

# Open Patient Meeting

## - Edinburgh -

### What's new in the treatment of glaucoma

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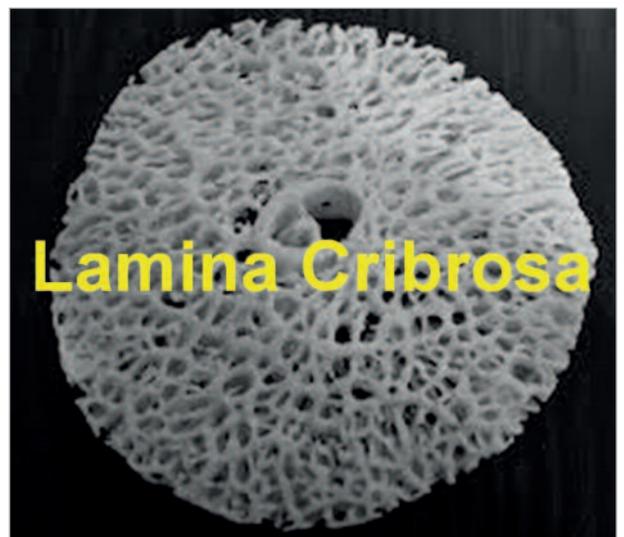
Good afternoon everyone, it's very nice to be here and thank you all for coming to the Scottish meeting of the International Glaucoma Association. For those of you who don't know me, my name is Andrew Tatham, and I am a consultant glaucoma surgeon here in Edinburgh, at the Princess Alexandra Eye Pavilion. The topic I wish to cover today is what's new in the treatment of glaucoma.

Although glaucoma affects about one per cent of those aged over forty and four per cent of those aged over 80 years, about 50 per cent of people who have glaucoma actually aren't aware that they are affected and have not been diagnosed. That's a huge problem, because although glaucoma is one of the most common causes of irreversible blindness, if we pick it up early there are effective treatments that can prevent loss of vision. It is therefore very important for us to raise awareness of glaucoma among the general population and encourage

people to attend their optometrist regularly, so that it can be detected at an earlier stage. So, what's new in glaucoma?

#### Lamina Cribrosa

First, we are beginning to understand more about what causes glaucoma. This structure, the Lamina Cribrosa, which looks like a little sponge, is

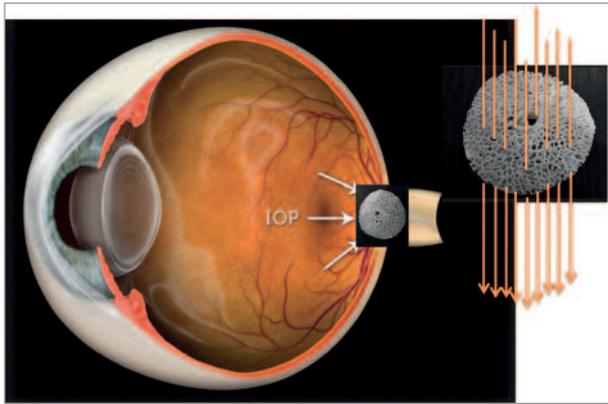


Slide 1

very important (slide 1). Glaucoma is damage to the optic nerve, (slide 2) which is a cable, made of one million individual fibres, that sends visual messages from the eye to the brain.

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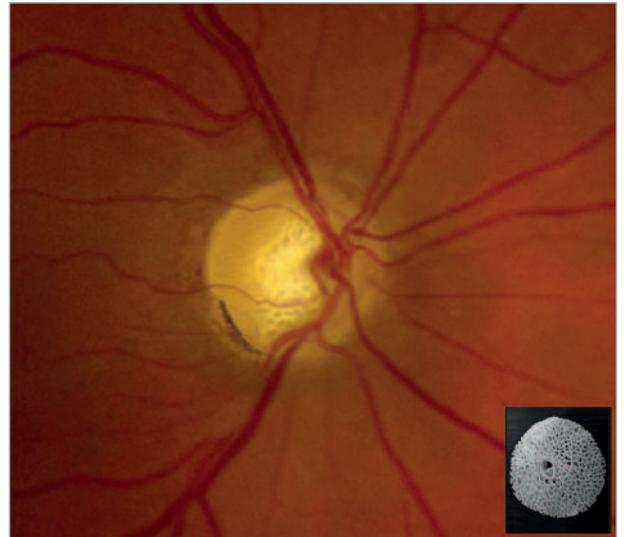
Slide 2

