

PARENT'S NEWSLETTER 2012

ICISS – 250 children now enrolled, well over half way to our target of 410 and on schedule to finish in the Spring of 2014!

UK, Germany, Switzerland, Australia, New Zealand all enrolling patients in the largest ever trial investigating infantile spasms

Dear Parents,

- First of all a *massive thank you* for agreeing to take part in ICISS. We really believe that your participation in this trial is going to help contribute to furthering our understanding of this difficult epilepsy syndrome and what is the best way to treat it.
- Since we last wrote to you we have made lots of progress that we would love to share.

Changes in management of the trial:

- Firstly, there has been a change of Chief Investigator of the trial: Dr Finbar O'Callaghan has taken over from Professor John Osborne as Chief Investigator. Professor Osborne has retired but is continuing to take an active role in the trial. He will maintain responsibility for developing the international sites.
- In the ICISS Trial office, Ewa Mapstone has joined us to assist Dr Stuart Edwards in co-ordinating trial administration.
- The trial steering committee remains unchanged and consists of:
Dr Finbar O'Callaghan (Bristol)
Professor John Osborne (Bath)
Dr Stuart Edwards (Bath)
Dr Ellie Hancock (London)
Dr Tony Johnson (Cambridge)
Professor Colin Kennedy (Southampton)
Catherine Carter (Parent Representative)
Dr Andrew Lux (Bristol)

Dr Richard Newton (Manchester)

Mark Scholefield (Parent Representative)

Dr Chris Verity (Cambridge)

Infantile Spasm Conference in Bath in November 2011

- Because of our interest in infantile spasms we organised a conference for international experts in the field to talk about various aspects of the disease and possible new avenues for research.
- The conference was held in Bath on 31st October to 1st November 2011.
- The conference was a great success and attracted speakers from, Italy, Germany, Canada, USA, France, Australia, Switzerland, China, and, of course, the UK.
- Topics covered included the genetics of infantile spasms (i.e. do genes predict who is going to suffer from spasms and do genes predict who is going to respond best to treatment), the significance of the EEG, animal models of infantile spasms, side-effects of treatment, possible new agents that may have a role in protecting the brain of children with spasms and possible new treatment trials.
- The conference was such a success that there is real interest in producing a book on spasms written by the participants of the conference. If this happens we will, of course, let you know.

Recent publications from the ICISS (and old UKISS team)

- As many of you will know, the ICISS trial grew out of a previous trial looking at the treatment of infantile spasms, called UKISS (the United Kingdom Infantile Spasm Study).
- We are still analysing the multitude of data that has come out of the UKISS trial and have published two papers in the international medical journal, *Epilepsia* since you last heard from us.
- The first paper looked at the underlying causes of infantile spasms. We found an underlying cause for the spasms in just over half of the infants in the trial (61%) but in one third (33%) we could identify no underlying reason for why children developed spasms. In some children it was not possible to decide whether an underlying cause could be found because they were not extensively investigated.
- Common underlying causes were: a lack of oxygen around the time of birth causing brain injury, genetic disorders (such as Down's Syndrome or Tuberous Sclerosis), stroke, and disorders that caused the brain to develop abnormally (so-called cortical malformations).
- The second paper looked at whether it mattered how fast spasms are treated and whether it mattered how young (or old) an infant was when spasms develop.
- This paper does seem to show that the earlier spasms are treated then the better the

chances of a good outcome are with regard to learning.

- The paper also showed that in the UKISS trial the younger the infants were when the spasms started the poorer the outcome in terms of learning abilities.
- It must be remembered that these papers were looking at all the infants in the UKISS trial and that while the conclusions may apply to the children in the trial as a whole, any individual child could, of course, be an exception to the general rule.

Update on MRI changes and movement disorders

- In our last newsletter we talked both about the changes on MRI scans (brain scans) that are sometimes seen in patients that take vigabatrin and the funny movements (other than infantile spasms) that have been noted in some children in the trial.
- The changes on the brain scans that can be seen on children taking vigabatrin seem to occur in about 1 in 5 patients.
- The changes seem to disappear even if treatment with vigabatrin continues.
- There is no reason to believe that the changes on the scan matter or cause any problems for the children.
- However, some doctors have tried to link the two things together, suggesting that the unusual movements are linked to the changes that are seen on the MRI scan in children taking vigabatrin.
- We have looked at this in some detail in the children in the ICISS trial.
- In the first 124 children enrolled into the ICISS trial, a movement disorder developed in 8 children after the onset of their spasms and after entering the trial.
- In 4 of the 8 cases, the funny movements persisted despite stopping the vigabatrin. In 2 of the 8 cases, the movements disappeared despite continuing with the vigabatrin.

- In only 2 cases did there appear to be any plausible relationship with the vigabatrin therapy i.e. the movements started after beginning vigabatrin therapy and stopped after vigabatrin was taken away.
- There did not appear to be any convincing connection between the MRI changes that we know to occur in patients taking vigabatrin and the funny movements. The MRI changes were seen just as commonly in children without funny movements as in those with the movements.
- It is worth remembering that funny movements have been seen and known about in children with infantile spasms for a long time... long before vigabatrin was ever used. The funny movements in children with infantile spasms are most likely to be caused by whatever underlying brain abnormality is causing the epilepsy.
- We have written a paper about all this and hope to publish this soon.

Who are we?

- We have told you who the trial steering committee is, but we thought you might like to know more detail about the people running the trial on a day-to-day basis. So here we are:
- Dr Finbar O'Callaghan (ICISS Chief Investigator) is a Consultant Paediatric Neurologist at Bristol Royal Hospital for Sick Children and at the Royal United Hospital, Bath. He has a big interest in infantile epilepsy and disorders such as childhood stroke and the genetic condition Tuberous Sclerosis.
- Professor John Osborne was the Chief Investigator on the UKISS study and, previously, before his retirement, the ICISS study. He may have retired but he is still very much in evidence and is employed part-time to help with the ICISS study. He has particular responsibility for the overseas sites.
- Dr Stuart Edwards (ICISS Trial Co-ordinator) has extensive

experience of coordinating trials in infantile epilepsy having earlier run the successful UKISS trial. Stuart is the day-to-day hands-on "supervisor" of the trial who makes everything work!

- Dr Andrew Lux is a Consultant Paediatric Neurologist from Bristol who has a major interest in early onset epilepsy and neurophysiology. His main responsibility is analysing the EEG data in the study. Andrew was previously the Research Fellow in the UKISS Trial.
- Mrs Ewa Mapstone (ICISS Trial Assistant Co-ordinator). Ewa is the new addition to our team. She has a background in NHS administration and is the essential liaison person between the trial, and doctors who enrol patients into the trial.
- Mrs Patricia Shepherd (ICISS Data Entry Assistant) has worked with us for many years in the Trial Office helping enter data in both the UKISS trial and now the ICISS trial.
- We hope you have found the newsletter informative and helpful. We will try and update you on a yearly basis about what is going on. Thanks again for your support... with your help we will make a difference to children in the future.
- If you want to contact us, please email:

iciss@ruh-bath.swest.nhs.uk

and feel free to look at our website! www.iciss.org.uk



The ICISS Trial Centre, The Children's Centre, Royal United Hospital, Combe Park, Bath BA1 3NG, United Kingdom.

Fax: +44 1225 821432

Email: iciss@ruh-bath.swest.nhs.uk

Web: www.iciss.org.uk