The Surrey, Sussex & Kent Regional Paediatric & Neonatal Research Network

Second Annual Research Day

Wednesday 17th September 2008

Audrey Emerton Building, Eastern Road, Brighton BN2 5BE

Lecture Hall – Level 2

Scientific Committee:

PD Dr Heike Rabe, BSUH NHS Trust
Dr Paul Seddon, BSUH NHS Trust
Dr Phil Amess, BSUH NHS Trust
Mr Scott Harfield, BSUH NHS Trust
Prof. Somnath Mukhopadhyay, BSMS
Dr Terry Pountney, Chailey Heritage Clinical Services

Brighton and Sussex University Hospitals NHS Trust

brighton and sussex medical school

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The Surrey, Sussex & Kent Regional Paediatric & Neonatal Research Network

Programme

08:30	Registration & Coffee	
09:25	Introduction & Welcome	PD Dr Heike Rabe
	Session I Chair: Dr Shankar Kanumakala & PD Dr Heike Rabe	
09:30	Lung Development and Allergies in Childhood	Dr Jane Lucas
10:00	Non-Invasive Assessment of Respiratory Mechanics from Pulse Oximetry Waveform	Emily Savage
10:15	Developing a Caregiver Quality of Life Score for Wheezy Pre-school Children	Cathy Olden
10:30	**Coffee Break**	
	Session II Chair: Prof. Somnath Mukhopadhyay& PD Dr Heike Rabe	
11:00	Current Concepts of BPD Treatment	Prof. Sailesh Kotecha
11:30	New Drug Formulae for Children	Dr Angela Macadam Dr Alison Lansley
12:15	The Experiences of Parents Administering Medicines to Children in the Home	Liz Leggo
12:30	SENCE Medicines for Children Research Network	Dr Shane Tibby
12:45	Umbilical Cord Milking Versus Delayed Cord Clamping in Pre-term Infants	Amanda Jewison
13:00	CLRN in Sussex & Surrey	Dr Terry Pountney
13:05	**Lunch** *(Business Meeting of Research Network)*	
	Session III Chair: Terry Pountney & Dr Paul Seddon	
14:00	Parents Perception of Randomised Trials	Kim Cartwright
14:30	Examining Needle Related Distress in Children & Adolescents Undergoing Outpatient Venepuncture	Liam Mahoney
14:45	The Soothing Power of Chocolate	Charlotte Masterton
15:00	Measurement of Haemoglobin Levels in Infants Using Non-invasive Transcutaneous White Light Spectroscopy	Tom Whitfield
15:15	Sleep and Children with Cerebral Palsy	Jessica Underhill
15:30	**Coffee Break**	
	Session IV Honorary Lecture and Opening of TMBU - Chair: PD Dr Heike Rabe	
16:00	Epicure II Study	Prof. Kate Costeloe

Paediatricians attending this event may claim up to 5 CPD points in accordance with the current RCPCH CPD Guidelines

We value your feedback.
Please hand in the feedback questionnaire either at registration or put them in the box at the exit of the lecture hall.

Oral Presentations

Invited Speaker (09:30 – 10:00)
Lung Development and Allergies in Childhood
Dr Jane Lucas – Senior Lecturer, Southampton University

Abstract 2 (10:00 – 10:15)
Non-Invasive Assessment of Respiratory Mechanics from Pulse Oximetry Waveform
Emily Savage – Medical Student, Brighton & Sussex University Hospitals

Background: Previous studies in adults and children have found that the pulse oximeter plethysmogram (pleth) trace can be affected by changes in respiratory effort.
Aims: The aim of this study was to examine if respiratory data could be obtained from the pleth trace in quiet newborn term infants.
Methods: A Nonin 4100 Digital Pulse Oximeter (Nonin Medical Inc., USA) was connected via Bluetooth to a notebook computer in order to collect saturation, pulse rate and pleth data. Flow rate was also measured by means of a face mask connected to an ECO MEDICS EXHALYZER D Infant pulmonary function system (ECO MEDICS AG, Switzerland). Twelve artefact free sections of the pleth waveform and corresponding flow data recorded from six babies were analysed using MATLAB (The MathWorks Inc., USA).
Conclusions: In recordings from two babies visual assessment of the recordings suggested that there was a regular slow variation (about 4 to 6 per minute) in pleth amplitude. In all 12 recordings frequency analysis of the pleth waveform demonstrated a peak at a frequency similar to the respiratory rate obtained with frequency analysis of the corresponding flow signal. These results suggest that it may be possible to derive respiratory data from the pleth trace in newborn infants.