As the optic nerve leaves the eye on its journey to the brain, it passes through the sieve-like openings in the Lamina Cribrosa. The optic nerve is vulnerable to damage as it passes through the Lamina Cribrosa, and it is here that the nerve fibres are thought to be damaged in glaucoma. When we look at a photograph of the optic nerve, we can sometimes actually see the small pores, the openings in the Lamina Cribrosa. These are the openings through which the nerve fibres pass as they exit the eye and travel towards the brain.

### Glaucoma and nerve damage

To give an example of how glaucoma may affect a patient, here is a picture of someone's optic nerve in 2008 (slide 3). Over time this person loses their optic nerve fibres one by one. Everyone starts with about a million nerve fibres and there is a natural

ageing of the nerve, but in glaucoma that process of nerve loss is accelerated. With this particular patient, the nerve changes appearance over the next six years, as the optic nerve fibres are lost. We can see the result of this for this person's vision. In 2008, when she

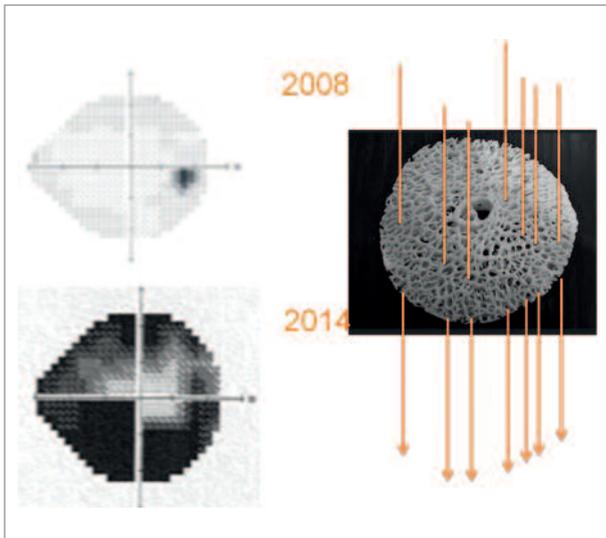


Slide 3

was first seen, the visual field test was normal (slide 4), but by 2014 she has lost a large amount of vision, as optic nerve fibres had been lost. So this person has progressed very quickly. Using new imaging devices we can now see the Lamina Cribrosa in greater detail, so for the first time we can see the location where optic nerve damage occurs in glaucoma. This has the potential to help us better understand the mechanism of nerve damage.

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Slide 4

### The challenges in glaucoma and what's new?

So, we are beginning to understand more about the mechanism of glaucoma. But what else is new? I would like to focus on three important challenges in the fight against this condition.

### Three challenges

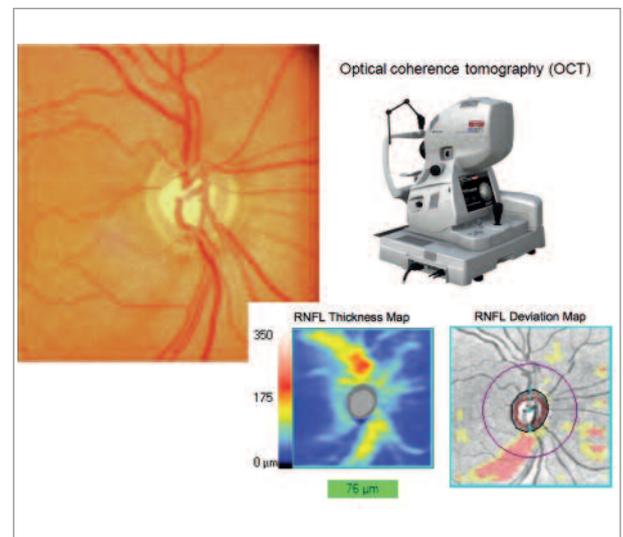
1. Detecting glaucoma earlier
2. Identifying those who are at most risk of losing vision
3. Developing better treatments.

