

NCUS NEWSLETTER



Newsletter for the National Collaborative Usher Study • Issue 4 • Winter 2006

The National Collaborative Usher Study is in its final phase. Recruitment of families required for the Study is completed, the clinical investigations on vision are finished, and all the DNA results have been sent out for verification. What remains to be done is completion of the hearing and balance tests, around April 2007, the final analysis of the DNA samples, writing up and publication of the results and most importantly reporting back to the collaborating families.

It is gratifying to be at this point but sadly, it has meant that the work of some members of the 'team' has come to an end. In July we said 'farewell' to Louise Thomasson who had assisted in the final stages of the recruitment by involving families further afield. At the end of September Liz Cook whom so many of you welcomed into your homes during the recruitment process completed her contract and her work in bringing families on board. Our Research Assistant Yasmin Hughes left to work at Guy's Hospital in October and by the time you read this Dr. Polona le Quesne

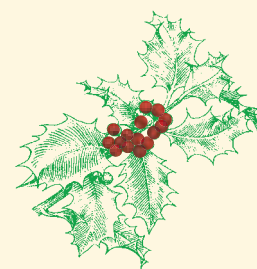
will have left her post as the Molecular Geneticist which she stepped into during Dr. Elene Haralabous' maternity leave.

On behalf of the NCUS partners and wider Usher family at Sense I want to record our thanks and deep appreciation for the hard and painstaking contribution which each of these women has made to the Study and to improving our understanding of Usher overall.

As we move into 2007 and the final year of the NCUS I hope that we will have the opportunity to meet many of you again to report on findings of this first UK study on Usher syndrome.

From everyone on the NCUS 'team' we wish you a happy and joyful festive time with your family and friends. Thank you for staying involved.

Mary Guest, Editor
Project Manager
E-mail:
mary.guest@sense.org.uk



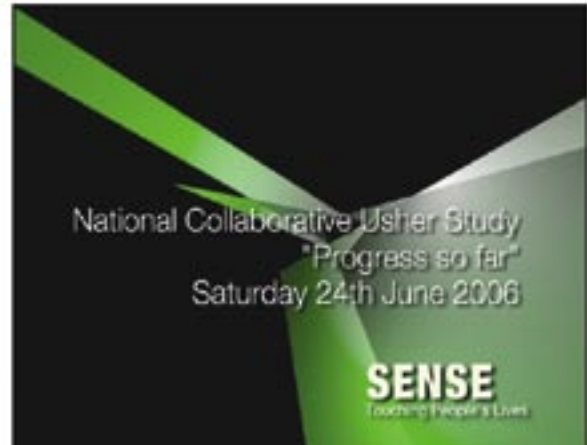
In this issue

- 'Progress so far' day on DVD
- Usher Symposium – Omaha
- Audiograms in the attic?
- Organ Donation
- Joint National Usher Clinic
- Farewells

'Progress so far' day June 2006 captured on DVD

It was good to meet up with so many families who have been taking part in the NCUS at the 'Progress so far' day on June 24th at the Institute of Child Health in London. Everyone involved in the research and recruitment attended as well as 90 family members.

The purpose of the day was to update families on progress in the NCUS and to explain in more detail why the tests are being done. Dr. Nell Rangesh gave some early audiological findings and covered many frequently asked questions, which come up when a person is being tested for hearing and balance. Dr. Zubin Saihan described the vision tests in detail and why the results are important for identifying patterns in types of Usher for possible future treatments. In her talk Dr. Polona le Quesne by using a simple sentence, 'the dog ate the cat' was able to illustrate the language which, is embedded in genetic codes and make what is for most people a mysterious subject more accessible.



John and Carol Lee, the Sign Language Video People, expertly recorded the meeting on DVD and order forms have been sent to all participating families. The 'Progress so far' DVD is available with British Sign Language and subtitles.

For an order form please contact Melanie Gonsalves at Sense on: melanie.gonsalves@sense.org.uk

Audiograms in the Attic?

NELL RANGESH, RESEARCH FELLOW

Finding old audiograms in the attic may not be as exciting as finding a hidden Picasso but is infinitely more precious for the Usher study. Why do we need old audiograms, when a new one is done as part of the study?

It simply comes down to studying the way age affects hearing in Usher syndrome. The normal ageing process can affect our ability to hear certain high pitched sounds and this is called **presbycusis**. In certain types of Usher (especially type III) the hearing loss progression

is greater than can be explained by age alone. This is a key finding and one of the suggested ways to separate Usher type III from Usher type II in the clinic, in the absence of genetic testing. We not only want to confirm this change, but also find out whether this happens in other types of Usher. This will then help us to understand better the progression of hearing loss in Usher syndrome and match it to the genetic change.