Abstract 3 (10:15 – 10:30)
Developing a Caregiver Quality of Life Score for Wheezy Pre-school Children
Cathy Olden – Paediatric Respiratory Nurse, Brighton & Sussex University Hospitals

Background: Assessing asthma control in the preschool age group is problematic. Lung function is difficult to measure and may not be closely related to the quality of life (QOL). Validated QOL tools exist for caregivers of school-age asthmatic children.
Aims: We aim to develop a QOL tool for wheezy preschool children and their families. As the first stage, we have explored QOL issues as perceived by caregivers and health professionals.
Methods: We interviewed 10 individual parents of children aged 1 to 5 years with recurrent wheezing, ran 2 parent focus groups involving a further 9 parents, and interviewed 6 health professionals.
Parents were asked open-ended questions about how wheezing illness affected
a) Their child's QOL
b) Their own QOL.
Professionals were asked what aspects of QOL were most likely to be affected by wheezing disease in
a) Pre-school children
b) Their carers
Conclusions: Prominent themes which emerged were as follows:
Parents on their child's QOL : Missing fun activities, need to limit exercise, sleep disturbance
Parents on own QOL: Anxiety about child catching respiratory infections, worry about spotting deterioration, missing work/college, concern about not being listened to by professionals
Professionals on child's QOL: Sleep disturbance, restriction of activity, upset about taking medications
Professionals on caregiver QOL: Stress of remembering to give medication, disturbed sleep, employment prospects.
Although there was considerable overlap, professionals focussed on the problems of medication impinging on quality of life, whereas caregivers rarely mentioned this. Compared to items in the Juniper caregiver QOL questionnaire for school-age asthma, issues about acute attacks, as opposed to chronic symptoms, predominated.

Invited Speaker (11:00 – 11:30)
Current Concepts of BPD Treatment
Professor Sailesh Kotecha – Professor of Child Health, Cardiff University

Invited Speaker (11:30 – 12:00)
New Drug Formulae for Children
Dr Angela Macadam & Dr Alison Lansley – Principle Lecturer & Senior Lecturer, Brighton University

Abstract 6 (12:15 – 12:30)
The Experiences of Parents Administering Medicines to Children in the Home
Liz Leggo – PhD Student, University of Brighton

This study is an on-going project. At present about 25% of the data have been collected, by the time of the conference it is anticipated that 75% will be ready to present on a poster.

Background: Previously published studies have shown that between 36 and 90% of hospitalised children receive one or more unlicensed or off-label medicines[1] and that approximately a third of parents experience problems obtaining prescriptions for unlicensed medicines in primary care[2].
However, no work has examined the experiences of parents in administering medicines to their children in the domestic setting, and moreover, the experiences administering unlicensed or off-label medicines, compared with those prescribed within a marketing authorisation.
Aims: The main objective of the study is to gain a deeper insight into the various factors which can affect medication administration and therapeutic outcome in paediatric patients. The impact that the licensing of pharmaceuticals has on these measures will play a central role in the research. The aim of the present study is to explore whether parents experience more problems in the administration of unlicensed or off-label medicines compared with licensed products.
Methods: Parents of children aged up to 11 years, admitted to the Royal Alexandra Children's Hospital, with a chronic condition have been recruited to the study. The licensing of the child's prescribed medicines has been ascertained from the patient notes in hospital.
Semi-structured face-to-face interviews are being conducted with parents, one month after the child is discharged from hospital to find out about their experiences in administering medicines, any reason for child refusal and methods employed to facilitate administration. They are also being asked about any changes to therapy, reasons for this, about the supply of medicines from pharmacies and about administration of medicines during the school / nursery day. Interviews are being coded using NVivo software and analysed using grounded theory.
Three months after discharge from hospital, structured telephone interviews are being conducted to find out about any further changes to prescribed therapy and reasons for this.
Conclusions: Interviews are currently being analysed. Results so far indicate that parents do experience problems with administration of medicines. The most commonly cited reason for this is the flavour of the medicine. To facilitate administration the most common method reported is to disguise medicine in food or drink. Parents have experienced problems with the supply of unlicensed medicines from community pharmacies and also have reported issues with administration during the school or nursery day. Parents who need to crush tablets and dissolve in water also report problems of administration, as well as concern over dosing accuracy.
The results from the interviews being conducted in this study will be used to develop a questionnaire to be distributed to a larger sample of parents.
References

