



THE ACHIEVER

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INSIDE

FROM THE PRESIDENT	2
FEATURES:	
MRS AMERICA FIGHTING FOR CURES FOR RETINAL DISORDERS	4
HOW BLIND PEOPLE'S BRAINS ADAPT TO ASSISTIVE TECHNOLOGY	5
TECHNOLOGY TOOLS AND TIPS FOR THE VISUALLY IMPAIRED	6
CHARLES BONNET SYNDROME	8
RETINAL PROSTHESIS APPROVAL	10
RESEARCH UPDATE:	
IRDR & DNA BANK UPDATE	11
ARVO 2011	13
PATIENT GROUP AMD ALLIANCE INT RESPONDS TO CATT TRIALS	14
VITAMIN D CONSUMPTION AND REDUCED RISK OF MD	15
AMD CAUSES	16
RESULTS OF ELECTRICAL STIMULATION STUDY FOR RP	17
RESULTS OF GENE THERAPY STUDY FOR BARDET-BIEDL SYNDROME	18
QUESTION TIME & LAST WORD	19

WARMING

WINTER NEWS

- Technology and the Vision Impaired
- IRDR and DNA Bank Update
- Focus on MD
- What are Charles Bonnet and Bardet-Biedl Syndromes?



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From the President - Leighton Boyd

It has been very exciting to see that during the previous three months there has been significant news regarding retinal research published online and in our local newspapers and other media. Information from a selection of these is included in this Achiever. We will continue to keep you up to date in the future.

Last week you may have read about the “bionic eye” that has been granted approval for implementation by European regulators. This is the same “bionic eye” that is referred to in the article about Retinal Prosthesis on page 10 of this Achiever. As mentioned, this device named the Argus II, has 60 electrodes and a camera attached to a spectacles frame. It is believed that after several months, people who have the device implanted will be able to learn to recognize objects and shapes. The cost for this device, which will be available in England, is \$86,000 and the training needed to use it will be an additional \$17,000.

The Argus II is one of 30 devices for artificial vision being worked on worldwide for patients with advanced inherited retinal diseases, including Retinitis Pigmentosa. It is the first device using bionic eye technology to gain approval for general use and the results of the trials of this electronic implant clearly indicate that such devices can reliably restore worthwhile sight. In the not too distant future we may hear about different types of “bionic eyes” being available for implantation in Germany and in Japan. Other teams who are in the developmental stage are located in Boston USA, Korea and Australia. The Australian “bionic eye”, which has featured in previous Achiever articles, is concentrating on utilising diamond based technology and an excess of 90, three dimensional, electrodes, compared to the 60 electrodes of Argus II, and is anticipated to deliver significantly clearer vision than other types of devices.

Details of the current stage of research involving “bionic eyes” as well many other projects investigating possible treatments and cures for inherited retinal diseases were presented recently at the annual meeting of the Association for Research in Vision and Ophthalmology (ARVO) and the 2011 meeting of the Scientific and Medical Advisory Board of Retina International (SMAB). Both meetings were held in Fort Lauderdale USA. Information about ARVO 2011 is included in this Achiever and one of the reports from that meeting is featured.

In keeping with our normal practice, the guest speaker at our AGM, which this year will be held on Saturday 1 October, will make a presentation about their own investigation into retinal diseases, as well as bringing us up to date with the latest world-wide research including news from ARVO and SMAB. Detail of the AGM will be sent closer to October but if you put this date in your calendar now, you will be free to come along and hear this news first hand.

Recently I represented Retina Australia at meetings held independently by Vision 2020 and the Centre for Eye Research Australia (CERA). These meetings are becoming regular events and enable us to network with many of the other organisations and agencies involved in the blindness and vision impaired

sector. As well as finding out about what is happening at Vision 2020 and CERA, these meetings enable us to tell other groups about the work that we do.

As flagged in the previous Achiever, there has indeed been much discussion about the proposed National Disability Insurance Scheme (NDIS) during recent months. I have been involved in contributing to responses to the Productivity Commission with both Vision 2020 and Blind Citizens Australia. The focus of these responses has involved the concern that the published draft documents about the NDIS are unclear as to the extent to which the blindness and low vision sector was included in the development of the scheme. Concerns were also raised as to how the proposed NDIS would meet the needs of blind and vision impaired individuals and their immediate carers. We will keep you informed about further developments of the NDIS as it unfolds.

I will be attending the annual Gerard Crock Lecture on Thursday 9 June at the National Gallery of Victoria. This year Professor Hugh Taylor, who is the Harold Mitchell Chair of Indigenous Eye Health at the University of Melbourne, will be presenting the lecture. His topic is, "*The challenges for eye care in Australia*". These lectures have been named in honour of Professor Gerard Crock AO who was the foundation Ringland Anderson Professor and Head of Department of Ophthalmology at the University of Melbourne. Of more relevance to us, Professor Crock was for many years a trustee of our organisation and assisted members through his work as their ophthalmologist at the Royal Victorian Eye and Ear Hospital or in his private practice.

