

**Hello, from all of us involved with the National Collaborative Usher Study.** This is to welcome you to the first edition of our NCUS Newsletter. The key to the NCUS is collaboration, collaboration with you the family with Usher, with us here at Sense and with the scientists at the Institute of Ophthalmology, the Institute of Child Health and the National Hospital for Neurology and Neurosurgery, Queen's Square. Good collaboration depends on good communication and we hope that with this our first NCUS Newsletter you will be kept informed and feel involved.

In this issue we feature profiles on the three research scientists who are carrying out the investigation. After some delays with getting the equipment for balance testing up and running we are pleased to report that both hearing and

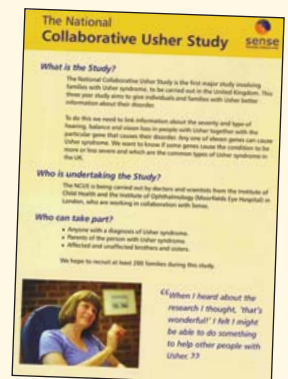
*Janet Cumming took part in the NCUS because she felt that it might help other people with Usher in the future*



balance testing is underway. Dr. Nell Rangesh describes what tests need to be done and why. We have an article from the Family Coordinator, Liz Cook on the benefits which arise when families get together to share information as well as donate blood. One of our collaborators Margaret describes her experiences taking part in the hearing tests, which will be interesting for those who have appointments coming up.

Our Molecular Geneticist, Dr. Elene Haralambous describes how we are determining the genetic cause of Ushers by using the DNA from families who have taken part already.

Finally, we have just produced a more attractive flyer to publicize the National Collaborative Usher Study, which is available from Liz Cook or Melanie Gonsalves at Sense.



If you have any queries about the NCUS please let us know, we will pass any research queries onto the scientist involved. We hope that you find the first issue of the NCUS useful and interesting.

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## Meet our researchers

In this first issue we would like to introduce you to the three scientists who are carrying out the research; we have invited them to write about themselves and their role within the NCUS.

### *Ophthalmic Scientist*

My name is Zubin Saihan. I have been involved in the National Collaborative Usher Study for 18 months now in my role as Research Fellow at the Institute of Ophthalmology. I am seeing all of you with Usher syndrome in the study and am responsible for performing and collecting the eye tests on everyone at Moorfields Eye Hospital. None of the tests that we do are

unpleasant or dangerous, although a lot of the technology is quite advanced.

I am involved in the genetics side of the study too and am responsible for performing and analysing our genetic results. I also work in collaboration with Dr. Elene Haralambous, the Molecular Geneticist. I am enjoying getting to know



*Zubin Saihan*

all the collaborating families as you come up for investigations into the vision aspects of Usher syndrome.

### *Molecular Geneticist*

Hello, allow me to introduce myself, my name is Dr Elene Haralambous and I have recently joined the group based at the Institute of Child Health (ICH) in London working on the genetic cause of Usher syndrome. I started being interested in the human genetic makeup and how it can confer susceptibility to one human condition or another back in 1994. Since then, I have completed an MSc and PhD in this area as well as two post-doctoral positions. My last position before coming to ICH was investigating the genetic susceptibility to meningococcal disease which

is the most common cause of meningitis and blood poisoning (septicaemia) worldwide.

As you are aware, Sense, the Institute of Ophthalmology and ICH are working together to further the understanding of the genetic causes of Usher syndrome. My role is to receive all the blood samples that you kindly give, analyse them and find the molecular causes of the Usher syndrome in all the families. This is a very lengthy process and so far, I am finding the work extremely rewarding. I must at this point extend a huge thank you to all of you who have agreed to take part



*Elene Haralambous (left)*

in the National Collaborative Usher Study as, without your willingness to participate; this project would not be possible. I am very happy to have joined the NCUS and look forward to meeting some of Sense's families at future meetings. Best wishes to you all  
**Elene**

### ***Audiological Scientist***

I am Dr. Nell Rangesh and I joined the team in July 2005 . I have a medical background and am a qualified Ear Nose and Throat surgeon. Currently I am a Research Fellow at the Institute of Child Health. I am

doing the audiological and balance tests for the National Collaborative Usher Study. My other interests include quality controls and maintaining standards in clinical medicine.



