

ANNUAL REPORT

Eye research in
the clinic and the
laboratory leads to
new treatments
to save sight



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CENTRE
YOUR SIGHT
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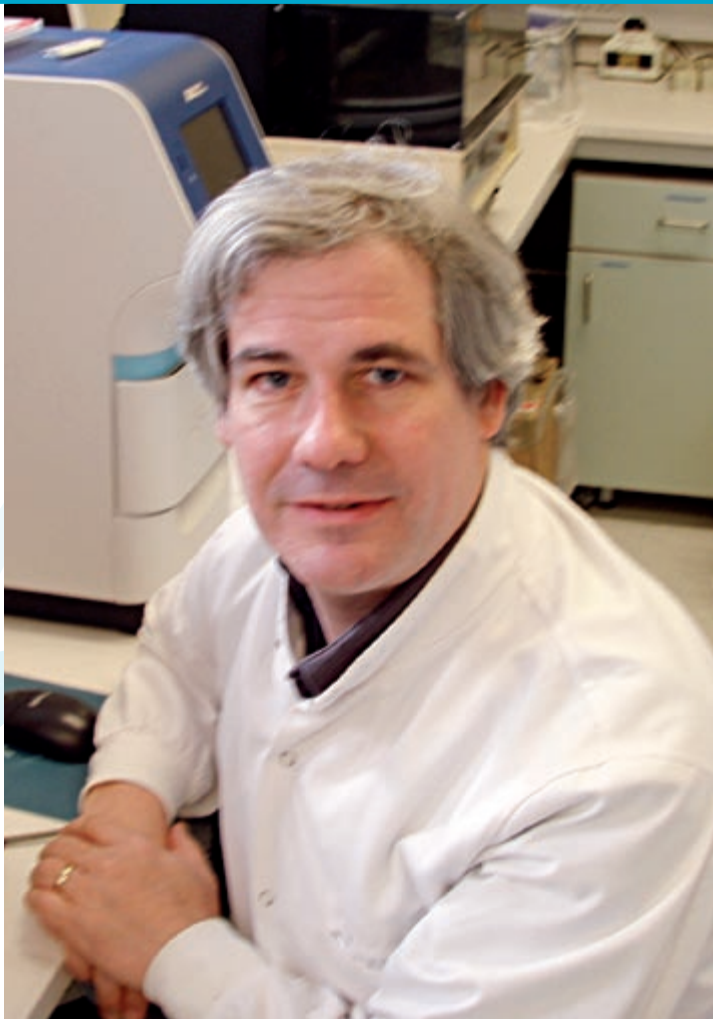
Third Decade of the National Eye Research Centre

The Centre enters its third decade in a strong position; reserves have been built up to carry the charity over difficult times which may be ahead and to cover an increased amount of research expenditure which it is committed to over future years.

The University of Bristol Department of Ophthalmology currently remains the principle beneficiary of the charity's support through a variety of projects and a Dowry for the Director of Research, Professor Andrew Dick. Dr Lindsay Nicholson who has headed the Inflammatory Eye Research Group for 5 years and been funded by the Centre, is now being funded by the University as a Reader in Research. The Centre is glad to be able to fund a number of PhD studentships countrywide.

The research staff, be they in the laboratories, the clinics or the Clinical Trials Unit are working tirelessly to discover more about the workings of the eye and collaborating with a multitude of scientists and clinicians both nationally and internationally and publishing the results of their research in an abundance of research papers and at conferences at home and overseas; the Centre is glad to support the annual "Looking into the 21st Century Vision Research Conference" held in Bristol.

Our branch in Yorkshire, Yorkshire Eye Research, has been through a difficult period but fundraising has improved and more research is being supported. Their Management Board has been boosted by some new members both from ophthalmology and the local community and the long term goal remains to establish a Chair of Ophthalmology in Leeds.



Dr Lindsay Nicholson, Head of the University of Bristol Inflammatory Eye Research Group

The cost of running research programmes is subject to inflationary pressure as is every other walk of life so it is vital to the continued progress of the development of new therapies for eye conditions and the prevention of sight loss that our supporters continue to provide the essential

financial support on which the success of eye research depends.

Most of our fundraising and administration is covered by the charity's investment income.

