PCD Day, June 2011

Fiona introduced herself and welcomed everyone. The children were entertained outside by a sports coach and inside with arts and crafts.

Michael Loebinger, Consultant Respiratory Physician at the Royal Brompton Hospital, gave a talk, "PCD, Progression and Pseudomonas".

He explained that there is a lack of research into PCD, and there are probably a lot more cases that are undiagnosed. PCD is a genetic disease associated with defective ciliary structure and function. The cilia form part of the defence of the respiratory tract and are the mucociliary escalator. Without this mucociliary defence system working properly, bronchiectasis can develop with irreversibly damaged and dilate bronchi leading to persistent or recurrent bronchial sepsis.

Research has shown that late diagnosis adversely affects lung function in PCD, and the age of diagnosis/treatment affects the outcome. Whilst treatment does have an effect however, the decline of lung function is not always stabilised with treatment, and there is certain unpredictability about PCD. There are gaps in medical knowledge and lack of research and evidence into PCD. It can be very difficult to decide how best to treat patients because of this.

He then talked about Pseudomonas Aeruginosa (PSA) which is an environmental pathogen and can infect the lungs of PCD patients. PSA lives in moist areas like sinks and drains. It is very hard to get rid of in the lungs because the bugs "talk" to each other and produce a green bio film that covers them and they become mucoid. This makes them difficult to treat with antibiotics. Sometimes they burst out of their "houses" and cause inflammatory exacerbation. Microbial infection causes inflammation and tissue damage, and a vicious cycle ensues, but physiotherapy helps to allay this. Pseudomonas is associated with increased disease progression and greater airflow obstruction. Lung function is worse, and quality of life is affected because of the probable need for intravenous antibiotics and increased hospital stays. Older patients with PCD are more likely to have pseudomonas and more likely to have lower lung function. It is not known whether this is a chicken or egg situation, i.e. association or cause.

In Cystic Fibrosis research has shown that aggressive antibiotic treatment of the initial colonisation of PSA can postpone colonisation and prevent deterioration of lung function, but there is insufficient evidence to determine the impact of this.

In bronchiectasis there are not enough studies to guide practice, but getting rid of PSA when it first appears seems to be effective, with the earlier the treatment starts the better the outcome.The treatment is oral Ciprofloxacin antibiotics for two weeks, and if this is not effective then two weeks of intravenous antibiotics, and/or nebulised antibiotics (Colistin) for three months. If this does not work, then not much can be done and the increased inflammation my cause more damage. The problem is that aggressive treatment may get rid of PSA, but the patient is re-exposed to it in the environment and it returns. PSA mutates and can become resistant to Ciprofloxacin. Mucoid Pseudomonas can be eradicated in some patients. PSA takes about six months/one year to become mucoid when it becomes more difficult to treat. If PSA is isolated, most clinicians would prescribe an eradication regimen similar to those used in cystic fibrosis.

He concluded by talking about his current research into PSA, and looking at its DNA/RNA which would enable early detection. This would be of great value because currently cultures have to be grown, and this takes several days. Early molecular detection could play a role in the future.

Nic Collins, Senior Paediatric Physiotherapist at the Royal Brompton Hospital, and Glenda Dalton, Senior Paediatric Physiotherapist at Milton Keynes Hospital, then gave a talk, "Physiotherapy and the importance of Exercise".

Nic explained that the large airways of the lungs are lined by cilia. The cilia normally waft in a co-ordinated manner, but in PCD this does not happen, and mucociliary escalation does not work properly. We were shown a video of a patient having a bronchoscopy and could see mucus, redness and inflammation because of infection. If sputum becomes trapped, this leads to infection and inflammation which in turn leads to airway damage, ie bronchiectasis. Sputum can completely block some airways and coughing alone is not enough to clear them. Inflammation, pain and wheeziness can result. Physiotherapy clears sputum, prevents inflammation and infection and delays/prevents lung disease.

Glenda then explained that different physio techniques can be used like a tool box. She explained that the active cycle of breathing technique is very flexible, easy to do and can be used with postural drainage positions. It uses breathing control and then thoracic expansion exercises which get the air

behind secretions and begin to move them. The forced expiratory technique then forces the secretions out. Postural drainage uses gravity assisted positioning to help clearance, but shouldn't be used if there are problems with reflux. Percussion also helps to loosen secretions and can be used with postural drainage whilst the patient is taking deep breaths followed by huff and "shakes". She demonstrated these techniques on her colleague Nic. Autogenic drainage is another technique which uses huffing and breathing cycles. It can be done in a sitting position and is often taught using a tube. We were shown a video of a boy using this technique.