### 1. Detecting glaucoma earlier

It is very easy to diagnose glaucoma at an advanced stage because it's very obvious when you do a visual field test that this person has lost vision. But do we want to diagnose glaucoma at an advanced stage, when

somebody has already lost vision? Clearly not, it is far better to detect glaucoma before it has caused significant visual loss. It is far better if we could diagnose glaucoma when a person has lost little visual field, or maybe we could actually diagnose glaucoma before a person has lost any vision at all. We can actually do that now with some of the latest developments.

This is a photograph of someone's eye (slide 5). This person has glaucoma and if you look really closely, you can see there is a little red spot here, a red spot of blood



Slide 5

indicating that they have a little haemorrhage at the back of their eye. There is also a little wedge shaped shadow where this person has lost some of their nerve fibres as

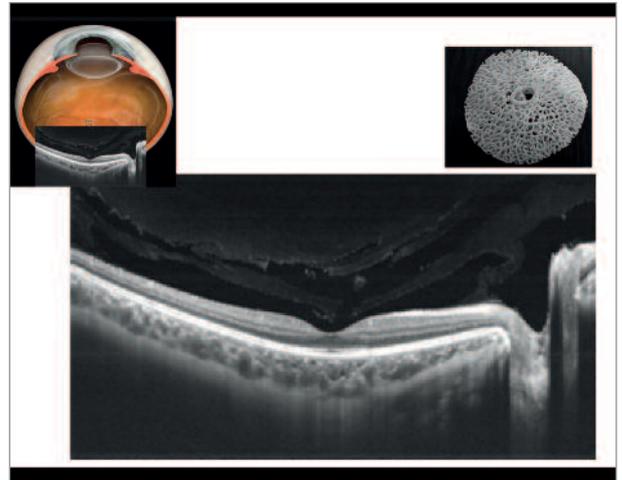
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well. Although this person has normal vision and visual field, when we look into the back of the eye we can tell that they have glaucoma. Using imaging devices like optical coherent tomography (OCT), which many of you would have had, we can actually measure the thickness of the nerve fibre and decide if somebody has glaucoma. OCT can produce a kind of heat map where the hot colours, like red, show that the nerve fibres are thick and the colder colours like blue, indicate that the nerve fibres are thin. At the top of the image there are a lot of hot colours indicating that the nerve fibres are thick (and so probably healthy). At the bottom of the image you can see a blue region where this person has had thinning of their nerve fibre layer. Thinning of the nerve fibre layer is not normal so this person has had an OCT scan of the optic nerve and it has confirmed that they have glaucoma, even though they haven't yet lost vision. So imaging, like OCT, can help diagnose glaucoma earlier than might otherwise have been possible.

### **Which parts of the eye is it useful to scan?**

Normally we use imaging devices to scan the optic nerve and surrounding structures, but improvements in

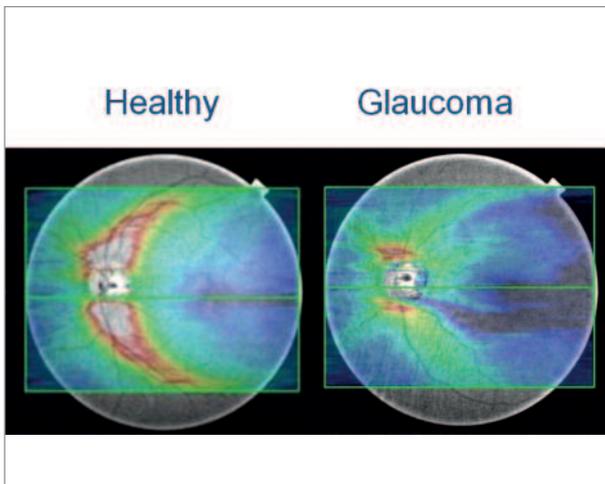


Slide 6

imaging devices mean it is now possible to gain further information about other structures in the eye that is damaged by glaucoma (slide 6). We can even see the Lamina Cribrosa, the main site where glaucoma damage is occurring. We can also measure the thickness of inner layers of the retina in the macula, the central region of the retina important for central vision. Some studies have shown that OCT imaging of the macula can be as good at detecting glaucoma as imaging of the optic nerve. So using imaging, we can obtain these amazing pictures of the back of the eye. Also, by taking measurements over time we can see whether people are actually getting worse and losing optic nerve fibres. This is somebody who is healthy, with (red) thick healthy nerve fibres, compared to somebody with glaucoma who looks

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Slide 7

very different: s/he has lost nerve fibre thickness (slide 7).