Director of Research's Report

by Professor Andrew Dick

There is certainly no platitude repeating in my reports that valued donations to NERC have continued our development both in Bristol and academic units nationally to improve ocular health and patient benefit. The work supported by NERC really does make a difference to our understanding of disease of the eye, develop improved therapies and assist in pathways of modernising healthcare delivery. Benefit nationally and internationally is tangible.

Our achievements this year have again been significant. With the great expertise of our scientists, clinicians and multitude of collaborators we have gained further insight in and presented and published our data of outcome measures of corneal transplantation and immunosuppressive treatment of sight threatening ocular inflammation (uveitis). Experimentally we have furthered and also published data on our understanding of immune cell function in intraocular inflammation, new therapies to suppress experimentally uveitis both of which we hope to lead into early clinical trials. Our Clinical Trials unit continues to expand, where we are undertaking over 15 clinical trials currently, including multicentred national trials such as CIRTED, a study of treatment for thyroid eye disease and trials of immunosuppression for uveitis. The unit, which is sponsored by both University Hospitals Bristol NHS Foundation Trust and University of Bristol, allows us to rapidly translate our scientific findings into man in the hope of developing better therapies.

Another substantial achievement this year is the consolidation of grouping collaborators of stem cell research with electrical engineers, chemists, physicists and industry. This work was initially driven by Dr Eric Mayer, who has since left to pastures new, but has left a legacy of hope with exciting developments in Bristol to generate repair and cell replacement of the retina. This work now continues to expand and to this end NERC have sponsored a stem cell biologist to come and work with

us from the USA. The reverse brain drain is testament to our progress in the field and strength of scientific leadership and innovation in multiple disciplines within University of Bristol.

Group leaders will in this report describe their individual research achievements and their optimism for better patient health in the future. I am proud and privileged to lead the department and work with them with the great support of NERC donors.



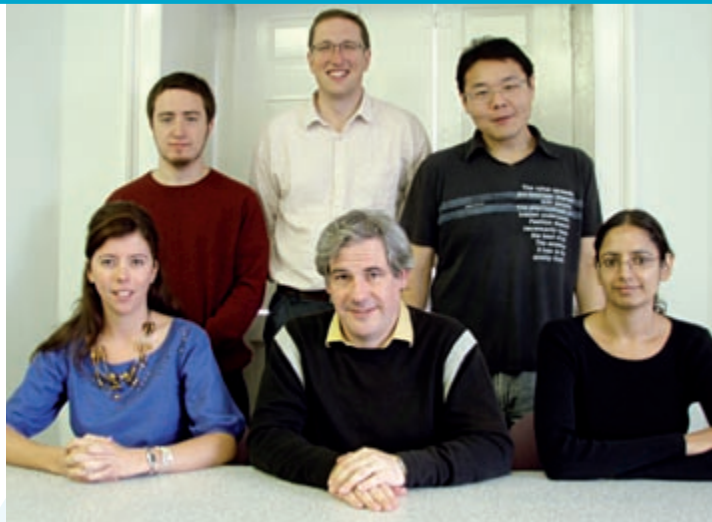
Head of the Inflammatory Eye Research Group in Bristol

by Dr Lindsay Nicholson

I came to Bristol University from Harvard in 2003 to bring my expertise in the field of organ specific autoimmune disease to the study of inflammatory eye disease (uveitis). Inflammatory eye disease is a potentially devastating condition, whose commonest cause in developed countries is the immune system attacking and damaging the retina. It shares many features with other autoimmune diseases, including a complex set of genetic influences and a tendency for the disease to wax and wane over time. With the support of NERC, I moved to the newly refurbished Wolfson Ophthalmology Laboratories in the School of Medical Sciences, which were opened officially by Prince Michael of Kent in July 2003, to focus on this blinding condition.

My first student, Carly Guyver, started working on a project to dissect in detail how one of the components of the retina was recognised by the immune system. I also began a fruitful collaboration with Professor Andrew Dick and Dr Claudia Calder, which began with an analysis of the importance of the cytokine receptor 'tumour necrosis factor receptor 1' in inflammatory eye disease. We chose this because treatments that target tumour necrosis factor had recently been shown to be effective in patients with inflammatory eye disease.