Every year about this time we have a Donation Drive to raise money specifically for research. During the last twenty years we have raised over \$400,000 from these donation drives and other specific events as well as through the sales of merchandise including our Owl Badges. Last year we raised money for the Inherited Retinal Disease Register & DNA project and for the Retina Australia research pool which funds approved Australian research. This year we are raising money specifically to support Australian Research.

One way in which some members and friends donate money towards research is through a regular Pre-authorized Credit Card Donation (PACC). Such donations are usually made monthly, with contributors choosing the regular donation amount. Donations of \$2 or more are tax deductible and a receipt for the total yearly donation is sent to PACC donors at the end of the financial year. An example of this scheme is where a person donates \$20 per month, which is an annual donation of \$240. This is a significant donation for us as recipients, but perhaps more achievable than a lump sum donation for the person involved. If you, or any member of your family or friends, are interested in contributing in this way please contact the office for details.

Finally, I remind you that July is the month for membership renewal and you should shortly receive your renewal notice. Monies raised through memberships help us to produce the quarterly newsletters, to send information to people who are newly diagnosed and to maintain the office. We would appreciate your prompt response so that we can budget appropriately.

FEATURES

Mrs America Fighting for Cures for Retinal Disorders

April Lufriu is just like many other women. She juggles being a mother, wife, counsellor, tutor, volunteer, organiser, and at times referee among many other duties sometimes demanded of us in our roles. There is one small detail that sets April apart. In April, April was aptly crowned Mrs. America in the televised Mrs. America pageant which took place in West Virginia. Along the way she was crowned Mrs. Florida America 2011 at the Mrs. Florida America pageant which took place in Orlando in February.

The purpose of these events is to celebrate married women, and also to give participants a chance to bring attention to issues important to them. The event afforded April the chance to spread the word about the importance of retinal research with a large audience.

April strives to educate others about the need for retinal research with the hopes of helping to find a cure for vision disorders. April is President of the Tampa Bay Chapter of Foundation Fighting Blindness. This cause is of vital importance to April as she herself, her sister, as well as both of her children are affected by different forms of Retinitis Pigmentosa. This past November students at the Trinity School for Children, including her two children who attend the school, participated in Tampa's first ever 5 km Vision Walk and raised \$4508.34 for the cause. April organised this event and put in many hours to encourage participation by as many Trinity students as possible.

For April, being Mrs. America isn't all about the beaded gowns and tiaras. It is about something much more important than that, the future of her children which are "her world".

April standing proud after being crowned Mrs. America.

The beautiful April Lufriu, ambassador for retinal research.

April pictured with her husband George, and their 2 children aged 11 and 7.



Source: Edited and adapted from various press releases.

How Blind People's Brains Adapt to Assistive Technology

If you observe an experienced user of a screen reading program, such as JAWS or NVDA, when browsing the web, you will be amazed at their level of skill at using assistive technology. New research recently reviewed in the Scientific American has demonstrated that the skill and precision at which these users are able to understand voice synthesis may be related to the way in which their brains have developed and learnt to adapt to their disabilities.

A large amount of the brain is devoted to processing visual stimuli. For many blind people, the area of the brain known as V1, which responds to light, cannot be utilised as it does not receive the environmental input it requires to develop appropriately. Functional brain imaging has demonstrated that some people who are vision impaired are using this area of the brain in a different way and for a different purpose than sighted individuals. Given that they are more reliant on listening to speech to understand their environment than vision, this area of the brain has been found to adapt and process speech and language instead of visual input, in order to be more functionally useful.

The ability of the brain to adapt in response to its environmental needs has resulted in some vision impaired individuals being able to process speech at a much higher rate than sighted individuals. Whereas sighted people can comprehend speech at a rate of 10 syllables per second, some visually impaired people can comprehend up to 25 syllables per second.

Sean Randall, an experienced screen reader user, has noticed a dramatic improvement in his comprehension over time, "I recently re-read Harry Potter and the Philosopher's Stone. I first heard it in audio form 11 years ago and the reading took eight and a half hours. My latest reading, at a comfortable, if leisurely synthetic pace, took precisely one-hundred and fourteen minutes and six seconds."

Like many screen reader users, Sean prefers speech synthesis that sounds clear at high speed, rather than more naturally sounding verbal output from his computer. "I don't want a computer that sounds like a human", he explains, "I've not yet met a human who can impart information to me at over 400 words per minute, be it fiction or source code, with the same level of efficacy."

Sean cautions against speaking quickly to people with vision impairments, "I can't process people who yammer at me at high speed; it seems a skill limited to synthetic speech."

The findings pose some interesting questions for Bionic Vision Australia (BVA), an Australian consortium of researchers who are in the process of creating a

neurostimulator, or 'bionic eye', to aid vision. Until clinical trials commence, researchers won't really know how the brain will respond to the visual information a bionic eye could deliver. As a result, it is hard to know how much 'rewiring' of the brain will be 'un-wired' and how this will affect patients ability to process audio from screen readers and other assistive technologies.

