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8th Annual Research Symposium

PAEDIATRICS

Incorporating the 4th Surrey, Sussex & Kent Regional Paediatric & Neonatal Research Network Conference

Programme and Abstracts

Tuesday 14th September 2010, 9.00am - 5.00pm
Audrey Emerton Building
Royal Sussex County Hospital
Brighton

Many thanks to our chairpersons, speakers, presenters and guests,

Brighton and Sussex Medical School

Brighton and Sussex University Hospitals NHS Trust

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

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Symposium Programme

Morning Programme		
8.00 – 9.00	Delegate registration	
9.00 – 9.15	Welcome: Duncan Selbie, Chief Executive, Brighton & Sussex University Hospitals NHS Trust	
9.15 – 9.30	Introduction: Professor Somnath Mukhopadhyay, Chair in Paediatrics, Brighton & Sussex Medical School	
Session I: Infections in childhood Chaired by: Professor Tony Frew		
9.30 – 10.10	Immune mechanisms of inflammation in RSV bronchiolitis	Professor Jürgen Schwarze, Edward Clark Chair of Child Life and Health, University of Edinburgh
10.10 – 10.25	Non-invasive measurement of lung function in infants and young children	Dr Paul Seddon, Consultant Respiratory and Neonatal Paediatrician, Royal Alexandra Children's Hospital
10.25 – 10.40	Neonatal sepsis - trials and tribulations	Dr Santosh Pattnayak, Consultant Paediatrician, Medway Maritime Hospital, Kent
10.40 – 11.00	**Coffee Break & Poster Viewing**	
Session II: A novel mechanism for children's allergy, eczema and asthma Chaired by: Dr Diab Haddad		
11.00 – 11.30	Filaggrin gene mutations as major predisposing factors to promiscuous atopic disease	Professor Colin Palmer, Chair of Pharmacogenomics, Biomedical Research Centre, University of Dundee
11.30 – 12.00	Filaggrin-related barrier defects in the skin but not the gut may increase peanut allergy risk in children	Dr Sarah Inglis, Senior Research Fellow, Biomedical Research Centre, University of Dundee
12.00 – 12.30	Filaggrin gene defects and the atopic march: could a poor skin barrier worsen childhood asthma and allergy?	Professor Somnath Mukhopadhyay, Chair in Paediatrics, Brighton & Sussex Medical School
12.30 - 13.30	**Lunch & Poster Viewing**	
Afternoon Programme		
Session III: NIHR funded paediatric and neonatal projects Chaired by: Professor Helen Smith		
13.30 – 13.50	How should we feed preterm infants? – the ADEPT study	Dr Kenny McCormick, Consultant and Honorary Senior Lecturer in Neonatology, John Radcliffe Hospital, Oxford
13.50 – 14.05	Randomised trial (RTC) on milking of the cord versus slight delay of cord clamping in preterms (VLBW)	PD Dr Heike Rabe, Consultant Neonatologist and Honorary Clinical Senior Lecturer, Brighton & Sussex Medical School
14.05 – 14.20	The efficacy of treadmill training with partial body-weight support, or static cycling training for children and young people with GMFCS level IV and V cerebral palsy – a randomised controlled trial	Dr Terry Pountney, Research Physiotherapist, Chailey Heritage School, Sussex
14.20 – 14.35	To do or not to do? Skin Prick Testing for children in general practice	Professor Helen Smith, Chair in Primary Care, Brighton & Sussex Medical School
14.35 – 15.20	**Tea Break & Poster Presentations**	
Session IV: Chronic respiratory problems: a foundation for healthy adulthood Chaired by: Dr Paul Seddon		
15.20 – 15.50	The growing lung and the early detection of lung disease	Dr Sarath Ranganathan, Paediatric Respiratory Physician and Senior Lecturer in Paediatrics, Brighton & Sussex Medical School
15.50 – 16.20	Pre-school wheeze – a problem for life	Professor Andy Bush, Professor of Paediatric Respirology, Imperial College, London
16.20 – 16.50	Respiratory function 'tracking' in adult survivors of prematurity and low birth weight	Ms Anne-Marie Gibson, PhD Scholar, University of Melbourne
16.50 – 17.05	Summing up and close	
17.05– 17.35	**Wine & refreshments**	

Welcome

On behalf of the Brighton and Sussex Medical School and Brighton and Sussex University Hospitals NHS Trust, we welcome you to the 8th annual research symposium, which this year focuses on paediatric research.

The Medical School and Trust are extremely proud of their evolving research portfolio in this area. As part of this strategy we have planned an exciting day showcasing the very best of local research and representing the breadth of local expertise.

The symposium is structured around the key themes of infection, allergy, local NIHR projects and respiratory complications.

Since building research partnerships is an essential part of our success, we have invited our valued collaborators from Kent, Oxford, London and further afield to be a part of today's event. We are also pleased to present the symposium in conjunction with the 4th Surrey, Sussex and Kent Regional Paediatric and Neonatal Research Network research conference.

We hope that today's symposium will be a stimulating, inspiring and beneficial experience, as well as an excellent opportunity to make connections for future research projects.