Over the succeeding years, I have built up my group to about 6 people. With the support of NERC, the James Tudor Foundation and the Multiple Sclerosis Society, we usually recruit



Dr Lindsay Nicholson and members of the Inflammatory Eye Research Group

one PhD student per year. We also raise funds to support one or two post-doctoral fellows. We have been successful in our studies of inflammatory eye disease and our paper on 'tumour necrosis factor receptor 1' was recognised, by the German Uveitis Patients Association, as the most important contribution to basic uveitis research published in 2005.

Over the last 5 years I have contributed to more than 15 published papers in the field of autoimmune inflammation. Our group has been greatly supported by generous equipment grants from NERC that have allowed us to keep pace with the rapid advances in technology that continue in immunology. Our most recent post-doctoral fellow, Dr Ben Raveney received a prestigious award from

the Japan Society for the Promotion of Science, and is now working on organ specific autoimmune disease in Japan. Two of our students have been awarded PhDs and more are on the way!

Looking forward, the group is well placed to have a significant impact on our understanding of inflammatory eye disease and on its treatment over the next 5 years. We are currently pressing forward with treatments that inhibit molecules that amplify the immune response and we are targeting the movement of immune cells into and out of the eye, with new drugs that are becoming available. To find out more about our work, you can visit our website www.bris.ac.uk/cellmolmed/air.

Optimising Immunotherapies for Patients with Inflammatory Eye Diseases

by Dr Richard Lee

Current therapies for inflammatory eye diseases aim to suppress the immune system. However, patients have differing responses to treatment. The core goal of our National Eye Research Centre (NERC) supported studies is to better understand these inter-individual disparities with a view to developing personally tailored immunotherapies.

Steroids are the most common immunosuppressive drug used in clinical practice, but they can cause significant side-effects, including weight gain, osteoporosis, high blood pressure and diabetes. They are therefore frequently used in combination with alternative immunosuppressants which aim to reduce steroid dependency. To investigate the benefits of two of these alternatives, tacrolimus and mycophenolate mofetil, we undertook a detailed analysis of their effectiveness and tolerance in patients attending the Regional Ocular Inflammation Service at Bristol Eye Hospital (serving a population of 5 million people). This generated concordant evidence supporting the use of these drugs, and we are now able to properly counsel patients on the likely success and outcome of

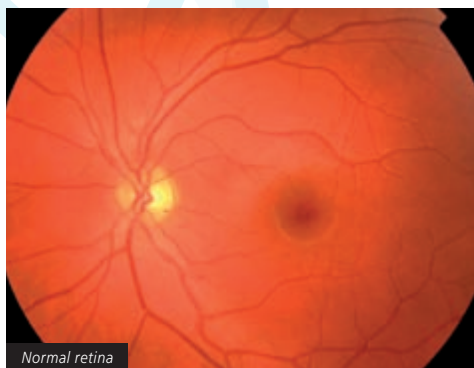
their treatment. These results have been published in *Ophthalmology* (the number one clinical eye journal worldwide) and the *American Journal of Ophthalmology*.

We have also been awarded a NERC PhD studentship for Lauren Schewitz to continue our studies of steroid resistance over the next 3 years. Our novel approach to the investigation of this widespread clinical problem has enabled us to identify a subgroup of immune cells which potentially prevent up to a third of patients responding adequately to steroids. As a result we have proposed a new strategy for combating this condition by specifically targeting these steroid resistant cells with a monoclonal antibody. The considerable interest this work has generated since its publication in the *Journal of Immunology* in December has led to the additional publication of two invited review papers, and has been further recognised with the award of an International Travel Grant by the Association for Research in Vision and Ophthalmology (the leading global organisation for vision scientists).

Our research also encompasses

Thyroid Eye Disease (TED), which is a cosmetically disfiguring and visually disabling condition caused by a misdirected immune response in the orbits of patients with an abnormally functioning thyroid gland. With NERC's support, we are conducting a clinical trial (www.cirted.org) which aims to determine whether using treatments in addition to steroids confers long-term benefits for patients with TED. Six UK teaching hospitals and their associated radiotherapy centres are now involved, creating a national network of experts which promises to deliver ongoing trials of immunotherapies in TED for many years to come.