Rewiring of the brain is more pronounced in people who lose their sight at a young age, but the conditions that the bionic eye targets, namely retinitis pigmentosa and age-related macular degeneration, are degenerative conditions, meaning that people lose their sight gradually over time. This means that bionic eye patients would generally be adults who have had well-developed vision in the past, thus the extent to which their brain would be rewired would be less.

"After a patient gets their first implant, there would be a fairly long period of adjustment and training to help the brain make sense of the information it is receiving from the bionic eye", explains Veronika Gouskova from BVA, "The potential psychological implications can also be quite serious. If a person has adapted to having no vision at all, the brain can become overwhelmed with the information it is suddenly flooded with."

"Our first patients will be very carefully selected and clinicians will work very closely with their families and support networks to make sure the adaptation process is as smooth as possible. But until we start working with our first patients, we really can't say what they'll experience and how this will affect them. It is also likely that the responses will vary from patient to patient, while the technology is still quite new."

Patient tests amongst BVA's international colleagues in Germany and the USA have indicated that some people respond very well to having their sight restored, but this research is still in its early stages.

Source: *Bionic Vision Australia.*

Technology Tools & Tips for the Vision Impaired

Modern technology can make life so much easier for everyone, including those with vision impairment, but with the trend towards making everything smaller, sometimes it can be difficult to utilise all the new tools and functions available.

Here we look at just a few ways to make things easier for those with poorer eyesight:



Large Button Mobile Phone

The Seniorphone has been designed specifically to be easy to use with its big buttons and easy to use menu style. The phone features:

- Large buttons
- Easy to use menu
- Loud ringtones
- Programmable SOS button
- Easy calling with speed dials
- Completely unlocked—will work with any simcard
- No contracts or monitoring fees

For more details go to www.seniorphone.com.au or phone 1300 821 660.

Microsoft Software Help

With every new version of Windows or the Office suite, Microsoft enhance the features for those who find it harder to see to navigate around the screen. When using Office, type “Accessibility Features” into the help section and it will bring up the helpful features for your version of Office. With Windows you can use the *Accessibility Wizard* (XP or earlier) or *Ease of Access Centre* (Vista & 7) which offer a number of features that allow you to change some of the settings on your computer to make them easier to see.

Some of the settings you can change include:

- Increase the font size for Windows title bars, menus and other features.
- Increases the size of items on screen including the text inside windows.
- Use Microsoft Magnifier which opens a floating window that displays an enlarged view of part of the screen.
- Select the size of scroll bar and window borders.
- Choose the size of icons on your desktop.
- Choose high contrast display colours that make text easier to read.
- Choose the size and colour of your mouse cursor .
- Change the blink rate and width of the cursor.

Additionally, many other programs and hardware are compatible with Windows and available to help individuals who are blind, including screen readers, Braille output devices, and other useful products. For more information, go to <http://www.microsoft.com/enable/>

Charles Bonnet Syndrome

The article below describes a little known and little understood syndrome which can affect those with severe sight loss. Hopefully, knowledge will soon grow as several research groups are currently investigating its cause and potential treatments.

Many people, particularly the elderly, who have suffered severe sight loss may also experience Charles Bonnet Syndrome (CBS). CBS is manifested by hallucinations or visions that can be quite frightening and unpleasant but may also be attractive and amusing. The condition was first described in 1760 when Charles Bonnet wrote of the images seen by his nearly blind grandfather - birds, patterns, buildings - none of which were there. Towards the end of his life, Charles experienced similar 'visions', although not as a consequence of failing sight.

Since then, very little has been heard about CBS because to admit to "seeing things" might risk being thought of as being mentally ill. There are an estimated 100,000 people in the UK with CBS caused by macular disease. If we include people with CBS caused by retinitis pigmentosa, glaucoma and diabetes, the number of sufferers will be far larger. Yet even now, relatively little is known about the syndrome, even in the medical world. Recently however, the Royal National Institute of Blind People (RNIB) and the Macular Disease Society (MDS) have helped raise awareness of the subject. Hopefully, as CBS becomes better known and understood, people will be able to express their experiences without fear of prejudice.

The "visions" can be in black and white or technicolour, static or mobile, frightening or fun, but no doubt very annoying. The most irritating seem to be complicated patterns such as netting, bricks or tiles, but they might be as bizarre as seeing little people in the dining room, a forest in the garden or a gargoyle sitting at the end of the bed.

There are a few drugs that help some people but they do have side effects, and the best way to cope is to talk about the frustration and incomprehension that attend this syndrome. It is thought that because the brain is receiving fewer signals from the eyes it compensates by producing fantasy pictures or old images that it has stored. Once people understand what is happening and are assured they are not suffering from a mental illness they are better able to fight back. The advice is to challenge the visions, sit if you are standing, if the light is on turn it off, move your eyes around and tell the visions - very firmly- to go away. The RNIB are shortly to publish a specific eye movement exercise which they believe may be effective for sufferers with macular disease.