So using scanning techniques like OCT we have made progress towards our first goal, of detecting glaucoma earlier.

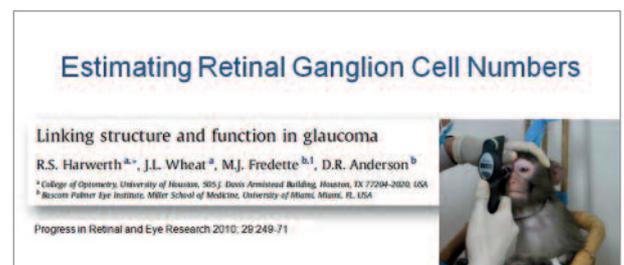
## 2. Identifying those who are at most risk of losing vision.

The second challenge I would like to address is identifying those who are at greatest risk of losing vision. Some people with glaucoma progress very slowly and without treatment they may never lose vision. But there are other people who progress very quickly and it's important we identify those people, so they can have the appropriate treatment early.

Glaucoma is loss of nerve fibres called retinal ganglion cells. These are the cells that send the connections

from the eye to the brain. If we could actually count how many ganglion cells somebody had, that might actually be the best way to detect glaucoma and also see whether somebody is getting worse.. If you remember, I mentioned that we all start off with about one million ganglion cells, so if you could look at somebody's eye and count the number of ganglion cells and find they had, for example, only 500,000 cells remaining, we would know they had lost half their expected number of cells. We might actually be able to better predict which patient's are at risk of losing vision and better measure change over time.

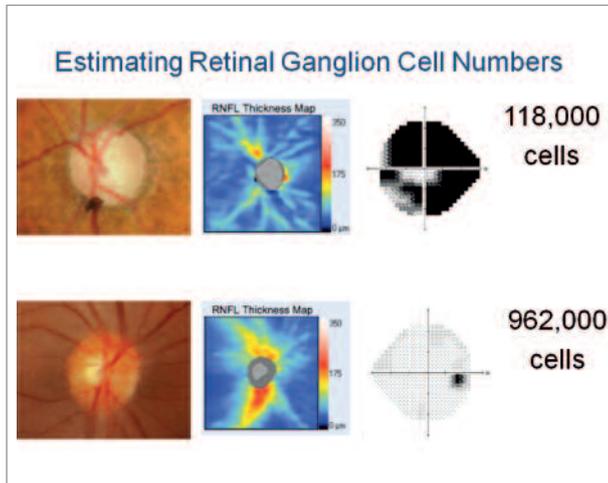
Unfortunately we can't actually measure the number of ganglion cells in people's eyes directly, but we can estimate them by using information from OCT and visual field tests. These estimates came from studies in monkeys (slide 8) with glaucoma (not funded by the IGA) who had OCT and were taught to do visual



Slide 8

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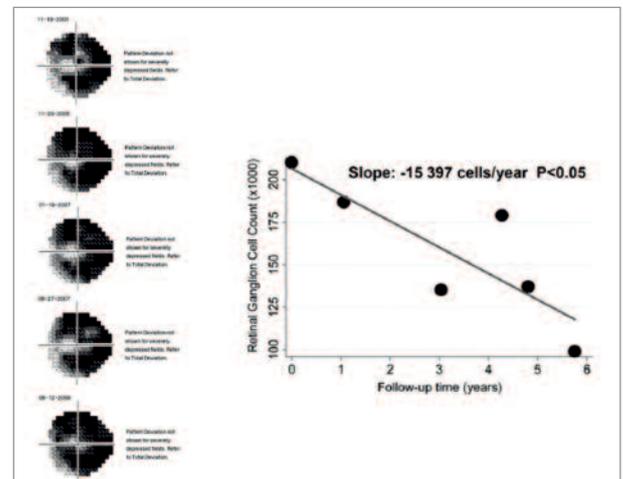
Slide 9

field tests. We all know visual field tests are difficult but the monkeys actually did the visual field tests better than some people can! I think the researchers bribed the monkeys with bananas! Anyway, the number of retinal ganglion cells was counted individually for each monkey and related to the OCT and visual field findings. These formulae are not perfect but it is possible to estimate the number of ganglion cells in an eye from OCT and how well they do the field test.