1. Cuzzolin, L. et. al (2006) Off-label and unlicensed prescribing for newborns and children in different settings: a review of the literature and a consideration about drug safety (review). *Expert Opin. Drug Saf.* 5:: 703-718
2. Wong, I. et al. (2006) Supply problems of unlicensed and off-label medicines after discharge. *Arch Dis Child* 91: 686-688

Abstract 7 (12:30 – 12:45)
SENCE Medicines for Children Research Network
Dr Shane Tibby, Co-Director – SENCE MCRN and Consultant

Description of scientific content and background
SENCE is one of six local research networks spread across England that form the Medicines for Children Research Network. It is part of the Department of Health, funded, UK Clinical Research Network (UKCRN), which aims to increase high quality research activity across the entire NHS.
SENCE is based on an equal partnership of three London health sectors and is co-ordinated by three organisations:
1. Great Ormond Street Hospital NHS Trust and the Institute for Child Health (GOSH/ICH) University College London with The Centre for Paediatric Pharmacy Research (CPPR) a collaboration between the School of Pharmacy (SoP) and GOSH/ICH
2. Bart's and the London NHS Trust (BLT)
3. Evelina Children's Hospital, Guy's and St Thomas's NHS Foundation Trust (GSTT)

SENCE supports paediatric clinical research. We facilitate clinical trials which are both publicly and privately funded. Our primary focus is improving the lives of children and their families through greater awareness and education.

The MCRN Local Research Networks (LRNs), of which SENCE forms part of, have been established to undertake the studies included in the MCRN portfolio. Our objective is to lead, support and promote research into medicines for children. This will facilitate recruitment to national clinical trials and other well-designed studies conducted by the network.
SENCE covers a diverse and substantial childhood population within a defined geographical area, whose health requirements are provided by an already established, world-class infrastructure, and clinical network of primary and secondary paediatric facilities. This concentration of children, healthcare and research facilities provide a powerful resource for the SENCE Local Research Network.

Abstract 8 (12:45 – 13:00)

Umbilical Cord Milking Versus Delayed Cord Clamping in Pre-term Infants

Amanda Jewison - Medical Student, Brighton & Sussex Medical School

Background: Delayed umbilical cord clamping can promote placental transfusion and increase circulating blood volume in preterm infants, decreasing the risk of hypotension and anaemia. Research has shown that clamping the umbilical cord after a delay of at least 30 seconds is associated with fewer blood transfusions and less risk of severe intraventricular haemorrhage. However, delayed cord clamping is not standard practice in many UK hospitals due to concern regarding the delay in resuscitation and assessment by the neonatal team. In a recent Cochrane review, milking the cord towards the infant was identified as an alternative method of achieving placental perfusion whilst minimising the delay before clamping the umbilical cord.
Aims: To investigate whether milking the umbilical cord 4 times towards the infant is an effective alternative to delayed cord clamping by 30 seconds, in achieving placental transfusion and reducing the need for blood transfusions in preterm infants.
Methods: Randomised controlled trial. Single-centre study. The study group consisted of preterm infants born between 24^0 and 32^6 weeks' gestation. The infants were randomised to either delayed cord clamping by 30 seconds or milking of the cord four times towards the infant. The randomisation was stratified by gestational age: 24^0-27^6 weeks' and 28^0-32^6 weeks. Outcomes of the intervention were analysed by looking at haematological status, number of blood transfusions required and incidence of intraventricular haemorrhage in the first 6 weeks of life.
Results: (please note this study is ongoing and results may be different at time of presentation) 21 infants were enrolled into the study. 14 infants were randomised to milking of the cord (median gestation 31.1 weeks, birth weight 1527.5g) and 7 were randomised to delayed cord clamping (median gestation 31.0 weeks, birth weight 1275.0g). The groups were comparable in terms of heart rate on admission, blood pressure, number of transfusions received. There were trends towards higher haemoglobin and haematocrit in those randomised to cord milking, but no significant difference. Two infants from each group received blood transfusions.
Conclusions: Milking the umbilical cord is comparable to delayed cord clamping by 30 seconds in terms of clinical outcomes and haematological status during the first six weeks of life.