When a hallucination starts, look from left to right about once every second for 15-30 seconds, without moving your head. As a guide to how far to move your eyes, imagine two points about a metre apart on a wall in front of you and look from one point to the other when standing about a metre and a half away. Your eyes should be held open during the movements. If the hallucination continues, have a rest for a few seconds

and try another 15-30 seconds of looking left and right. If the hallucinations have not diminished or stopped after 4 or 5 periods of looking left and right for 15-30 seconds, the treatment is unlikely to work and you can stop. It may be worth trying again on another occasion or for a different type of hallucination.

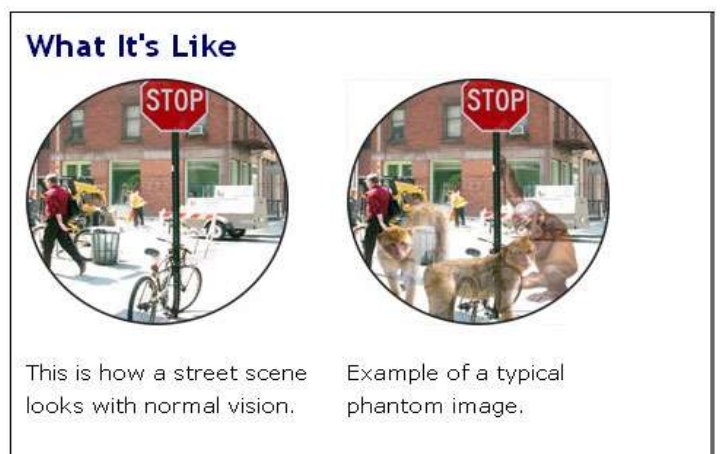
CBS can be very frustrating but at least the symptoms are silent and usually disappear after about eighteen months. When they start a medical check is advisable to make sure there is no other cause, but CBS sufferers are assured they are not suffering from a serious mental illness. Their problems are caused by poor sight and nothing else.

My uncle developed CBS when his RP became particularly bad, and the brick walls and looming patterns frightened him. A forest appeared in his tiny garden but when he understood what was happening he enjoyed the trees and the little people in brightly coloured clothes who were waving to him - as he said it was better to have that scene to watch than see nothing at all.

Recently my brother rang, for months he had had an enormous eye looking at him, then rows of type, and now chessboards that prevent him from using what little sight he still has. He feared he had a brain tumour or was going crazy. I mentioned CBS but he lives in northern Canada where none of the medics had heard of the syndrome. After some research and a lot of discussion, he understands what is happening and is coping much better and is reassured to know that the symptoms are usually temporary.

It occurs to me that the images seen by my uncle were related to his move from a house with a huge, well-loved garden with many trees to one with a tiny patio. My brother was a journalist and a fanatical chess player, so his images may have been stored in the brain, but could there be a psychological element as well - a sort of wish list of important elements in life which poor sight has destroyed? Hopefully, as the syndrome becomes better understood the bricks, the monsters and the little people will be made to go away.

Dr Dominic Ffytche, Clinical Senior Lecturer King's College London and Honorary Consultant Psychiatrist, has commented on this article. He says, "The explanation of your uncle's and brother's experiences in terms of their wishes is entirely plausible. In fact, wish fulfilment was the main account of hallucinations up until the 1960's. The problem is that most people who see chessboards and gardens do not have specific links to these experiences that reflect a wish or desire."



Source: Jane Canelle, RP Fighting Blindness Quarterly Members' Magazine, Spring 2011, Issue No. 138.

Retinal Prosthesis Approval

After more than 20 years of research and development involving a team of international specialists, Second Sight Medical Products, Inc., has announced that its Argus II Retinal Prosthesis System ("Argus II") is now approved for sale in the European Economic Area (EEA). After a successful clinical trial involving more than 30 blind patients around the world, and a very thorough review of the product's safety and performance by an independent expert body, this device becomes the first approved treatment available for sightless people.

"After years of research, we are very happy to be able to offer a viable long-term solution for people suffering from advanced retinal degenerative diseases such as retinitis pigmentosa (RP)," said Robert Greenberg, MD, President and CEO of Second Sight. "The CE Mark approval, which comes after intense regulatory review of our trial and our device, represents a huge step forward for the field and for these patients who have, until now, had no proven treatment alternatives."

Argus II is Second Sight's second generation implantable device intended to treat profoundly blind people suffering from degenerative diseases such as RP. The system works by converting video images captured from a miniature camera, housed in the patient's glasses, into a series of small electrical pulses that are transmitted wirelessly to an array of electrodes on the retina. These pulses then stimulate the retina's remaining cells resulting in the corresponding perception of patterns of light in the brain. Patients learn to interpret these visual patterns thereby gaining some functional vision. Thirty patients participated in the clinical trial, using the device at home and in their daily lives since the trial started.

Although the resulting vision is far from normal, investigators in the clinical trial of the Argus II are excited by the results. "After more than 3 years of clinical trials, we were happy to demonstrate the performance, safety and long-term reliability of Argus II," explained Professor José-Alain Sahel, Chairman, Department of Ophthalmology: Quinze-Vingts National Ophthalmology Hospital, Paris, France.

Adds Dr. Lyndon da Cruz, MD PhD Consultant Retinal Surgeon at Moorfields Eye Hospital in London, UK, "The fact that nearly all patients had a stable, safe and functioning system and that a majority of patients could recognise large letters, locate the position of objects and the best could read short words impressed us beyond our most optimistic expectations."

