

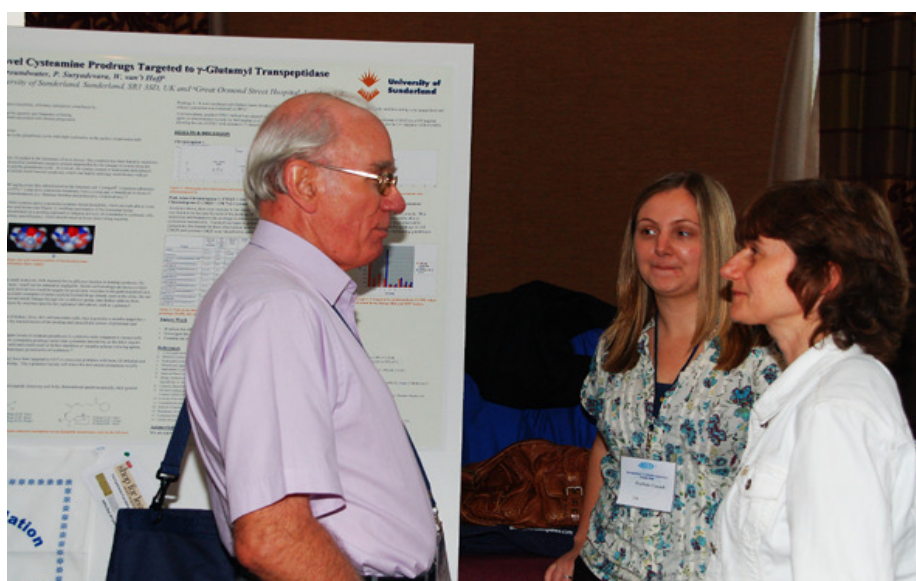
## The International Conference - A Personal Report

John Terry, Secretary to the Foundation

I am not able to give a complete scientific report on all the presentations at the Dublin Conference but I will focus on the contributions that relate to the treatment of the condition since I think that will interest our members most.

The genetic defects that cause Cystinosis are being identified with increasing precision. However, there was only one (poster) presentation related to work on gene therapy. This is being done by a group at Cork University led by Dr Harrison. They have been working on the challenge of gene repair for cystic fibrosis for some years but are now starting similar work for Cystinosis. A related, intriguing experiment was reported by Jerry Schneider in his Keynote Address. For some years now, a group in Paris have been experimenting with mice that have been made cystinotic by gene modification. They display some but not all the characteristics of human cystinotics. However, an experiment was done in which non-cystinotic bone marrow was injected into bones of these mice and they were given anti-rejection drugs as well so that the marrow was not rejected. All traces of cystinosis disappeared! This is exciting because it leads to the dream (at the moment) that bone marrow cells could be extracted from cystinotics, the genes corrected by gene therapy and then the marrow put back with no need for immunosuppressants.

A development that should take much less time to be delivered was reported from the USA. Dr Dohil carried out experiments using a nasal enteric tube to introduce cysteamine (the active in Cystagon) into the stomach, the colon or the small intestine of cystinotic volunteers. Measurements of blood cysteamine level were much higher when it was introduced into the small intestine and also it persisted longer. This led to the use of enteric coated Cystagon (enteric coatings have been used for years on aspirin tablets for example to avoid dissolution in the stomach where irritation can result). A small number of patients took part in experiments in which they were given double their normal four-times-a-day dose of Cystagon, but enteric coated and just twice a day. This was found to be too high a dose under these conditions, presumably because much less was wasted in the stomach, and something nearer 60% of the double dose looks very promising. A clinical trial sponsored by Benu Pharmaceuticals is planned for 2009.



*John Terry talks to Roz Anderson about the research the Cystinosis Foundation UK is funding at Sunderland University.*

It is very important to establish the correct dosage in the situation when none is destroyed in the stomach or colon. The dangers of overdosing on Cystagon came to light at the last International Conference two years ago. Cases of apparent 'bruises' were reported on elbows in patients who had taken high doses of Cystagon and one child unfortunately died. Since 2006 this condition has been studied and bone defects have been shown to arise as well, but use of the correct dose of Cystagon leads to full recovery. So that all doctors are aware of this, it is to be published in the medical/scientific literature and animal studies will be used to gain an understanding of the 'bruising' effect which is actually caused by the development of blood vessels under the skin surface. It is important to remember that Cystagon is the only treatment for cystinosis but a dose of 1.3g/sq.m/day should not be exceeded.

The development of the enteric-coated Cystagon could be a great step forward. In the longer term, if gene therapy continues to be elusive, the Prodrug work supported by the Foundation at Sunderland University and parallel work at Aberdeen could yet prove to be hugely beneficial. The aim here is to 'hide' the cysteamine active in a compound that can get through the stomach and the other organs right into the cells where it is needed and then be released. This would be so much more efficient that doses could be greatly reduced. Experiments are continuing and so far the results on some formulations look extremely promising.

Dr Zhang from Australia reported work on an eye gel made with cysteamine hydrochloride and paraffin. He stated that it is stable for up to 2 months at room temperature and is being used twice a day by 4 patients without problems. However, in response to a question he could not say if it is as effective as eye drops in removing corneal crystals.

Although Cystagon therapy can delay renal failure, most cystinotics will need a kidney transplant at some point. Dr Sarwal from Stanford University presented some very encouraging results on the use of non-steroidal immunosuppressants. So far the experience suggests that rejection rates are reduced and patient condition improved compared to the steroidal drug regimes.

As always at these conferences it is not only the formal presentations that benefit everyone so much, it is the opportunity to talk to the world's experts on Cystinosis about any aspect of a patient's condition that is concerning the patient or his/her parents. Apart from that, there are the friendships made or renewed with other families who face similar stresses and concerns. Once again I recommend that as many as can try to attend the next International Conference which is to be in Italy in 2010.