Abstract 9 (14:00 – 14:30)

Parents Perception of Randomised Trials

Kim Cartwright – Psychologist & Lecturer, Southampton University

Background: Enrollment of a newborn into a randomised controlled trial (RCT) requires asking parents to make important and complicated decisions for a third party, their newborn baby, regarding possible procedures that may have significant risks and implications for their baby's health and possibly survival. Little, however, is known about how parents make sense of their baby's participation in a clinical trial or about parents' actual experiences of their newborn taking part in a RCT.
Aims: To explore parents' (of surviving and deceased babies) perceptions of their newborn's participation in neonatal RCTs, including their views about enrolment and being approached, the period whilst the trial was running and after the trial. To investigate the perceived implications of participation for both parents and babies.
Methods: Semi-structured interviews were carried out with 16 parents (11 mothers, 5 fathers) of newborns who had participated in a neonatal RCT whilst receiving intensive medical and nursing care following birth. The neonatal RCTs were INIS, TOBY and INNOVO. Systematic thematic analysis revealed seven key themes: parental reactions to being approached, parent-clinician communication, decision-making process, perceived consequences for parents, perceived implications for newborn, effects on baby's care, overall experience and attitudes towards neonatal research.
Results: Most parents reported having mixed feelings such as shock, anger or worry when initially approached by clinicians to enrol their newborn into a trial. Negative thoughts were common immediate reactions, however, when parents had time to reflect on the situation, parents were generally pleased to be enrolling their baby into neonatal research. The most commonly reported reasons for participation were possibility of helping newborn, possible benefit to future babies, few risks/no harm to baby, and positives outweighed negatives. Many parents described "clutching at straws" and their willingness to "try anything" to help improve the chances of their newborn's survival. The majority of parents of surviving infants believed the trial had improved their baby's health, played a part in their child's survival and their baby had truly benefited from the study. Parents' thoughts about the effects of the trial on their newborn's care were mixed. Some thought their baby's care was the same and more than half the parents believed that during the trial their baby received more care from medical and nursing staff such as an increase in the number of observations and tests

carried out and access to better equipment. After the trial, parents were pleased with regular follow-ups as a result of their child's participation. Perceived implications for parents differed according to the trial and as to whether their baby survived or died.
Conclusions: Overall both parents of surviving and deceased newborns perceived their newborn's participation in a neonatal RCT as a positive experience. Clinicians should feel confident to ask parents to participate in neonatal research, particularly as most parents were glad to have been given such an opportunity. Nevertheless, an empathetic approach and good communication throughout the trial is essential, particularly as parents are often distressed, in shock and still coming to terms with having a critically ill baby.

Abstract 10 (14:30 – 14:45)
Examining Needle Related Distress in Children & Adolescents Undergoing Outpatient Venepuncture
Liam Mahoney – Medical Student, Brighton & Sussex Medical School

Background- Needle distress is a common problem in paediatric medicine. The anxiety, distress and pain that are associated with needle related procedures can produce profoundly negative physiological and psychological effects on children. Jay *et al* (1987) found that the anticipatory concern in children with cancer was so great in the days preceding bone marrow aspirations that they experienced nausea, vomiting, and insomnia. Furthermore, many children consider needle related procedures as one of the most distressing experiences of medical care. Despite increasing knowledge, the aetiology of needle related distress remains ambiguous, with studies displaying contradictory findings. Whilst increasing body of research relating to paediatric needle distress has emerged, much of the research has focused on particular populations (e.g. children with cancer) or procedures (e.g. immunisations).
Aims:

1. To examine verbal interaction between the carer, health care professional and children in the treatment room and how it may relate to child distress.
2. To investigate how procedural and situational variables such as child age, previous needle procedural experience and pre-procedural anxiety, and the relationship with child behaviour during venepuncture.