As an example, I've estimated the number of cells in the eyes of these two people (slide 9). The first person is healthy and we can see s/he has a healthy looking nerve on the photograph and the OCT scan also looks okay; there is a nice thick (red) nerve fibre layer, and the visual field

is good. We can estimate that this person has about 960,000 retinal ganglion cells – close to the one million we expect in a healthy person. We can see that the second individual has quite bad glaucoma. S/he has lost a lot of the visual field and we estimate that s/he has only 118,000 retinal ganglion cells. So we can have an idea of how many ganglion cells this person has lost; they really haven't got very many left.

Being able to estimate the number of retinal ganglion cells could be very useful for trying to identify if glaucoma is worsening. At the moment we tend to use the visual field and appearance of the optic nerve to decide whether someone is getting worse. This person (slide 10) has a bad field and it's getting worse over time. The estimated number of ganglion cells can be plotted at each

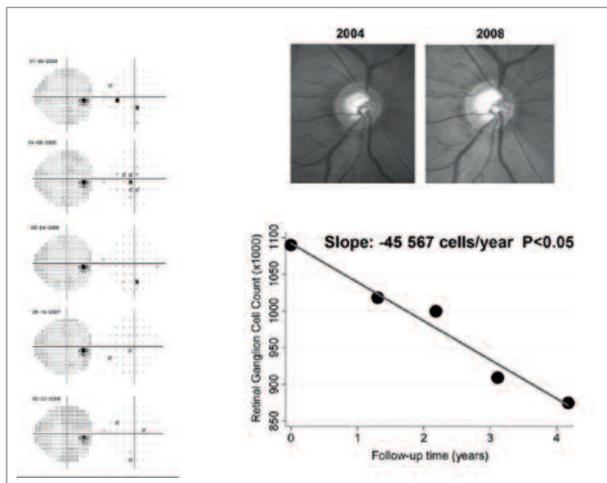


Slide 10

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visit, so we can gauge how quickly the glaucoma is changing over time. If we know this person's age we could extend the plot to predict how many retinal ganglion cells might be left should they live to, for example, 100



Slide 11

years of age. Are they still going to be seeing okay at this age?

We can use visual field alone to look for progression, however, consider this next person. Would we say this person is getting worse? (slide 11) Probably not, because their visual field has not really changed but as we've said, some people can actually have large changes to the optic nerve without losing visual field. You can probably appreciate the difference in the appearance of this person's optic nerve over time. The nerve has changed and if we estimate how many retinal ganglion cells this

person has lost it comes to approximately 50,000 cells per year. So this person is losing a large number of optic nerve fibres, even though the tests of vision remain normal. This might not be a problem in an elderly person, but in a young person this rate of ganglion cell loss could well result in loss of vision later in life. This illustrates why it is important to use measurements of optic nerve structure, as well as visual field tests, in monitoring glaucoma. We can then better decide if somebody needs extra treatment or lower eye pressure.

### Tasks of daily living

What matters most to you? It is probably not how many retinal ganglion cells you have, or even how well you do on visual field tests. What matters most is likely to be the ability to live life fully, the ability to take part in activities important for day-to-day life, activities like shopping or driving. Unfortunately we don't know very much about how the results of tests like visual field actually relate to ability to perform important daily tasks. This is an important area for research, and several groups have been trying to investigate and answer this important question.

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Recently I have been involved in a study to examine the effect of glaucoma on driving. Loss of a driving licence is something that worries many people, and although drivers with glaucoma have been shown to be at increased risk of accidents, many people with glaucoma are likely to be very safe drivers. It is important to better understand the relationship between conventional tests of vision, like visual field, and the ability to drive and detect potential hazards when driving. Recently, in conjunction with University of California in San Diego, USA, we have been looking at this, using a driving simulator. The driving simulator tests how well drivers can divide their vision between tasks when driving. This is different to visual field testing which tries to minimise distractions.