The progress I have made as a NERC Clinical Research Fellow has led to my recent appointment as a National Institute of Health Research Clinical Lecturer in Bristol. This new and prestigious post is part of an initiative by the Department of Health to generate a new cadre of young clinicians to take forward the challenge of translating science for patient benefit. With NERC's continued support I hope to successfully fulfil this ambition for patients with sight-threatening diseases.



Normal retina



Inflamed retina

Sight loss due to multifocal choroiditis despite being treated with currently available therapies and why eye research is so important.

Research into Visual Development

by Dr Cathy Williams, Paediatric Consultant in the Bristol Eye Hospital

NERC has made major contributions to our programme of research into visual development within the Avon Longitudinal Study of Parents and Children (ALSPAC).

The current projects are –

CARDIOVASCULAR DISEASE

This project uses photographs of the retina (camera provided by NERC) of 12-year old children to see the earliest signs of cardiovascular disease, and relate this to events in utero or in early life (eg being born with low birthweight). This work is in collaboration with a world-leading group of researchers at St Mary's Hospital London (Dr Robyn Tapp, Prof N Chatuverdi and Dr Simon Thom) and has led to two publications in paediatrics, with several more papers due to be submitted.

MYOPIA

This project aims to identify the most important aspects of children's lifestyles and their genetic make-up that lead to myopia (short-sightedness). This is in collaboration with a leading myopia researcher Dr Jez Guggenheim of Cardiff School of Optometry and Vision Science. NERC are supporting George McMahon, a PhD student who is working with Dr Guggenheim and myself to obtain the optometrists' records of children in the ALSPAC study, then will link these records with ALSPAC data on their genetic susceptibility and their pastimes eg reading, to see which factors are most important for developing myopia. 3 papers on



Successful eye research will help this patient

myopia have already been published from ALSPAC and George has already submitted another.

OPTIC NERVE DISEASE

This project aims to establish a unique library of graded pictures of the optic nerves of children – a valuable resource to help us understand which factors might affect early optic nerve development and then how these factors may lead to blinding disease affecting the optic nerve eg glaucoma and optic atrophy. This is in collaboration with Bristol Eye Hospital senior clinicians Jeremy Diamond and Paul Spry, with Mr James Morgan of Cardiff who developed the grading software and with Mr Mike Burdon of Birmingham Eye Centre, a leading expert on neuro-ophthalmology and optic

nerve disease. The team are piloting a specially designed grading protocol and will check it is fully repeatable and valid. They will then use this protocol to grade the optic nerves of the 7,000 children who had their eyes photographed at the age of 12.

The ALSPAC study holds the most detailed collection of information about a group of young people, from before birth to the brink of adulthood (they are now 16 - 17), available anywhere in the world. NERC has enabled vision researchers to join closely with the study. All the projects described above will make important contributions to reducing ill-health (CVS disease) or blindness/visual impairment (optic nerve disease, myopia).

Genetic Eye Research

by Dr Amanda Churchill, Head of the Genetic Research Group

We are very fortunate in Bristol to be able to offer an exceptional Genetic Eye service and one that is rarely available in Europe. Our team of Ophthalmologists, Geneticists, Counsellors and Genetic Researchers offer a comprehensive monthly clinic dedicated to help families who may have inherited eye conditions. This is designed as a one-stop shop where investigations can be performed and questions answered. Of course, in some case families choose to attend on more than one occasion. Where possible, individuals are offered the opportunity to take part in research which may serve to identify the gene responsible for their condition. This is the first stage in understanding

how inherited eye conditions occur and what possible treatments could be offered in the future. In Bristol we also have a research facility, generously supported by The Underwood Trust, where we are able to screen a small number of genes that are responsible for impaired vision that begins in childhood. We also have links with research units around the UK and Europe for testing other genes that cause inherited eye disease. In this way we believe we offer the very best service to families in the South West of England.

However, it is not just causes of inherited conditions that we specialise in. Over the past few

years we have been working hard to identify genetic markers that may highlight individuals who are at greater risk of developing common eye diseases, such as 'wet' age-related macular degeneration. We have also been investigating whether genes can influence how mild or severe a common disease might be. We have recently completed and published our work on diabetes showing that specific DNA profiles are associated with those people who develop the most severe form of blinding diabetic eye disease. What this means is that a simple blood test could be developed that would inform the doctor and enable treatment to be tailored to an individual. For instance the DNA profile might suggest very close monitoring or early laser treatment because the genes predict severe blinding eye disease or less frequent checks because the genes predict only mild eye disease.