Various oscillatory and PEP devices were also demonstrated. These help to mobilise secretions, splint the airways open and can help with compliance. The acapella is oscillatory and can help loosen secretions. The flutter was also demonstrated but it has to be used whilst sitting otherwise it is not effective.

Physiotherapy needs to adapt through the patient's life time. In the newborn, chest clapping but not shaking can be used to help clear secretions. This is usually done one hour after a feed. Assisted autogenic drainage and infant PEPs can also be used. Toddlers (between 2 and 4 years of age) can do blowing games to help with sputum clearance. Shakes can start to be introduced as well as songs, games and rewards. It is usually best to establish a routine and do physio at the same time of day. DVDs and books can also help with compliance. Older children aged 4 to seven years can use the above methods. Huffing should be encouraged. Rewards and stickers usually help with compliance. Adolescents can be difficult because they are trying to consolidate their identities and establish relationships outside the family. They are trying to become independent and looking for a vocation. It must be remembered that they are not small adults or big children. It can also be a difficult time for parents who are trying to "let go" a little. Physiotherapists usually see patients most often when they are newly diagnosed and techniques need to change as the patient becomes more independent, prepares for work, and also during pregnancy.

Exercise is important and should be encouraged. It mobilises secretions, improves body image, maintains bone density, improves quality of life, promotes increased muscle strength, improves cardiovascular fitness and slows down lung function decline. Fairly active children tend to do well.

Mucolytics can also help. Nebulisers can loosen secretions. Dnase and hypertonic saline can be used before physiotherapy, but they are not suitable for everyone. Airways can be opened up with an inhaler, then should be cleared with physiotherapy techniques and inhaled antibiotics can then be used. Douching of sinuses can also be helpful.

Physiotherapy is effective if it reduces infection and fits into your lifestyle and should be reviewed periodically. PCD should be managed with regular sputum samples being tested and prompt antibiotic treatment when necessary.

We all then had a delicious lunch and mingled and chatted to each other. Some people had never met anyone with PCD before and it was a good opportunity to do so in this informal friendly environment.

After lunch, whilst the children were being entertained by "The Great Gappo", Hannah Mitchison, Senior Lecturer in Molecular Genetics at UCL and the Institute of Child Health gave us an "Update on Genetic Research".

She said that interest in the genetics of PCD is growing, and that she has collaborated with Scientists at Chapel Hill in America who are studying the same field as well as others.

She explained that there are 200 to 300 cilia on the top of each cell which co-ordinate into a beat pattern. There are cilia on the ventricles of the brain, in sperm, the airways, fallopian tubes, kidneys and eyes. In rare cases hydrocephalus can result when cilia are defective. Laterality (ie when organs are reversed) in PCD has been understood since the late 90's through experiments with mice. It was discovered that in embryonic mice nodal cilia set up our left right asymmetry. A cilium is made up of 600 proteins. Dynein arms make up the motor of the cilia with their self propagating motion. In PCD some of the structures are absent. The most common defect of the cilia in PCD is absent dynein arms.

She then went on to explain that we are our genes, and our genes control everything about us, including our health. Genes are made from DNA and a change in the DNA sequence can cause a genetically inherited disorder. Researchers therefore look at DNA sequencing analysis. She explained that if two parents are carriers then there is a 25% chance that any children they have will have PCD. Blood samples are taken from PCD families and the genes are hopefully identified to try to understand what has gone wrong so that then we can see what can be done about it. With new technology and DNA sequencing it can only takes about 2 weeks to identify a new gene because the painstaking mapping does not have to be done. This is a great step forward.

Thirteen genes cause 40% of cases of PCD. DNAH5 and DA11 cause 30% of cases. Ten PCD genes are essential components of the cilia structure and cause outer dynein arm defects. Two genes are in the cell body and assemble proteins. There is also a gene that specifically links PCD and Retinitis Pigmentosa. A total of 15 genes have now been found that are implicated in PCD, and with the help of new technology five of these have been found in the last two years.