During the driving task, the driver was asked to follow a car in the road and at the same time, detect a small target out in the periphery. The driver was asked to press a button on the steering wheel when the target appeared and we measured the reaction time to this target. This was repeated several times as the driver continued to follow the car. We found that by combining information from visual fields and

OCT we were better able to predict drivers with problems on simulated driving. In the future, we might be able to relate rates of change in visual field or OCT to changes in the ability to perform daily tasks like driving. If we are also able to estimate numbers of retinal ganglion cells, we might even be able to see that somebody is losing a certain number of retinal ganglion cells per year, and because of this, identify that this person is at risk of losing their driving licence. We might be able to then recommend that this patient consider extra treatment or an operation to slow down the rate of ganglion cell loss and prevent the loss of their driving licence. Further studies that investigate the relationship between common measures of glaucoma severity and the ability to perform important daily tasks, will mean we have much better information to make these important decisions about treatment.

### **Intraocular pressure**

We know that intraocular pressure is important in glaucoma, but we also know that many people have “normal pressure”, or a pressure not above 21 mmHg. Population based studies have shown that up to about 50 per cent of people with glaucoma have

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“normal pressures” but there are geographic variations and in Japan 90 per cent of people with glaucoma have normal pressures. The term normal pressure glaucoma is a little controversial, due partly to the fact that we are really bad at measuring pressure and many people may in fact have higher pressure at other times. A single pressure-reading is like a snapshot, like taking one frame from an entire movie. We’re just seeing what the pressure is like at one second in time. In contrast, glaucoma is a 24 hour condition and so really we need to be able to measure pressure over 24 hours.



Slide 12

One way this can be done is in sleep labs. There are actually laboratories where patients can spend a comfortable night, sleeping in the laboratory, only to be woken up every hour to have their intraocular

pressure checked. About two-thirds of people have their peak pressure during the night. Recently I saw a patient whose pressure was only about 15mmHg during the day, and if you remember a normal pressure is about 10 to 21 mmHg, but when the pressure was measured in the sleep lab, it actually went up to 30mmHg during the night. So there may be people who appear to have normal pressure, who actually don’t have normal pressure at all. Despite this some people do have low pressure all the time and their optic nerve is just very sensitive and vulnerable to damage. The pressure might be normal for other people, but for them it is too high.

Another way to measure the effects of eye pressure over 24 hours is using this contact lens sensor (slide 12). This contact lens can be fitted by the doctor and then worn at home for 24 hours. The lens has a tiny pressure sensor that sends information wirelessly to a device worn on the waist. After 24 hours the patient needs to come back to the clinic to have the lens removed and the stored data can be downloaded by the doctor. The lens does not measure intraocular pressure directly but instead measures the changes in the shape of

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the cornea that are believed to occur as a result of changes in eye pressure. Although more work needs to be done to see how these changes relate to eye pressure, and whether fluctuations in pressure actually increase the risk of glaucoma, these sorts of developments could help us better understand glaucoma.

### 3. Developing better treatments.

What is the ideal glaucoma treatment? Perhaps the ideal would be something you need to use only once, or at least less often than the current treatments. Definitely something that has few side effects; something that doesn't irritate the eyes or make them red or make the eyelashes grow longer. And probably something that doesn't involve putting any drops in your eye at all; you could just throw the drops away. What about something that could protect the nerve and re-grow the nerve: something that might actually improve vision? We are still a long way from being able to improve damage from glaucoma, but there is some progress being made to improve current treatments and develop new ones.



Slide 13

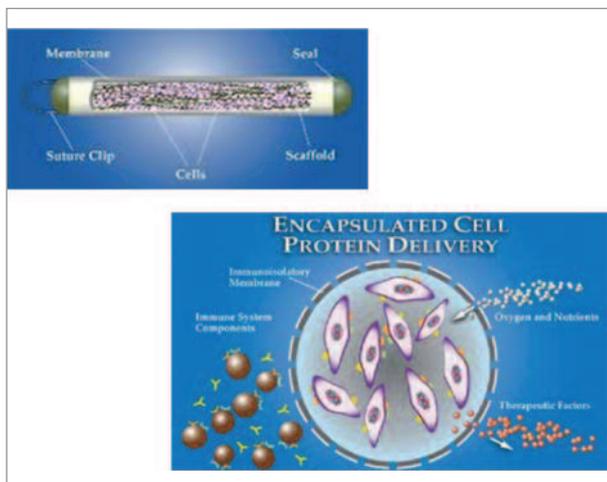
There are new ways to deliver drugs to the eye in development. This is an implant that can be placed into the tear duct, which slowly releases the drug over time (slide 13). This is a potential alternative to daily use of eye drops. Other ways of delivering drugs could include implanting a slow release drug under the conjunctiva or directly into the eye. Perhaps if we are able to deliver a drug closer to the optic nerve it will have a better effect, and reduce side-effects such as red eye that occur with some eye drops.

