asia Pac J Clin Nutr, 2006. 15(2): p. 178-88.
29. Murray, R.B., et al., *Sustaining remote-area programs: retinal camera use by Aboriginal health workers and nurses in a Kimberley partnership.* Med J Aust, 2005. 182(10): p. 520-3.
30. Xie, J., et al., *Prevalence of self-reported diabetes and diabetic retinopathy in indigenous Australians: the National Indigenous Eye Health Survey.* Clin Experiment Ophthalmol, 2011. 39(6): p. 487-93.
31. Jaross, N., P. Ryan, and H. Newland, *Prevalence of diabetic retinopathy in an Aboriginal Australian population: results from the Katherine Region Diabetic Retinopathy Study (KRDRS). Report no. 1.* Clin Experiment Ophthalmol, 2003. 31(1): p. 32-9.
32. Lee, S.J., et al., *Costs of mobile screening for diabetic retinopathy: a practical framework for rural populations.* Aust J Rural Health, 2001. 9(4): p. 186-92.
33. Ferris, F.L., 3rd, *How effective are treatments for diabetic retinopathy?* JAMA, 1993. 269(10): p. 1290-1.
34. Australian Diabetes Society, *Guidelines for the Management of Diabetic Retinopathy 2008*, National Health and Medical Research Council.
35. Tapp RJ, et al., *Diabetes care in an Australian population: frequency of screening examinations for eye and foot complications of diabetes.* Diabetes Care., 2004. 27: p. 688-693.
36. Muller, A., et al., *Utilization of eye care services in Victoria.* Clin Experiment Ophthalmol, 2006. 34(5): p. 445-8.
37. Bylsma GW, et al., *Utilization of eye care services by Victorians likely to benefit from eye care.* Clin Experiment Ophthalmol, 2004. 32: p. 573-577.
38. Arun CS, et al., *Long-term impact of retinal screening on significant diabetes-related visual impairment in the working age population.* Diabet Med., 2009. 26: p. 489-492.
39. Lamoureux, E.L., J.B. Hassell, and J.E. Keeffe, *The impact of diabetic retinopathy on participation in daily living.* Arch Ophthalmol, 2004. 122(1): p. 84-8.
40. Fenwick, E., et al., *Social and emotional impact of diabetic retinopathy: a review.* Clin Experiment Ophthalmol, 2012. 40(1): p. 27-38.
41. Fenwick, E.K., et al., *The impact of diabetic retinopathy on quality of life: qualitative findings from an item bank development project.* Qual Life Res, 2012. 21(10): p. 1771-82.

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