Method- 51 children aged between 7-16 years accompanied by their carer were video taped whilst having venepuncture. Prior to the procedure parents completed a sociodemographic questionnaire. Basic medical information was ascertained through direct questioning of the subjects and from the patients medical notes and the level of anxiety felt by the child was assessed though the use of a visual analogue scale of anxiety. The behaviours were coded according to the Child-Adult Medical Procedure Interaction Scale-Revised, of which the six super ordinate coding categories are outlined below (Blount *et al.*, 1997).

- *Child coping behaviours* *Adult coping promoting behaviours*
- *Child distress behaviours* *Adult distress promoting behaviours*
- *Child neutral behaviours* *Adult neutral behaviours*

Results: Children exhibited marginally more coping behaviours than distress behaviours during outpatient venepuncture. The most frequent child coping behaviour was that of non-procedural talk. Crying and verbal pain were the most frequent child distress behaviours exhibited. Regression analysis revealed that neither child age or trait anxiety of the child made independent contributions to the rate of child coping or distress behaviours. The regression analysis showed that, respectively, parental and staff distress promoting behaviours accounted for 64% and 4% of the variance seen in child distress behaviour, indicating that parental distress promoting behaviours have more of an influence on child distress behaviours during venepuncture. In addition, the regression analysis showed that staff coping promoting behaviours accounted for 37% and parental coping promoting behaviours accounted for 15% of the variance seen in child coping behaviour, signifying that staff coping promoting behaviours have more of an influence on child coping behaviours during venepuncture.
Conclusion: This research demonstrates that both parents and staff both have important influences on child coping and distress behaviour during venepuncture. It extends on previous research by showing that these relationships are stable across diverse situational variables and in different samples of children. It also reiterates the importance of the use of child coping promoting strategies during needle procedures, such as distraction, especially by medical professionals.

Abstract 11 (14:45 – 15:00)
The Soothing Power of Chocolate
Charlotte Masterton – Medical Student, Brighton & Sussex Medical School

Background: Venepuncture is one of the most common painful clinical procedures carried out on children in hospital. It is inevitably painful and is associated with a certain degree of anxiety and distress. Oral sucrose has been proven to reduce pain and distress in neonates having heel-prick test, another common painful clinical procedure.
To extend this view further we wanted to see if chocolate could be used to decrease the pain and distress associated with pleasure and increased mood.
Methods: All children aged 5-10 year old who were attending for a routine blood test were identified by the phlebotomist and approached by the researcher to discuss participation in the study. All children had EMLA cream and all children were guaranteed the same amount of chocolate.
The aim of the study was to recruit 60 children as part of a pilot study. After parents had given their consent, each child was randomly assigned to one of two groups. Group A were given chocolate after venepuncture (the control group), whereas group B were given chocolate bars before venepuncture (the intervention group).
After venepuncture all children were taken to a nurse blind to randomisation who helped them to score their plan on a Wong-Baker faces scale without parental influence. Independently of this, the parent scored their perception of the child's pain on a Wong-Baker faces scale. The researcher also completed a CHEOPS form as an objective measure of the child's distress and pain.
Interim: This study is still ongoing, the following are interim results. 48 children were recruited, 28 to Group A and 20 to Group B. These provisional results were analysed.
No significant differences were found between the child scores of the two groups, however, there was a significant difference in the CHEOPS scores between the groups ($p=0.03$), showing less pain and distress in Group B. There was also a significant difference between parent and child pain scores in Group A ($p=0.02$), with parents overestimating their child's pain.
It was also found that males were scoring slightly higher than females, with no females scoring 3 or more, but 18% of males scoring 3 or more out of 5 for their pain($p=0.05$).
Conclusions: The difference in CHEOPS scores suggests that chocolate is effective in reducing the pain and distress associated with venepuncture, although this was not evident from the children's pain scores. Parents also seemed to overestimate their child's pain, but this was only seen in Group A – those children who received chocolate after their blood test. It also became evidence that boys were scoring higher than girls.
One possible explanation for the similarity in scores of children could be that the children in Group A know they are about the receive chocolate when they score their pain, and the anticipation and excitement of this could reduce their pain. The figures from the CHEOPS scores suggest that chocolate is effective in reducing pain and distress in venepuncture, but more numbers are needed to show this is significant in the children's scores.