"This 'artificial retina' brings hope to thousands of people with advanced retinal diseases" added David Head, Chief Executive of the British Retinitis Pigmentosa Society. "The restoration of an element of vision may bring with it the restoration of independence and mobility that would greatly improve a patient's quality of life."

Source: Adapted from Second Sight Press Release, Lausanne, 2 March 2011.

RESEARCH UPDATE

IRD and DNA Bank Update

The purpose of the Australian Inherited Retinal Disease (IRD) Register and DNA Bank project is to maintain a public and enduring Australian resource for use by approved scientists and clinicians embarking on inherited retinal disease research. The resource consists of (1) a register of consenting Australians affected with an IRD and their family members, and (2) a DNA bank containing DNA from consenting individuals.

A short-term aim of this project is to collect 3000 DNA samples, with associated clinical and family history information, from IRD-affected individuals and appropriate family members by March 2012. We are on track to meet this aim. The table below provides some statistics relating to the register and DNA bank.

	Aug 2004	Aug 2005	Aug 2006	Aug 2008	Apr 2011
General Statistics					
Subjects in register	1014	1209	1285	1680	3279
Families in register	616+	715	735	882	1382
Genetic Testing					
DNA samples stored	252	405	444	724	2080
DNA samples analysed	0	0	0	52	314
No. of subjects with mutation(s) identified	0	0	0	12	191
No. of families with mutations(s) identified	0	0	0	4	95

Genetic Analysis

The current status of genetic analysis for various diagnoses is summarised below.

Autosomal Dominant Retinitis Pigmentosa (adRP)

So far we have identified disease-causing mutations in 24 individuals on the register. The genes in which mutations have been identified in our population are RP1, PRPF3, RDS, RHO and USH2A.

Autosomal Recessive Retinitis Pigmentosa (arRP)

Over 35 disease-causing genes have been identified for arRP. Because of this, we have analysed arRP DNA using SNP genotyping analysis, which allows the elimination of genes from a set of possible disease-causing genes. DNA from 93 individuals sourced from 21 families diagnosed with arRP have been analysed. The number of candidate disease-causing genes for each family was reduced to between two and 18 genes. In over half of the families analysed, the number of candidate genes was reduced to between only two and nine. Mutations in the gene PDE6B have been identified as disease-causing for two individuals.

X-Linked RP (xLRP)

A collaboration is being established with laboratories in Melbourne and Manchester which will enable the genetic analysis of DNA arising from xLRP diagnosed families to be carried out at low cost in laboratories that specialise in this analysis.

Juvenile X-linked Retinoschisis

Juvenile X-linked Retinoschisis is caused by mutations in the RS1 gene. DNA from 9 subjects sourced from 4 families in the register has been genetically analysed by sequencing the RS1 gene. A mutation was found in each DNA sample analysed. Three distinct variants were identified, with all subjects within a family exhibiting the same variation. Two of the variants have been previously reported, while one is novel.

Stargardt Disease (Fundus flavimaculatus)

Stargardt Disease is the most common juvenile macular dystrophy. Inheritance is usually autosomal recessive with mutations in the *ABCA4* gene. DNA of affected members from families diagnosed with Stargardt Disease or Cone- Rod Dystrophy were sent for microarray analysis of 501 genetic variants in the *ABCA4* gene. Known disease-causing mutations in the *ABCA4* gene were identified in 108 individuals.

Macular Dystrophies

In addition to its implication in adRP, the RDS gene is thought to be implicated in some macular dystrophies, including the Pattern Dystrophies, Vitelli-form Dystrophy and CACD, and the currently less well-defined macular dystrophies. We are currently preparing to carry out genetic analysis on DNA from individuals clinically diagnosed with these dystrophies.

Choroideraemia

Choroideraemia is caused by mutations in a single gene, known as CHM. We have sequenced the CHM gene from six affected families. Results of genetic analysis are not ready for reporting.

Usher Syndrome

We are currently genetically analysing the DNA obtained from Usher's-affected families. To date we have identified disease causing mutations in 31 individuals. Genes implicated in our population so far are USH2A, CRB1 and MYO7A.

Leber's Congenital Amaurosis (LCA)

The IRD register currently contains 11 families having at least one member affected with LCA. The disease-causing gene has been identified in four of those families. A mutation in the gene CRB1 was identified for two families, and in CEP290 for two other families.

Website

Our website is:

http://www.scgh.health.wa.gov.au/departments/medical_technology/inherited.html

The website invites interested scientists and clinicians to apply to make use of this resource. The website includes a link to a document which lists (1) all DNA samples collected, (2) the best diagnosis relating to the subject from whom each DNA sample was obtained, (3) the probable causal mutation where identified and (4) the place of origin of the DNA. No subject identification information is available on this website. This website is updated every six months.