Furthermore, we have been looking at the influence that our genes have over the likelihood of developing potentially blinding infections following cataract surgery. We have shown that, once more, particular DNA profiles are associated with individuals who contract infections versus those who do not. We believe that this is an important step towards understanding why infections occur in some people and in improving not only the treatment but also prevention of infections after future surgery.

Dr Amanda Churchill (left) and members of the Genetic Research Group



Corneal transplantation – is tissue matching needed?

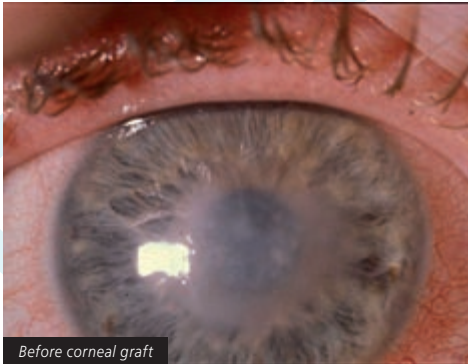
by Professor John Armitage

Corneal transplants have successfully restored the sight of many thousands of people. However, some transplants do fail and the main reason is that the body recognizes the transplant as 'foreign' and rejects it. Most organ transplants are tissue matched, a similar process to matching blood groups based on red blood cells but using the markers carried on white blood cells. These markers are critical for the normal functioning of the body's immune system in its fight against infectious disease. Unfortunately, transplants can also be attacked. One of the ways to reduce the risk of organ rejection is to match these white cell markers of the organ donor with those of the transplant recipient. With corneas, the evidence for a beneficial effect of this 'tissue matching' is not so clear cut as it is for organs. Many corneal

transplants survive well with little evidence of rejection; but there are some well-defined circumstances where the risk of corneal transplant rejection is substantially increased. An improved understanding of how tissue matching works in corneal transplants could reduce the reliance on drug treatments for treating rejection.

In Bristol, Professor John Armitage has been conducting a national, multi-centre study into tissue matching, which is funded by NERC. The aim is to recruit 1,200 corneal transplant patients that are at increased risk of rejection their transplants and where the level of tissue matching for each transplant is determined beforehand in the same way as in a clinical trial. In addition, all of the tissue matching uses advanced DNA methods to

avoid the errors in tissue typing that undermined previous studies. The patients will be followed up for five years, checking for signs of transplant rejection. In this way, the impact of different levels of tissue matching can be assessed. Already, almost 1,000 patients have been recruited. This is clearly a long-term study lasting many years; however, preliminary analysis of data from 800 patients two years after their transplants is currently being undertaken and this suggests that the type of tissue matching required for cornea is different from an organ transplant. This could be good news for those patients needing matched corneal transplants as their waiting times could be reduced.



Contact Lenses and Dry Eyes

by Dr Monica Berry

Many people with dry eyes will know that the way their eyes feel is not necessarily reflected in results from tests in the clinic. This disconnect is most frustrating also to clinicians and ocular biologists.

With a number of clinical colleagues from Cardiff and Weinheim we started to address this issue by comparing patients' self evaluation, clinical examination of the ocular surface, and the mucins adhering to their contact lenses. Mucins were chosen because they form the scaffold of the tear film covering the ocular surface. Other groups as well

as ours have shown that, and how, mucins change in dry eyes.

Because we have some knowledge of the general behaviour of human ocular mucin – support from the National Eye Research Centre has been very important for those initial studies – we can now identify mucins adhering to a single contact lens, or contained in a small tear sample. We can evaluate the relative abundance of each type of mucin found on the surface of the eye. (Mucins are gregarious, many species contributing to the stability of the tear film and the health of the

ocular surface). Furthermore we can assess some of the characteristics, for example how fragmented these initially long polymers are in tears or when they adhere to a contact lens.

Our results suggest that, while the relative decrease in mucin quantity is associated with clinical tests, it is the quality of mucins that is associated with symptoms. Studies we hope start in the near future will tease out which changes in the structure of the mucin molecules themselves are implicated in itchy, dry and sandy eyes.