Abstract 12 (15:00 – 15:15)
Measurement of Haemoglobin Levels in Infants Using Non-invasive Transcutaneous White Light Spectroscopy
Tom Whitfield - Medical Student, Brighton & Sussex Medical School

Background: Venepuncture-related blood loss is a common cause of anaemia in neonates. Currently, this is the only way to obtain haemoglobin levels. Not only does this cause distress for the infant but it can also lead to the need for blood transfusions. Recently, new techniques for measuring haemoglobin levels non-invasively have been developed to reduce iatrogenic blood loss. A pilot study by Rabe et al showed that haemoglobin levels measured using a spectroscopic device (Mediscan 2000) were comparable with those obtained from venous blood samples.
Aims: To further compare haemoglobin levels obtained using the transcutaneous spectroscopic device Mediscan 2000 with venepuncture obtained blood samples, the current "gold standard" in preterm and term infants requiring blood tests. Secondly, to develop a conversion factor that takes into account the inhomogeneous distribution of haemoglobin in the capillary bed.
Study Design: Single centre prospective cohort study of term and preterm infants. Infants with major congenital abnormalities including chromosomal aberrations, fetal hydrops and congenital skin disease were excluded.
Method: 33 female and 42 male infants (mean age at measurement was 5.4 weeks; mean gestation 28.5 weeks; mean birth weight 1160g) were enrolled into the study. A white-light spectroscopic device (Mediscan 2000) was placed on the forearm for 60 seconds to measure haemoglobin content in each infant, on at least one occasion. Measurements from

blood samples were obtained from the hospital pathology system. The readings from the two methods for obtaining haemoglobin values were taken within a two hour time period. The Mediscan results were analysed using computer software and compared with the venepuncture obtained samples
Results: From the 75 infants, a total of 220 recordings were taken. The spectroscopic haemoglobin values were corrected for the inhomogeneous distribution of haemoglobin in the microcirculation. Using the Bland –Altman method, the venous blood sample and Mediscan recorded results were compared which gave a correlation coefficient of 0.9657.
Conclusions: The results show good correlation between the haemoglobin levels from the blood samples and Mediscan measurements. This supports evidence from the pilot study that the Mediscan 2000 could be used to determine haemoglobin levels.

Abstract 13 (15:15 – 15:30)
Sleep and Children with Cerebral Palsy
Jessica Underhill - Research Fellow, Chailey Heritage

Background: Sleep is a necessary yet often overlooked element of daily life. It is taken for granted that we all sleep with little in-depth exploration of the meanings and experience of sleep for people. Research on these important aspects of sleep is beginning to be carried out within the field of sociology. For instance, within the sociology of childhood a few studies have sought to describe the experience of sleep from the point of view of children and young people. This is novel as much research on the sleep of children relies on parental accounts. This work has not extended to the experiences of sleep for children with disabilities. Children with cerebral palsy (CP) make up the largest group of children with a physical disability in the UK yet there is little research on the sleep of children with CP or that of their families.
Aims: The primary aim of this PhD research is to obtain an in-depth understanding of the sleep of children with CP and the sleep of their families.
Secondary aims include:

- To explore and compare family members constructions of 'good sleep' compared to 'poor sleep'.
- To obtain an understanding of the impact of 'poor sleep' of young people with CP on their lives and relationships, and on their families and the coping strategies used.
- To explore how experiences of sleep change or vary when young people with CP regularly spend nights away from home i.e. in respite care.
- To develop recommendations and resources about sleep for young people with CP and their families on the basis of the research findings.