She then talked about the Ciliopathy Alliance which enables a bigger voice on ciliopathy disorders and explained that some of the ciliopathy diseases overlapped. The first International Conference is being held on 17th and 18th May 2012 on Cilia in Development and Disease at the Institute of Child Health in London.

She explained that with the genes already identified, it was possible to tell if someone is a carrier, but gene testing is very expensive. In 15-20% of PCD cases it is not possible to find a structural defect in the cilia although the motility is abnormal. At the moment it is too expensive to do gene testing here.

The PCD Family Support Group AGM Minutes.

Fiona, the Chairman, introduced herself and explained that she is the mother of two boys with PCD. The minutes of last year's meeting on 19th June 2010 were agreed, and then she went on to talk about the achievements of the Family Support Group this year.

- CAUK (Ciliopathy Alliance United Kingdom) was launched in November with a scientific meeting and there will be another one next year in May 2012
- We went to Rare Disease Day at the House of Commons and talked to various MPs about PCD.
- We attended the ARNS conference and talked to nurses
- We attended the BTS Conference
- We held a coffee morning at Luton and Dunstable where families with PCD were able to meet each other
- Fiona attended clinics in the Royal Brompton Hospital and Southampton Hospital
- We obtained a grant of £2,500 from Genes for Jeans to fund the PCD Day
- We had a lunch for PCD adults and twelve people attended. Some had never met anyone else with PCD.
- The website is being well used with 17,723 hits and an average of 4 pages being accessed each time. The discussion board is being used a lot more.
- Fiona is working with the three centres to improve patient care
- 77 people completed the PCD survey. About half saw a consultant between two and four times a year, but less than 40% currently attend a specialist PCD clinic. 84% would like to see a PCD specialist.
- Standards of care for PCD adults have now been drafted
- Fiona took part in the Duathalon, the Great South Run and BUPA London 10,000
- Fiona met Princess Alexander at the Biomedical Research Centre opening at the Royal Brompton Hospital
- Fiona spoke at the Genetic Alliance Conference

Mick Wilkin, Treasurer, than gave us his Financial Review. He explained that 2010 had been difficult for the economy and charities, but that there were signs of recovery now. The cash reserves have dropped from £16k to £12k. He thanked everyone who had donated. He said that we need to keep our costs down and not pay for medical equipment as we have done in the past. £1200 has been spent on sponsoring delegates to go to conferences. The accounts have been checked by the auditors and he asked for their approval and they were formally agreed. The Independent Examiners would also be reappointed - they do not charge us for their services.

Looking forward, he said that the economic climate in 2011 was difficult, and asked if anyone could help with fundraising or by looking at potential trusts who may give us funds. The annual running costs with our current plans are about £11,000. He explained that the PCD Family Support Group is a going concern for the future, but some requests for funds may have to be refused for the time being

Fiona then addressed the meeting again. She explained that the Family Support Group goals have been revised and updated because they were originally drawn up 21 years ago.

These are as follows:-

- To provide support to patients and their carers who have or are suspected of having PCD.
- To maintain the website, create a specified tab for medics, and monitor the discussion forum
- To have a designated telephone number with an answer machine that will be answered by committee members
- To send newsletters by email
- To bring PCD to the attention of medics working in respiratory, cardiology and ENT medicine whilst continuing to provide and up to date information service via the website, leaflets and DVD.
- To promote research to aid diagnosis and treatment of PCD patients by being part of CAUK
- To support the NHS and other bodies to ensure PCD patients have access to diagnostic services and on-going care, and work with AGNSS

- To help the three diagnostic centres to obtain centralised funding for paediatric patients
- To help the transition to adult care
- To produce a blue print for standards of adult PCD care at the Royal Brompton Hospital that can then be adopted throughout the UK
- Fundraise to support the above activities
- Manage day to day activities to ensure that they meet Charity Commission rules within the law and without political bias.

Fiona then asked for volunteers to help with the above activities, but specifically:-

- To manage social media like Twitter and Facebook
- To update the website on a monthly basis
- To attend the ARNS conference every two years at Warwick University
- To attend Genetic Alliance Meetings
- To help with surveys and find patients for research
- To promote and manage fundraising activities

The officers were then re elected, i.e. the Chair, Secretary, Treasurer and Committee Members. Fiona thanked everyone and asked for new committee members explaining that the meetings are about three times a year.