*Nell Rangesh*

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## **Genetic Analysis in Usher Families**

ELENE HARALAMBOUS

**We are using three approaches to analyse the genetic cause of Ushers in the individuals who have agreed to participate in the UK Collaborative Usher Study:**

### ***1. Microchip Technology***

A thorough literature review of mutations in type 1 Usher has shown that there are very few genetic changes or mutations which are common i.e. observed in lots of families with Usher (with the exception of Usher type 1C). One approach was therefore to trial an 'Usher mutation' microchip, developed by researchers in Holland, on some of the first samples. This screens for ALL previously described mutations (n=305) in all the Usher genes in one go. It doesn't pick up any mutations which have not appeared in the medical literature and may be a cost effective screen. Results indicated that we detected at least one mutation in half of the Usher samples that were sent. Verification of results indicated 100% accuracy.

### ***2. Consanguineous Families (cousin marriages)***

Investigating each of the twelve known genes that cause Usher syndrome in each family is very time consuming. However, where an Usher individual is from a cousin marriage, a technique called 'homozygosity mapping' can be used which can indicate the position of the Usher causing gene in the genome, rather than analysing all the known causative genes. We have currently collected 11 consanguineous families.

### ***3. Sequencing***

Through a collaboration all the Usher causing genes will be sequenced in all of our Usher volunteers. This is especially necessary to verify data from the mutation chip and also to identify mutations in those people where the mutation chip did not detect anything and where the patients do not come from a consanguineous family.

## News from the Hearing and Balance side of NCUS

When you take part in the Usher study you will undergo different types of hearing and balance tests. Most people with Usher syndrome would have had a hearing test as part of their diagnostic workup or during hearing aid fitting sessions, but tests that identify the precise site of the problem within the inner ear or brain pathways are not done as a routine. Detailed testing of a large group of people with Usher syndrome will help to establish patterns of hearing and balance changes and provide some answers as to how certain genes cause this disorder.

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*“Detailed testing of a large group of people with Usher syndrome will help to establish patterns of hearing and balance changes and provide some answers as to how certain genes cause this disorder.”*

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### Hearing tests

The hearing tests are done at the Neuro-otology Department of the National Hospital for Neurology and Neurosurgery. The first test is called audiometry and determines the hearing levels across a range of frequency of human hearing. This is then followed by tests to assess middle ear function (tympanometry and acoustic reflex thresholds). (Information on how the tests are done is available from the patient information leaflet of the NCUS)

In ear clinics, otoacoustic emission testing and auditory brain stem responses (ABR) are normally used to screen infants and children for hearing impairment. In adults these tests provide detailed information on the function of the inner ear and brain pathways for hearing and have been included as part of the protocol.

*Investigation into balance is a very important area of the NCUS*



If the hearing loss is severe, there may not be enough sound to stimulate the inner ear and reach the nerve of hearing. All the hearing tests including an examination take about two hours to complete.

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*“So far twenty-five of you have completed the hearing tests and you have given us helpful feedback.”*

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So far twenty-five of you have completed the hearing tests and you have given us helpful feedback. You have not reported that it was too tiring or time consuming. Some of you have given us copies of your previous audiograms and this has been very helpful to assess any progression or change in the hearing levels. Please do let us have any earlier tests you may have undergone. We can certainly copy the originals and return them to you at the time of your appointments with us.

### ***Balance testing***

Balance testing can be done as a single session immediately after the hearing tests. If you live close to the hospital we may ask you to come in on two separate days to reduce the tedium of being tested for several hours. The equipment is housed at the Hospital for Children at Great Ormond Street, next door to the National Hospital and has only recently been commissioned. It is new, highly sophisticated; state of the art equipment and we are pleased to have access to it for this exciting and valuable project.

The balance system of the body is extremely complex and highly developed in human beings. Balance and co-ordination depend on information received from the ear, eyes, muscles and joints. The balance tests used in this study are designed to give information on

- whether balance is normal or affected.
- whether the balance problem is arising in the ears.
- whether the problem is arising from areas in the brain that integrate balance information.

Once enough data has been collected, the results can be analysed and correlated to visual changes and genetic information. The results may also help towards designing screening tests and to provide a more accurate diagnosis of Usher syndrome in the future.

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*“The equipment is new, highly sophisticated, state of the art equipment and we are pleased to have access to it for this exciting and valuable project”*

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We are extremely grateful to all of you who have taken part in our study so far and would be delighted to receive any feedback.