Methods: This research aims to involve all participating family members in the research and will allow participants to explore and describe their experiences of sleep from their own perspectives. Because sleep is a complex phenomenon the research will use multiple qualitative and quantitative methods of data collection. The qualitative methods to be used are in-depth interviews, sleep diaries and the use of photography. The quantitative methods are sleep quality questionnaires and the use of actigraphy (a small movement sensor, worn on the wrist, which provides an indication of sleep-wake patterns).
Conclusions: Development of recommendations and resources about sleep for young people with CP and their families is an expected outcome based on the research findings.

Poster Presentation Abstracts

Gene Environment Interactions Influencing Inflammation in Young Children

Dr Shrabani Chakraborty – Clinical Fellow, Brighton & Sussex University Hospitals

Background: Detailed population based prospective studies have indicated that polymorphic variation in genetic status could interact with environmental factors to influence the course of many common adult illnesses. This means that patients with individualised genetic profiles may react differently to environmental influences like smoking, pollution etc. This could lead to different patterns of risk for individuals exposed to similar degrees of noxious environmental stimuli.

Researchers in Dundee have conducted cross-sectional studies in children and young adults (aged 4-22 years). They have shown that the polymorphic variation in genes interact with environmental variables thus regulating asthma and eczema outcomes (for exemplar studies, see poster by Basu *et al* at this meeting).

However studies done in older children are unable to provide us insights into these interactions when they influence the early origin of these diseases.

Aims: To study the relationships between variation in inflammation-related genes and allergy and asthma phenotype in infants and young children.

Methods: It is intended that mothers will be approached at their 20 weeks appointment for ultrasound scan at the Royal Sussex County Hospital and hospitals in Scotland in order to inform them regarding the study. They will be approached later at their subsequent hospital visit near term to obtain consent.

The baby's cord blood will be collected, stored at -80^{o}C, and genotyped in batches at the Biomedical Research Centre at Dundee. A questionnaire regarding other factors that influences the disease course of allergy, asthma and inflammation will be completed by the mother. Microvasculature studies will be performed during the neonatal period. Lung function measurements will also be obtained on the infant during the neonatal period. In case of difficulty in obtaining cord blood, a saliva sample may be collected from the infants. DNA will be extracted from the blood or saliva sample. Assays for genetic polymorphisms will be performed according to standard procedure.

The proposal is currently being discussed with obstetric and midwifery staff. We have received advice from the Ethics Committee and will be preparing our final submission to the Committee following the consultation.

A follow up would be performed at 1 year and 2 years of age to assess the development of eczema and wheeze during early childhood. This will be performed using a questionnaire developed and validated in the UK for young children. 200 children with heterozygous filaggrin gene (*FLG*) variation and wild type filaggrin gene status will be randomly selected for detailed evaluation of clinical symptoms of eczema and asthma, and skin prick testing at their first and second years of life.

Conclusions: The birth cohort genotyped for common, relevant polymorphisms, and phenotyped for asthma and eczema, will be a powerful tool for exploring gene-environment interactions of relevance in the field of asthma, allergy and eczema in children. We expect that this line of research will help develop an individualized approach to the management of these illnesses and facilitate the development of novel therapeutic interventions for these conditions in the future.

Management of Congenital Cytomegalovirus infection (CCMV): An evidence based approach

Dr R Fernandez – Neonatal Consultant, Brighton & Sussex University Hospitals

Objective: To develop an evidence-based structured approach to the management of neonates with CCMV.

Materials/Methods: MEDLINE/OVID database and Cochrane Collaboration Library were searched for related papers and graded for their level of evidence.

Results: 39 papers were identified including 9 reviews**.** Neonates with abnormal neurological signs i.e. microcephaly, seizures, abnormal cranial ultrasound, sensorineural hearing loss (SNHL), chorioretinitis or signs of disseminated infection i.e intrauterine growth restriction (IUGR), thrombocytopenia or abnormal liver function tests should be evaluated for CCMV infection.

Asymptomatic neonates: Current evidence does not support treatment of babies who only have positive CMV-PCR.