The Future of the Resource

As this resource has matured we have begun receiving increasing numbers of requests from ophthalmologists and genetic counselling services to provide genetic results which we may have obtained for their patients. We are currently actively instituting protocols allowing us to report genetic analysis results to appropriate ophthalmologists or genetic counselling services where we have established information that may be beneficial for the medical management or counselling of a research participant. This will involve our contacting the research participant to obtain their written consent for the release of this information. As we have so far established the disease-causing mutation in less than 10% of subjects for whom we have collected DNA this new initiative is not initially expected to affect many participants.

A detailed proposal for the further development of this resource is provided in the document "Discussion document for the further development and use of the Australian Inherited Retinal Disease Register and DNA Bank for the period 1st April 2012 to 31st March 2015". This document proposes a greater emphasis on the genetic analysis of collected DNA and a lesser emphasis on DNA collection.

Source: Dr John de Roach, Principle Medical Physicist, Sir Charles Gairdner Hospital.



This year the annual meeting of the Association for Research in Vision and Ophthalmology ("ARVO 2011") was held at the beginning of May in Fort Lauderdale, Florida. The theme of the meeting was visionary genomics and the objective of the meeting was to provide a forum for the worldwide exchange of information that will lead to discoveries and better treatments for eye and vision disorders. Approximately 11,000 scientists and clinicians from around the globe were in attendance.

We learned of significant advances in the field of retinal degenerative diseases. Perhaps the biggest news at ARVO 2011 came from a report of the 1-year results of the Comparison of AMD Treatments Trials (CATT) - see next page. Among the many other areas were potential treatments related to the use of neurotrophic compounds, small molecules and anti-neovascular agents, gene therapies, retinal prostheses and stem cells treatments.

Patient Group AMD Alliance International Responds to CATT Trials

Results of the Comparison of AMD Treatments Trials (CATT) study have been published in The New England Journal of Medicine (NEJM). The CATT study was designed to compare two drugs currently used to treat wet-AMD: Lucentis (ranibizumab) and Avastin (bevacizumab) - a drug that is used off label for ocular use in a number of countries around the world.

"As an organisation representing more than 30 million people around the world living with age-related macular degeneration, we have been anxiously awaiting the results of the CATT study," said AMD Alliance International CEO, Narinder Sharma. "Proven safety and efficacy should be the only concern of any treatment debate. With the guidance of our respected Science Panel Chair, Dr. Alan Cruess, we have reviewed the report and believe that it is important to put this high profile study into context and encourage frank and open dialogue between patients and doctors about all treatment options and potential risks."

What Does CATT Tell Us?

The highly anticipated CATT study, sponsored by the National Eye Institute (NEI) is reporting non-inferiority of bevacizumab (Avastin®) monthly intravitreal injections in terms of efficacy for choroidal neovascularization (CNV) secondary to age-related macular degeneration (AMD) relative to the gold standard therapy, ranibizumab (Lucentis®) injected monthly. As widely anticipated by the worldwide community of retina sub-specialist ophthalmologists, bevacizumab injected monthly appears to preserve vision in this disease as well as ranibizumab intravitreal injected monthly. Furthermore, it means secondarily that bevacizumab appears to reduce retinal thickness, reduce sub-retinal fluid and resolve sub-retinal bleeding as well as ranibizumab.

What Does CATT Not Tell Us?

Safety signals, of new medicines, especially for relatively uncommon events such as endophthalmitis, stroke or myocardial infarction are notoriously difficult to detect, often times for years following the approval and licensing of a new drug therapy. Examples of this abound, such as the recall of Vioxx®, the black box safety warnings for systemic bevacizumab and rosiglitazone (Avandia®), to name some cases in point.

Fortunately, in this case, we do have access to a large amount of accumulated data concerning both the ocular and systemic safety of ranibizumab, through the pooling of results from many large clinical trials. In fact, stroke has been recognised with a label warning as a legitimate risk of intravitreal ranibizumab therapy, especially if a given patient has been afflicted with prior stroke before undertaking therapy. We do not have this information regarding intravitreal bevacizumab, and, unfortunately, CATT does not put these relevant safety concerns to rest.

Next in the Comparative Effectiveness Research (CER) pipeline is IVAN, and subsequently trials from around the world notably from Australia, France, Germany, Brazil, Norway and the Netherlands are due to report in the coming years. At a minimum these trials should all be brought to completion, regardless of the results of CATT and IVAN, because the accumulated data from these trials will be crucial to a better understanding of the relative safety risks of these two drugs. The accumulated CER clinical trial data of bevacizumab vs. ranibizumab will hopefully make possible a high quality meta-analysis to compare the safety signals mentioned.

Safety concerns are legitimate in the debate about off label use of unproven yet inexpensive and readily available alternatives to proven licensed therapies. Safety comparisons, notwithstanding efficacy similarities, are not yet powerful enough to make conclusions that should alter public policy. The gold standard for the treatment of "wet" age-related macular degeneration remains intravitreal ranibizumab. Cost savings should not trump safety concerns in ocular disease any more than in cardiac disease.