**DR NELL RANGESH**  
**PROFESSOR LINDA LUXON**

## Undergoing the tests

We asked one of our collaborators, Margaret Pickess, to give her reactions to the vision and hearing investigations done at Moorfields and the National Hospital for Neurology and Neurosurgery. Margaret kindly responded to our questions with the following:

### ***Why did you take part and did the investigation meet your expectations?***

"I must admit I was a reluctant participant for various reasons, one of which is I don't like blood tests! Another being that I was diagnosed late with Usher, I have no parents and I am also an only child so there is no other family to test apart from my children and grandchildren who all have normal hearing and sight".

### ***Were the tests explained in enough detail so that you understood what was involved and why the tests were being carried out?***

"Yes, everybody was very helpful in explaining everything and I felt confident in asking questions that I had never asked before. I did seem to have a death wish on the researchers because the day I went to Moorfields, Zubin had started an awful streaming cold! Then, when I went for my hearing tests, Albert was off work sick - was it something I said? However, Professor Luxon was very helpful and explained a lot to me".

### ***Did you find the testing itself OK, interesting, boring, enlightening?***

"A lot of the eye tests you did I have had in the past. I found the hearing tests very interesting



*Margaret Pickess*

as I had never seen so many different testing machines. My local hospital seems to be way behind with their technology".

### ***Was it organised efficiently?***

"Yes, I found the maps and directions were very clear, especially as I was in strange parts of London".

### ***Would you encourage other people with Usher to take part and why?***

"Yes, definitely, the more that can help the better".

### ***What more would you like us to do?***

"I think it would be useful for us to know how the study is progressing and I think this newsletter is a good way of doing this. It may even be a tool to encourage others to get involved".

## “We have never really talked about it before!”

One of the most interesting aspects of my job is meeting people. As I travel up and down the country, talking to families about the National Collaborative Usher Study, I am fortunate enough to be able to renew some old acquaintances and hear how people with Usher have faced the challenges brought about by their condition. I also meet families newly diagnosed with Usher syndrome who are just starting to face some of the uncertainties that the condition can bring.

My role brings me into contact not only with people with Usher, but also their parents and unaffected brothers and sisters. Often the meeting that I have with a family to discuss whether they wish to participate in the study is the first time that they have sat down together to talk about Usher syndrome and how it affects the whole family.

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*“Families who have come together to discuss the research have a better practical understanding of the condition and how to support each other”*

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For some people with Usher, a major challenge can be talking about their condition with other family members. Emotional, psychological and practical influences can affect family dynamics to the extent that many families only discuss Usher syndrome at a basic level. This can result in misconceptions and misunderstandings. For example, some people do not understand how much their affected relative really sees or why they suddenly stop moving when entering a darkened room. Non affected relatives and their

partners may have misconceptions about the genetic implications of Usher syndrome in the family for their children.

Parents may have difficulty coming to terms with the fact that they have both passed a gene for Usher Syndrome to their child. Partners may use denial to cope with changes they observe in their husband or wife.

A positive outcome for families coming together is that they talk and begin to share more freely what Usher means for each one of them.

I work in partnership with colleagues in the National Usher Team at Sense and regularly refer families to them who might require additional support from the organisation.

Marylin Kilsby who is the National Usher Coordinator at Sense observes that, families who have come together to discuss the research have a better practical understanding of the condition and how to support each other. Involvement in the research provides a reason for families to come together that in turn may be the start of a process of better communication. Marylin summarised this when she said “we can provide family members with information about Usher syndrome, but they will only start to really understand the condition by talking to their brother or sister, son or daughter”.

**Liz Cook**  
**Family Co-ordinator**  
**National Collaborative Usher Study.**



## Recruitment update

The National Collaborative Usher Study is a three -year study, which started in 2003. We aim to recruit at least 200 families to take part in the NCUS, ideally by Autumn 2005. So far we have fully recruited 131 families and have had contact with several more who are interested in taking part.

If you know of any families with Usher who would be interested in finding out more about taking part, please ask them to contact Liz Cook, Family Coordinator, National Collaborative Usher Study on 020 7561 3331 or E-mail: [liz.cook@sense.org.uk](mailto:liz.cook@sense.org.uk) Information on the study is also available on the Sense website: [www.sense.org.uk/usherstudy](http://www.sense.org.uk/usherstudy)

### Editor's note:

We hope to send out the next issue of our NCUS Newsletter in late Autumn 2005. If you have news, letters or questions, please send them to Mary Guest by Sept. 30th 2005. [mary.guest@sense.org.uk](mailto:mary.guest@sense.org.uk)  
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