Symptomatic neonates: Evidence recommends treatment of all newborns with positive CMV-PCR and CNS related/sensorineural symptoms to prevent further neurological deterioration. IUGR newborns are thought to have systemic involvement including CNS and could also therefore be considered for treatment. There is evidence to suggest that newborns with no CNS symptoms but other signs of systemic involvement could be treated to avoid neurological sequelae if their viral load in the peripheral blood is high. Neonates with normal neurology but lower viral load should be closely followed up for evidence of SNHL. Treatment should be with intravenous Ganciclovir. Increasing evidence suggests oral Valgancilcovir for 6 weeks as an effective alternative. Close follow-up for evidence of toxicity and neurological deterioration is required.
Conclusion: Evidence for neonates who would benefit from treatment is growing. We have tried to formulate this structured protocol in order to treat neonates with signs and symptoms that would affect long-term prognosis.

Gene-Environment interactions and Clinical Asthma and Eczema Phenotype in Children – *Breathe* (TAYSIDE) AND *Breathe II (SUSSEX)*

Dr Kaninika Basu - Research Fellow, Maternal and Child Health Sciences, University of Dundee

Introduction: The industrialised world is in the middle of a natural epidemic of eczema and asthma in children. It is hypothesised for our studies that a range of gene-environmental interactions may influence the course and severity of these diseases in children and their response to medication. The report presents two exemplar studies from our work. Firstly, the presence of the Arg/Arg-16 variation on the β_2-agonist receptor gene is associated with poorer response to β_2-agonists in adults and we have explored the effect of this variation on asthma phenotype in children. Secondly, the presence of variation in the filaggrin gene apparently leads to poor epithelial barrier function and greater entry of allergens into the body. The study explores whether this leads to worse asthma phenotype.
Aims: To conduct a hypothesis-based study of the above gene-environment interactions through the development of a database of children and young adults with asthma that contains information on patient genotype, environmental factors contributing to asthma, and clinical asthma severity.
Methods: A cross-sectional survey was undertaken using electronic records and direct interviews of asthmatic children and young adults aged 3-22 years attending primary and secondary care clinics in Scotland. Saliva samples were collected for genotyping and archiving. Currently, 1500 children and young adults have been enrolled in the database.
Results: The results of the two exemplar studies are presented below. *β_2-agonist receptor gene variation:* There is an increased hazard for asthma exacerbations in children with homozygous arginine-16 (Arg/Arg16) genotype of the β_2-agonist receptor gene, especially those on regular salmeterol (OR 3.40, 95% CI 1.19 to 9.40, p = 0.022). Arg/Arg patients had a greater risk of overall exacerbations (OR 1.80, 95%CI=1.24-2.62; *P*=0.002), were more likely to require oral steroids (OR = 1.78, 95%CI=1.17-2.70; *P* = 0.007) and experience school absences (OR = 1.76, 95%CI=1.21-2.57; *P* = 0.003).
Filaggrin gene (FLG) variation: Individuals bearing *FLG* null alleles were more likely to be prescribed increased asthma medication (*P*=0 .001), with the homozygote null individuals having an odds ratio of 6.68 (95% CI, 1.7-27.0; *P*=0 .008) for being prescribed long-acting β_2-agonists in addition to inhaled steroids. FLG null alleles were also associated with increased rescue medication use (*P*=0.004).Exacerbations were significant for R501X mutation and the combined genotype compared to the wild type with odds ratios of 1.97 (95% CI, 1.19- 3.22; p= 0.006) and 1.61 (95% CI, 1.08-2.40; *P*= 0.013) respectively. Children with *FLG* null alleles were more likely to require oral steroids (31.4% vs. 19.5%; OR= 1.89; *P*= 0.016) for their exacerbations. There was an increased risk (42.6% vs. 30%; OR=1.71; *P*= 0.026) of school absence owing to asthma exacerbations in children with *FLG* null mutation.
Conclusion: The BREATHE database describes the phenotype and genotypic characteristics of children with asthma in Scotland and has been a powerful tool for the exploration of various gene-environmental interactions, and for pharmacogenetic studies in children with asthma. We are currently extending the database to other centres the UK – hospitals in Brighton and Hove and other parts of Sussex, and other centres in Scotland.