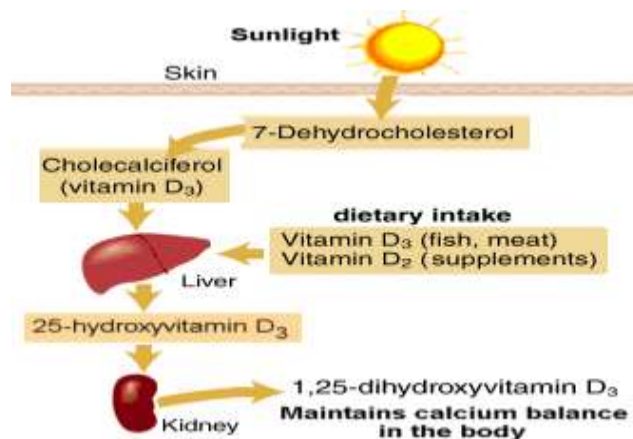
Caveat: Scientists from the Johns Hopkins University, presenting a late-breaking paper at ARVO 2011, reported on adverse effects of Avastin and Lucentis when used to treat AMD. Their findings are based on an analysis of the Medicare claims database and include over 77,000 patients. The results of this analysis seem to indicate a higher risk of overall mortality, hemorrhagic stroke, ocular inflammation, and subsequent cataract in patients treated with Avastin group. Also here, additional research is needed to explain the findings, which could be influenced by confounding factors such as smoking, lipid and blood pressure levels, and age.

Source: *Retina International.*

Vitamin D Consumption and Reduced Risk of MD: 2011 Study

As reported at ARVO, consuming vitamin D from foods or supplements might reduce the risk of developing age-related macular degeneration (AMD) in women younger than 75, according to a study published this week by the Archives of Ophthalmology.

A team led by researchers at the University at Buffalo, N.Y., examined data on blood levels of vitamin D among 1,313 women, 50 to 79, enrolled in the ongoing Women's Health Initiative study. In women younger than 75, vitamin D from foods and supplements (but not from time spent in direct sunlight) was linked with decreased risk of developing early age-related macular degeneration. Those who consumed the most vitamin D had a 59 percent decreased risk of developing it compared with women who consumed the least.



Sources: www.arvo.org
www.naturaleyecare.com May 2011
Newsletter

Age-Related Macular Degeneration Causes

While the exact causes of AMD are not fully understood, recent scientific evidence points to chronic vascular disease, including cardiovascular disease, as a potential cause. Scientists believe that slow degradation of the blood vessels in the choroid, which provides blood to the retina, may lead to macular degeneration.

A number of factors have been identified that may contribute to or cause macular degeneration such as:

- Family genetics (Patel 2008).
- Health conditions such as high blood pressure (Fraser-Bell 2008), and/or poor circulation (Kaufmen 2003), elevated cholesterol.
- Abnormalities in the enzymatic activity of aged retinal pigment epithelium (RPE) cells lead to accumulation of metabolic byproducts.
- Oxidative stress due to inflammation (Hollyfield 2008).
- Exposure to sunlight without protective sunglasses is a risk factor for AMD (Fletcher 2008).
- Insufficient intake of the B vitamins, lutein, zeaxanthin, and meso-zeaxanthin are linked to AMD (Ahmed 2005).
- The therapeutic efficacy of lutein and zeaxanthin in AMD is significant, according to the Lutein Antioxidant Supplementation Trial (LAST), which showed improvement in several symptoms accompanying AMD (Richer 2004).
- The Women's Antioxidant and Folic Acid Cardiovascular Study (WAFACS) in 5,442 female health professionals showed that daily supplementation with folic acid, B6 and B12 resulted in significantly fewer AMD diagnoses than a placebo (Christen 2009).
- Higher intake of specific types of fat, rather than total fat intake, may be associated with a greater risk for advanced AMD. Diets high in omega-3 fatty acids, fish and nuts were inversely associated with risk for AMD when intakes of linoleic acid (an omega-6) was low (Tan 2009).
- High trans fat consumption has been linked to an increased prevalence of late AMD in a study of 6,734 individuals. In the same study, olive oil consumption offered a protective effect (Chong EW 2009).
- Researchers have now found that bio-markers predictive of cardiovascular risk, such as elevated homocysteine and C-reactive protein (CRP) levels, are risk factors for AMD (Seddon 2010, Boekhoorn 2007).

Source: April 2011 Newsletter, www.naturaleyecare.com

Results of Electrical Stimulation Therapy Study for RP Patients

Okuvision GmbH, which specialises in the field of electrical stimulation therapy (EST) for early and intermediate stage retinitis pigmentosa patients, presented data from the company's first sham-controlled pilot study at ARVO's annual meeting. The study included 24 patients suffering from early and intermediate stage retinitis pigmentosa who were separated into three groups and received EST at varying strengths for 30 minutes once a week for six weeks. The presentation was delivered by lead author, Dr. Florian Gekeler of the Centre for Ophthalmology, Tuebingen University Eye Hospital.