We would like to collect as many audiograms

as possible for each person in the study and then analyse all these audiograms for age related changes. Pictured right: this is how an audiogram looks. If you find any of these in your attic or in your long forgotten desk drawer, no matter how old it is, can you **please** make a copy and post it to us (the address is also given below).

Address for Posting:

Dr N Rangesh

Academic Unit of Audiological Medicine

Institute of Child Health

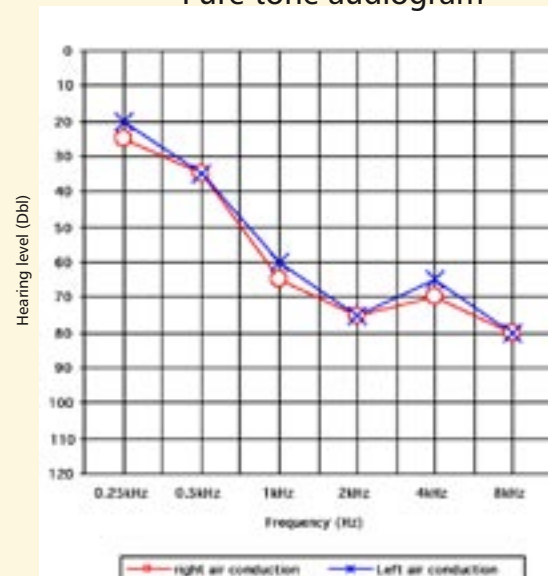
30 Guildford Street

London WC1N 1EH

As we near the end of the study, thank you all once again for taking part in the study and for

your extraordinary patience in undergoing all the hearing and balance tests

Pure tone audiogram

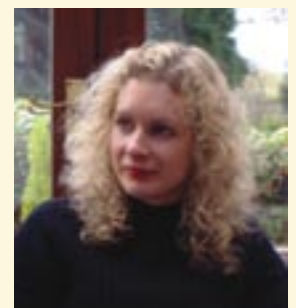


Joint National Usher Clinic-Proposal

Thank you taking time to answer the Joint Clinic questionnaire and for the extra comments which some of you sent in on the value of bringing hearing, balance, vision and molecular genetic services together under one roof.

The response to the questionnaire which we gave out at the 'Progress so far' day in June has been overwhelmingly supportive of the proposal to set up a Joint National Usher Clinic in London. About 60 questionnaires were given out and 46 were returned. Nearly everyone was prepared to travel to London. Even people living in Scotland and the South West said they would attend if they could see clinicians who understood Usher syndrome as a whole and be put in touch with the recent research advances.

The Joint National Usher Clinic questionnaire has now been sent to all families who have taken part in the NCUS. If you have not yet replied please think about the questions, talk to your family and let us have your views. The more evidence we have that a Joint National Usher Clinic is what you want the more this will help when we try to get it started and seek for funds in the future.



Penny Rudge

Penny Rudge, who has Usher herself, has kindly offered to collate your replies and summarise any comments, which you send in. Please don't let the Christmas rush stop you from sending your views!

Has it really been three years?

LIZ COOK, FAMILY COORDINATOR

In September 2006 my contract with the National Collaborative Usher Study ended and with sadness I left Sense. Reflecting back on the last 3 years as Family Coordinator on the study, I am however very pleased to have been able to contribute in some way to this exciting, challenging and innovative project.

The positive response that we received from families far outweighed our expectations. In the first two years I was kept very busy travelling up and down the motorway to recruit families. I had the pleasure of meeting many old acquaintances. and also making contact with some families who had perhaps only recently been diagnosed. As well as informing them about the study, I hope I was able to offer such families information and reassurance, and provide them with access to long-term support through the Usher team at Sense.

“Through my contact with families and with the research team, I feel that I have learnt an immense amount over the last three years”

My background is in social work and prior to this job I had never taken blood and only had a very rudimentary knowledge of genetics. I learnt to take blood through attending an intensive course on phlebotomy at the Middlesex Hospital in Central London. However, I am also extremely grateful to the doctors and scientists working on the study who patiently answered my questions and helped me to develop the practical skills needed for my job, even to the extent of letting me practice sticking needles in them!

As I travelled around the country I had many long and fascinating conversations with people keen to discover more about their Usher syndrome. Some families had researched their family history in an attempt to discover where the genes had come from, others contacted members living abroad in order that we could obtain a complete set of blood samples.

For many families, I believe the study has stimulated a process of learning and understanding. Family members have shared information about Usher syndrome not only with the researchers, but, often for the first time, amongst themselves. Individuals felt empowered to ask questions. Hopefully through developing a better understanding of their own condition and through actively contributing to research many people feel better able to face the future.

Through my contact with families and with the research team, I feel that I have learnt an immense amount over the last three years. I have recently moved away from London and hope to continue working with families with Usher. In the meantime, I remain in regular contact with Sense and greatly look forward to hearing about some of the outcomes from the research in the coming months. Good luck everyone!