What about protecting the optic nerve? The current approach to protecting the optic nerve depends on lowering intraocular pressure but there are other treatments being explored. One such treatment uses a capsule containing a naturally

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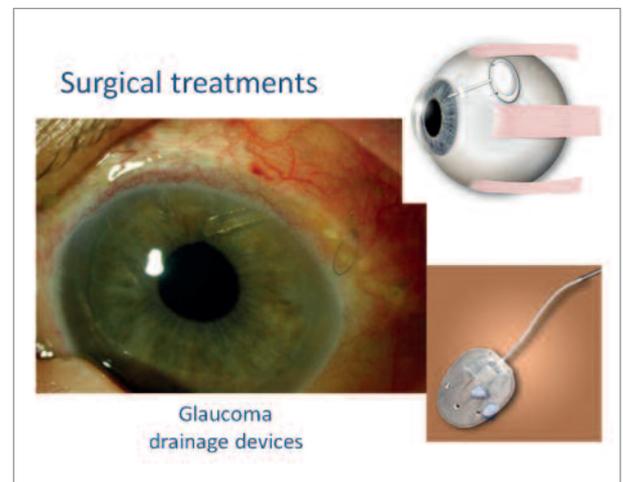
produced chemical called Ciliary NeuroTrophic Factor (CNTF). Living cells can be engineered to secrete CNTF and then trapped within a capsule that can be implanted into the eye. The purpose of the capsule is to protect the cells from the patient's immune system but the capsule also has little openings that allow oxygen and nutrients to gain access to the cells, keeping them alive and producing CNTF. The CNTF can leak out of the capsule through the same tiny openings and then nourish the optic nerve and retinal ganglion cells. One way to think about this is like plant food for the optic nerve (slide 14). There have been some early studies using CNTF in a handful of patients with glaucoma. The studies have concentrated on safety and so far it seems to be safe but we really don't know whether it will be an effective



Slide 14

treatment for glaucoma yet. Larger studies are needed. The initial hope for CNTF and other nourishing factors is that they might offer a way to preserve the optic nerve that does not depend on lowering pressure. There is also much interest in the use of stem cells to improve vision. Stem cells are beginning to be tested in some inherited eye diseases of the retina, and disease of the cornea, but using stem cells to regrow the optic nerve in glaucoma is a more challenging prospect.

It is also important to think about some newer surgical treatments. One thing that's changed recently is the growing number of operations available for glaucoma. One of the main operations for glaucoma is called trabeculectomy (Slide 15). This operation involves making a small opening in the eye, which is



Slide 15

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covered by a trapdoor, secured with stiches. Trabeculectomy works well for many patients, but is not suitable for all. Glaucoma specialists are increasingly using glaucoma drainage devices, or glaucoma tubes. A glaucoma drainage device is particularly suited for people who have had previous eye surgery or with more complex conditions. There is also a range of procedures known as Minimally Invasive Glaucoma Surgery (MIGS). These include various devices that are injected into the eye to create channels to increase drainage of fluid from the eye and lower pressure. There is also a procedure known as trabeculotomy, in which the wall of the trabecular meshwork is removed. The trabecular meshwork is part of the eye's drainage channel that can become blocked in glaucoma. These procedures have good safety but as yet do not seem to lower intraocular pressure as much as trabeculectomy or glaucoma drainage device surgery.

Finally I wanted to mention an important study of which several Scottish centres are involved. The **Treatment of Advanced Glaucoma Study (TAGS)** is a national study, based in Nottingham, which aims to answer the question 'is

initial medical or surgical treatment best for patients with advanced glaucoma?' We really don't know the answer to this. Many glaucoma specialists feel that when somebody presents with advanced glaucoma it might be best to go for early surgery, as these patients tend to need very low pressure, and trying various eye drops may delay a more definitive treatment. However surgery has risks and medication may work. It will be interesting to see the results of this study.

### Summary

So to summarise, what's new in glaucoma? Well, we are making progress in the three key areas I have discussed. We can diagnose glaucoma earlier than before, we can detect progression better and improved treatments are emerging. However, much more needs to be done.

### Andrew Tatham

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