Dr. Gekeler's poster presentation titled, "Transcorneal Electrical Stimulation in Patients with Retinitis Pigmentosa," highlights findings from Okuvision's first clinical trial which began in 2007 using a thread electrode to stimulate the retina with small amounts of current. Twenty-four patients with early and intermediate stage retinitis pigmentosa were randomised and separated into three different groups. Each group received different levels of stimulation-the first was treated without electrical current, the second with 67 percent of the individual threshold, and the third with 150 percent of the patient's threshold for 30 minutes a week for six weeks. Final evaluation showed a +20 percent statistically significant improvement in the field of vision by patients who received the 150 percent stimulation. The findings from this study emphasise that electrical stimulation of the retina liberates growth factors which may be able to delay retinal degeneration.

"Our team began this study with the goal of determining whether electrical stimulation therapy could safely and effectively preserve vision for early stage retinitis pigmentosa patients," said Dr. Florian Gekeler, consultant at the Centre for Ophthalmology of the University of Tuebingen, Germany. "The visual results achieved surpassed our initial expectations and it is our hope that these results will be the first step in ensuring that EST is considered a viable treatment option to slow the degenerative progress for retinitis pigmentosa patients."

"The results of our study show promise that a treatment option, while not a cure for retinitis pigmentosa, could be available in the future," said Dr. Walter-G. Wrobel, chairman and founder, Okuvision GmbH. "While much is still unknown about EST technology, the results of the study are a great step toward determining efficacy of this treatment and we look forward to conducting further studies to potentially reach out to those who are hopeful in delaying the effects of retinitis pigmentosa."

The study findings were also reported online on April 5, 2011 in *Investigative Ophthalmology & Visual Science*, the official journal of ARVO (A.Schatz *et.al.*, IOVS Papers in Press).

Source: 4 May 2011, www.medicalnewstoday.com

Gene Therapy Preserves Vision in Lab Study of Bardet-Biedl Syndrome

In a groundbreaking effort, scientists at Baylor College of Medicine used gene therapy to preserve vision in mice affected with a form of Bardet-Biedl syndrome (BBS), a devastating, multi-faceted disorder that causes significant vision loss from RP. This research advancement represents the greatest success thus far in the development of a treatment for RP associated with BBS.

BBS can affect many parts of the body, causing intellectual disabilities, learning problems, obesity, genital abnormalities, and serious kidney dysfunction, as well as significant vision loss from RP. The range and severity of disorders varies from person to person, though individuals with BBS are usually legally blind by the age of 16. Genetic researchers have identified variations in approximately 15 genes that can cause the disorder.

Led by Samuel Wu, Ph. D., Camille and Raymond Hankamer, Chair in Ophthalmology at Baylor College of Medicine, the research team injected the treatment underneath the retinas of mice affected by variations in the BBS4 gene. The therapy consisted of a corrective BBS4 gene that was delivered to photoreceptors in the retina by an adeno-associated virus, the same mechanism used in successful gene therapy clinical trials for Leber congenital amaurosis (LCA). The team observed that photoreceptors treated with the BBS gene therapy survived and continued to provide vision while untreated photoreceptors died.

The BBS4 gene plays an important role in facilitating the transport of rhodopsin, a light-absorbing protein essential for vision, to the outer segments of photoreceptors. When BBS4 is defective, rhodopsin doesn't reach the outer segments, and as a result, vision is lost and photoreceptors degenerate.

"We are very pleased with this advancement, because it holds promise for preserving vision for people affected by an extraordinarily challenging condition. We are delighted to have a treatment option emerging for them," says Stephen Rose, Ph. D., chief research officer, Foundation Fighting Blindness. "Furthermore, it is great to see the research community leveraging the success of our landmark gene therapy trials for Leber congenital amaurosis. This is just one of many examples of how the LCA work is opening the door to treat a variety of retinal degenerative diseases."

David Simons, an investigator on the BBS gene therapy project, says that the team's work has strong clinical potential. "It is a little early to predict when this treatment would be ready for a clinical trial. There's more work to be done. But this is a huge step forward," he says. "Our success also opens the door for treating Bardet-Biedl syndrome caused by other genetic variations."

Source: *Foundation Fighting Blindness, 28 March 2011.*

Question Time *with Bev Sellens*

In this edition, Bev Sellens has kindly agreed to volunteer for Question Time.



1. What's your earliest memory?

Sitting on a big pink iron bed at Christmas with my presents.

2. What's your idea of a good time?

Going out to lunch with family and friends.

3. What's your ideal holiday destination?

Tasmania and Merimbula.

4. Who inspires you?

Friends and family.

5. What makes you angry?

Greed.

6. What's the hardest thing you've ever done?

Saying goodbye to my grandson when he went to live in Japan.

7. What's the best thing you've ever done?

Getting married and having a family.

8. What do you like about Retina Australia (Vic)?

That they keep in contact and the friendship.

9. If you could change one thing about the world, what would it be?

That all wars end today and no more were to start.

10. What's the most important thing you've learnt about life?

If it is to be it is up to me.

Last Word

Knowing is not enough; we must apply.

Willing is not enough; we must do.

JOHANN WOLFGANG VON GOETHE, 1749 - 1832

Nothing will ever be attempted if all possible objections must first be overcome.

SAMUEL JOHNSON, 1709 - 1784

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