Liz Cook

First International Symposium on Usher Syndrome and related disorders

3rd-6th October, Omaha, Nebraska.

Editor's note : In October three of us, Dr. Maria Bitner who oversees molecular genetics, Dr. Zubin Saihan, the vision researcher and Mary Guest the NCUS Project Manager attended an Usher symposium on Omaha. Zubin presented a poster on vision findings from the NCUS and Mary presented a paper on vision care for deaf children. Maria kindly summarised this important gathering of researchers working in our field.

This conference, sponsored by Boys Town National Research Hospital and Sahlgrenska University Hospital, Göteborg, Sweden, was hosted by Professor Bill Kimberling and Professor Claes Möller who have collaborated on the genetic and clinical aspects of Usher syndrome for two decades. Bill Kimberling's group was responsible for mapping (finding the genetic localization) of the first Usher genes and in the following years, for the identification of the USH2A gene, underlying the commonest form of Usher syndrome, as well as the USH2C gene. It was therefore fitting and exciting for us to go to the 'homeland' of Usher syndrome!

Molecular genetics and cellular function

The 3 day symposium started with a session on 'Molecular genetics and cellular function of Usher genes and proteins' and a keynote speech and overview from Dr Christine Petit on what is currently known about the function of the Usher gene products in the eye and the ear. Dr Petit's research group in Paris has been responsible for identification of several genes for type 1 Usher as well as work investigating what these genes actually do. This information will be vital for the development of treatments for Usher syndrome. This was followed by three excellent research talks by Dr Wolfrum



Boys Town National Research Hospital, Omaha

from Germany, Dr Cosgrove from Omaha and Dr Mueller from California on Usher proteins. An afternoon focussed on the Usher genes and progress in gene testing by geneticists from France, Holland and the US, outlining some potential strategies for diagnosing Usher syndrome in potentially affected people. As is the case in the NHS in the UK, diagnostic tests are still not available in Europe or the US outside research projects, although this will soon change with our current progress.

Clinical Aspects of Usher syndrome

The second day continued with sessions about clinical aspects of Usher syndrome and then an afternoon session on 'Current' treatments, including Vitamin A and omega-3 rich diets, data on fatty acid metabolism in mice and a very nice overview on cochlear implantation in Usher patients. This continued with research talks on more 'experimental' strategies for the treatments of specific types of Usher syndrome

(Myosin 7A-based, treatment of PCDH15-Usher syndrome and development of animal model for Usher type 3, each of which produced promising data). The second day ended with a visit to Boys Town founded in the 1920's to provide shelter and education for abandoned and orphaned boys. After the conference dinner at Father Flanagan's Boys Home Great Hall we saw the first showing of 'Silence with a Touch' about living with Usher syndrome. This excellent DVD was produced by the National Technical Institute for the Deaf, Rochester with New York Technical Assistance Project for Deafblind Youth. Sense hopes to obtain copies when it is released.

Animal models for Usher syndrome

The final day started with a session devoted to animal models of Usher syndrome, describing both zebra fish and mouse models, since again, it will be important to have animal models on which to try any therapies for Usher syndrome. The mouse, which is the most commonly used animal model (and one about which we know most) has been disappointing as a model for the human disease because essentially although Usher type 1 mice are deaf, they do not so far develop any signs of RP and so any treatments for RP cannot be easily tried out on mice. However, an exciting talk detailed the recent development for a mouse model for type 2 Usher syndrome (the USH2A mouse) which does appear to have both hearing and vision loss and should serve as a useful model on which

novel treatments can be assessed. Hopefully this should be a real advance in the development of treatment for this type of Usher.

The closing session was dedicated to Psychosocial and Rehabilitative Aspects of Usher syndrome

Mia Kelley-Bock from Helen Keller National Center for Rehabilitation talked about the effect of loss in the lives of people with Usher and how grieving can be an uncertain life long process occurring at different times. She described the value of the peer support group at HKNC in helping individuals recognise these stages and work through them. Mary Guest took the subject of 'Vision Care for all Deaf Children' in which she emphasized the importance of vision to all deaf children in the development of communication and socialization. She cited studies on vision in deaf children which show a consistently high level of vision impairment in deaf children and described a vision care pathway which is being taken up in the UK.

For me the most exciting parts of the symposium were:

advances in genetic diagnosis of Usher syndrome,
novel experimental treatment strategies for type 1 Usher,
development of the USH2A mouse
and seeing the facilities at the Boys Town National Research Hospital.