(Part of the National Eye Research Centre)
Reg. Charity No. 294087

Eye Department, Clarendon Wing, Leeds General Infirmary, Leeds LS2 9NS
Tel: 0113 292 2837

Appeal Administrator: Ms Susannah Voke

Mr Martin McKibbin, Eye Consultant, Trustee and Chairman of the Management Board writes:

Yorkshire Eye Research is currently raising money to fund a three year project in which Professor Inglehearn at the University of Leeds seeks to identify the faulty genes which lead to the inherited blinding conditions of Retinitis Pigmentosa, Cone Rod Dystrophy and Microcornea in children. As well as the scientific benefits of this work, it will be of great benefit to patients and their parents as it will give a precise diagnosis, confirm information about the way in which these conditions are inherited and give a more accurate guide to future eye sight. Given the recent gene replacement therapy trials for retinal diseases, it brings the prospect of treatment for these inherited conditions closer, but first scientists need to know which genes are responsible.

To find out more about this project and the work of Yorkshire Eye Research please visit its website at www.yorkshireeyeresearch.org.uk or contact the Administrator.

Report from the Director

Last Year

The generosity of our supporters boosted voluntary income and enabled an increasing amount of eye research to be supported, despite a decrease in grant income. We are most grateful to all our supporters, particularly those who donate on a regular basis; their support remains very important in the current difficult financial climate when only a very limited amount of eye research is supported by the Government.

A successful Garden Party was held in the extensive gardens of Highnam Court near Gloucester and in the autumn supporters enjoyed a performance of 'Il Trovatore' at the Bristol Hippodrome.

An increasing number of people worldwide are accessing our website www.nerc.co.uk to learn about our charity and the research we are supporting. Donations can now be made on-line.

Legacies

We realise rightly that leaving gifts to their family and loved ones is everyone's first priority. We thank all those who have left a legacy to our charity. We were in receipt of over £500,000 last year which greatly benefited eye research.

Remember how important it is that everyone should make a Will, legacies to registered charities can reduce liability to Estate Duty. Shares can be left to a charity with savings to the Estate. Ask for our legacy leaflet before making or changing your Will.

In Memoriam Gifts

The passing of a loved one can be marked by an 'In Memoriam' gift and is a much more lasting tribute than flowers. Many suggest the National Eye Research Centre as a beneficiary of collections at funerals or memorial services.

Thanks

We thank all our supporters who help eye research in so many different ways and particularly those who donate in a tax efficient manner. There is still much to be discovered about the workings of the eye and great potential to develop new treatments but this can only be done with the help of our supporters.



The Director receiving a generous donation from Mr Melvyn Griffiths, Captain of Shirehampton Golf Club

Comparative Balance Sheet

As at 31 March 2008

(For Trustees' purposes only)

	Bristol	2008 Yorkshire	Total	2007
	£	£	£	£
Fixed assets				
Tangible assets	5	5	10	10
Investments	1,806,374	-	1,806,374	1,941,556
	<u>1,806,379</u>	<u>5</u>	<u>1,806,384</u>	<u>1,941,566</u>
Current assets				
Debtors	4,919	-	4,919	21,280
Cash at bank and in hand	708,832	152,907	861,739	953,042
	<u>713,751</u>	<u>152,907</u>	<u>866,739</u>	<u>974,322</u>
Creditors: amounts falling due within one year	(637,542)	-	(637,542)	(906,345)
Net current liabilities	<u>76,209</u>	<u>152,907</u>	<u>229,116</u>	<u>67,977</u>
Total assets less current liabilities	1,882,588	152,912	2,035,500	2,009,543
Creditors: amounts falling due after more than one year	(323,233)	-	(323,233)	(727,062)
	<u>1,559,355</u>	<u>152,912</u>	<u>1,712,267</u>	<u>1,282,481</u>
Funds				
Unrestricted funds	1,209,348	152,912	1,362,260	865,947
Restricted funds	350,007	-	350,007	416,534
	<u>1,559,355</u>	<u>152,912</u>	<u>1,712,267</u>	<u>1,282,481</u>

Committed future expenditure

Included in creditors above are the following amounts relating to committed future charitable expenditure:

	2008	2007
	£	£
Amounts falling due within one year:		
Grants committed	716,189	719,971
Research creditors	105,742	132,105
Amounts falling due after one year:		
Grants committed	425,729	727,062
	<u>1,247,660</u>	<u>1,579,138</u>

The summarised accounts may not contain sufficient information to allow for a full understanding of the financial affairs of the charity. For further information the full annual accounts and the auditors' report on those accounts should be consulted. Copies of these can be obtained from the National Eye Research Centre, Bristol Eye Hospital, Lower Maudlin Street, Bristol, BS1 2LX. The full financial statements were approved on 15 July 2008 with an unqualified audit opinion from the auditors, R S Porter & Company have been submitted to the Charity Commission.

These accounts were prepared by: R S Porter & Company
77-81 Alma Road
Clifton
Bristol BS8 4AN

COMPARATIVE STATEMENT OF FINANCIAL ACTIVITIES

For The Year Ended 31 March 2008

	Unrestricted funds		Total £
	Bristol £	York £	
Incoming resources			
Voluntary income	671,635	24,985	696,620
Grants received	-	-	-
Clinical trials	11,272	-	11,272
Income from investments	105,102	4,796	109,898
Total incoming resources	788,009	29,781	817,790
Resources expended			
Charitable expenditure			
Cost of activities in the furtherance of the charity's objects:			
Research grants paid during the year	265,530	63,211	328,741
Committed future charitable expenditure b/fwd	(1,189,572)	(63,529)	(1,253,101)
Committed future charitable expenditure c/fwd	791,911	-	791,911
Laboratory equipment grants paid during the year	138,924	-	138,924
	6,793	-318	6,475
Cost of generating funds			
Fund raising	21,651	21,160	42,811
Publicity costs	11,274	-	11,274
Portfolio management	12,907	-	12,907
Support costs	56,546	893	57,439
Governance	1,527	-	1,527
Total resources expended	110,698	21,735	132,433
Net (outgoing)/incoming resources	677,311	8,046	685,357
Transfers	-	-	-
	677,311	8,046	685,357
Realised gain on disposal of investments	79,296	-	79,296
Unrealised loss on investments	(268,340)	-	(268,340)
Net movement in funds	488,267	8,046	496,313
Balances brought forward at 1 April 2007	857,927	8,020	865,947
Balances carried forward at 31 March 2008	1,346,194	16,066	1,362,260

Restricted funds			Total Funds 2008			2007
Bristol	York	Total	Bristol	York	Total	Total
£	£	£	£	£	£	£
-	-	-	671,635	24,985	696,620	549,025
148,447	50,000	198,447	148,447	50,000	198,447	529,968
-	-	-	11,272	-	11,272	32,987
-	-	-	105,102	4,796	109,898	91,491
148,447	50,000	198,447	936,456	79,781	1,016,237	1,203,471
331,501	-	331,501	597,031	63,211	660,242	478,504
(416,534)	-	(416,534)	(1,606,106)	(63,529)	(1,669,635)	(1,181,268)
350,007	-	350,007	1,141,918	-	1,141,918	1,669,365
-	-	-	138,924	-	138,924	31,442
264,974	-	264,974	271,767	-318	271,449	998,043
-	-	-	21,651	21,160	42,811	68,196
-	-	-	11,274	-	11,274	11,822
-	-	-	12,907	-	12,907	8,951
-	-	-	56,546	893	57,439	1,215
-	-	-	1,527	-	1,527	48,440
264,974	-	264,974	375,672	21,735	397,407	1,136,667
(116,527)	50,000	(66,527)	560,784	58,046	618,830	66,804
-	-	-	-	-	-	-
(116,527)	50,000	(66,527)	560,784	58,046	618,830	66,804
-	-	-	79,296	-	79,296	-
-	-	-	(268,340)	-	(268,340)	(46,025)
-116,527	50,000	-66,527	371,740	58,046	429,786	20,779
416,534	-	416,534	1,274,461	8,020	1,282,481	1,261,702
300,007	50,000	350,007	1,646,201	66,066	1,712,267	1,282,481



Every day forty people are registered blind.
Your support today could help many
people look forward to a brighter future

**NATIONAL
EYE
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CENTRE**
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