Sense Telephone Numbers

In 2007 Sense is moving office from Finsbury Park, where we have been since 1993, back to Kings Cross. We do not have a moving date yet but when we do everyone will be sent our new address. But we already have our new telephone numbers which can be used from now on. Our new 0845 numbers are published in 'Editor's note' at the end of this issue. Our existing numbers: 0207 272 7774 etc. can be used until we move but if you start using our new 0845 numbers now you will not need to change your records when we finally leave Finsbury Park.

Organ donation

Another subject which came up at 'Progress so far' day ' was the question of donating eyes and ears or temporal bone to research. In September 2006 the Human Tissue Act became law which has changed the rules governing the donation of human tissue for research purposes. For post mortem tissue donation you now need to have signed consent, which is witnessed, from the person before death, to say that they will donate their tissue. For a child parents can consent on their behalf although the child should be consulted where possible. If the deceased person was not asked about donation before death, their named representative can be asked to consent. The Human Tissue Act has strict guidance on what is now required. To find out about the new rules consult the website given below. If you already carry an eye donor card check that it is still valid under the rules of the Human Tissue Act.

The British Retinitis Pigmentosa Society has

information on their Eye Donor Scheme, although the scheme is under review in the light of the new regulations as a result of the Human Tissue Act. Contact details for the BRPS are: e-mail info@brps.org.uk tel: 01280 821334 (office hours).

Temporal bone donation

Currently there is no system in the UK in place for donation of the temporal bone (the ear). Recently, Professor Linda Luxon and Mary Guest met Emeritus Professor Leslie Michaels from University College London, whose primary interest is in ear disorders. We discussed the steps needed to set up temporal bone donation in the UK, one of which will involve more key people from ear research. Linda and Mary will report back in the next NCUS newsletter.

For more information about the Human Tissue Act you can look at the government web site: http://www.hta.gov.uk/_db/_documents/2006-07-04_Approved_by_Parliament_-_Code_of_Practice_1_-_Consent.pdf

A year with the NCUS project

POLONA LE QUESNE

I joined the NCUS project one year ago to replace Dr. Elene Haralambous during maternity leave. Elene is back to work and it is now time for my maternity leave.

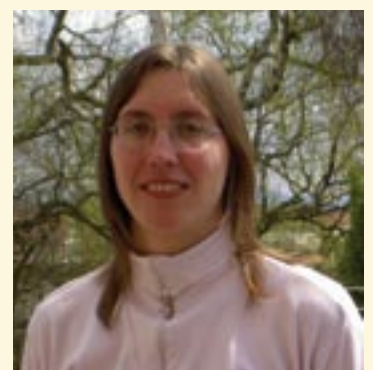
Working on the NCUS project has been very enjoyable and challenging. The cooperation between Sense, families, clinicians and molecular geneticists has been very good and it was a privilege to work in a group with such a high standard. I especially enjoyed meeting some of you involved in the project at the 'Progress so far' day in June. After maternity leave, I plan to return to

veterinary research. I mentioned in one of the previous NCUS newsletters that I studied veterinary medicine and

have been working on a heart disease called cardiomyopathy in Dobermanns prior to joining the NCUS team.

I would like to thank you all for your enthusiasm and great contribution to the project and wish you all the best in the future.

Polona



Recruitment of families

The Family Co-ordinator, Liz Cook, in her final report to the NCUS Steering Panel meeting held 12th Sept 2006 informed the members that 220 individuals with Usher had been recruited into the Study from 191 families. Out of the 191 families 3 people had been found

not to have Usher syndrome. Six families had withdrawn but 2 of these families were happy for their genetic data to be included in the Study. Full data had been collected on 182 families.

Yasmin Hughes moves on



Hello everyone,

It seems like it was just the other day that I was writing to introduce myself to you as the new Research Assistant working

on the genetics side of the project at ICH. I have had a brilliant 13 months working as part of the NCUS and feel that I have gained a great deal of practical experience in the field. Armed with this knowledge I will begin a career as a Clinical and Molecular Geneticist at Guy's Hospital, working for the NHS. At Guy's I will undergo a two year training programme in which I will learn about

different genetic conditions such as Cystic Fibrosis and Huntington's and the laboratory methods used to diagnose them in patients' DNA samples. I am very excited about the new job but am naturally very sad to be leaving the NCUS. The major highlights for me have included chatting with many of you at the family day held at ICH during the summer and visiting Steven Slocombe and his lovely family at home in Barry. I would like to say goodbye and a big thank you to all of you – without you the project would not be able to happen!

Yasmin

Editor's note

We plan to send out the next issue of the NCUS Newsletter around June/July 2007
Please send your views, news, letters or questions to Mary Guest by May 31st 2007
mary.guest@sense.org.uk, Sense, 11-13 Clifton Terrace, Finsbury Park, London
N4 3SR, Tel: 0845 127 0060 Fax: 0845 127 0061 Minicom: 0845 127 0062

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