Professor Somnath Mukhopadhyay

Chair in Paediatrics, Consultant Paediatrician

Brighton and Sussex Medical School

PD Dr Heike Rabe

Honorary Clinical Senior Lecturer, Lead for Neonatal Research

Brighton and Sussex Medical School

Professor Somnath Mukhopadhyay*, Chair in Paediatrics, Consultant Paediatrician*

Professor Somnath Mukhopadhyay became Chair of Paediatrics at BSMS in October 2007. In a landmark discovery published in Nature Genetics 2006, he described a novel mechanism causing eczema and asthma in children. Subsequent to this, he described the role of this gene defect on a number of aspects of the development of allergy and asthma in children, e.g. the development of more severe asthma, or interactions with exposure to allergens from pets. The discovery of the role of this protein change, and its subsequent characterization, has potential for future treatments that could reduce the risk of developing eczema and asthma in children.

In another important discovery published in the Journal of Allergy and Clinical Immunology, impact factor 9.2 and reported prominently by Radio 4, ABC, and in paper editions of all leading newspapers in the UK in October 2009, Professor Mukhopadhyay led research into the detection of a gene change that substantially

reduces the efficacy of the commonest asthma medicine, the 'blue inhaler', in children. He has now completed a randomised controlled trial further testing this hypothesis. The results, expected for publication later in 2010, are likely to generate further international interest.

His current research aims to further unravel the wider picture of gene-environment interactions and their role in guiding treatment for childhood eczema and asthma.

PD Dr Heike Rabe, *Honorary Clinical Senior Lecturer, Lead for Neonatal Research*

PD Dr Heike Rabe is an Honorary Clinical Senior Lecturer and Consultant Neonatologist since November 2002. Her research interest is mainly focused on neonatology, especially on developing non-invasive methods of studying microcirculation. Other areas of interest include prevention and treatment of anaemia of prematurity and neonatal neurology.

The Department of Neonatology is participating in several multi-centre trials and local studies which include topics on microcirculation in neonatal sepsis, reduction of red cell transfusion in preterm infants by delaying cord clamping, oral versus nasal intubation and onset of feeding, parents' perceptions of randomised trials, and neonatal follow-up.

PD Dr Rabe has run the highly successful Surrey, Sussex and Kent Regional Paediatric and Neonatal Research Network Conferences since 2007 and co-founded the network.

About BSMS research

- At BSMS, we identify research areas in medicine where we believe we can make a rapid and real difference.
- Our focus is on the continuous improvement of medical treatment to deliver more personalised healthcare for patients, by applying basic science to answer fundamental clinical questions.
- BSMS brings together the combined expertise of the universities of Brighton and Sussex and the local NHS health economy, to deliver research which is directly applicable to our local population, but also of national and international standing.
- BSMS research directly impacts health and resource policy within the NHS, as well as bringing indirect economic and social benefits to the wider population.

Paediatricians attending this event may claim up to 5.5 CPD points in accordance with the current Royal College of Paediatrics and Child Health CPD Guidelines

We value your feedback. Please place your feedback questionnaire in the box at the exit of the Lecture Theatre at the end of the day. Thank you

DELEGATE SPEAKER ABSTRACTS

Delegate Speakers

Session I: Infections in childhood

(9.30 – 10.10am)
Immune mechanisms of inflammation in RSV bronchiolitis
Professor Jürgen Schwarze, Edward Clark Chair of Child Life and Health, Child Life and Health and Centre for Inflammation Research, University of Edinburgh

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Session II: A novel mechanism for children's allergy, eczema and asthma

(11.00 – 11.30am)
Filaggrin gene mutations as major predisposing factors to promiscuous atopic disease
Professor Colin N.A. Palmer, Chair of Pharmacogenomics, Biomedical Research Centre, University of Dundee

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Session III: NIHR funded paediatric and neonatal projects

(1.30 – 1.50pm)
How should we feed preterm infants? – the ADEPT study
Dr Kenny McCormick, Consultant Neonatologist, John Radcliffe Hospital, Oxford on behalf of the ADEPT Study Group

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Session IV: Chronic respiratory problems: a foundation for healthy adulthood

(3.20 – 3.50pm)
The growing lung and the early detection of lung disease
Dr Sarath Ranganathan, Senior Lecturer in Paediatrics, Brighton and Sussex Medical School and Consultant Respiratory Physician, Royal Alexandra Children's Hospital, Brighton

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Immune mechanisms of inflammation in RSV bronchiolitis

Professor Jürgen Schwarze, Edward Clark Chair of Child Life and Health, Child Life and Health and Centre for Inflammation Research, University of Edinburgh

The Queen's Medical Research Institute, 47 Little France Crescent, Edinburgh, EH16 4TJ
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Viral bronchiolitis in infancy is a severe inflammatory disease of the distal airways, caused in the majority of cases by respiratory syncytial virus (RSV). The immune pathology of bronchiolitis is not fully understood. The immune response to RSV can be subdivided into: 1) the epithelial phase in the first hours after infection during which epithelial cells and some macrophages release pro-inflammatory cytokines and chemokines, 2) the innate immune response which is characterised by an early influx of natural killer cells and concomitant recruitment of granulocytes, macrophages and dendritic cells (DC), 3) the adaptive immune response by antigen-specific effector T-cells and activated B-cell following activation by DC. T-cells are involved in cytotoxicity, clearing the virus, and in both pro-inflammatory and regulatory pathways. Activated B-cells produce antigen specific antibodies which contribute to viral clearance, in particular in secondary infections.

Given the apparent role of T-cells in viral bronchiolitis, we studied the impact of RSV infection in vivo on phenotype and function of pulmonary DC, the professional antigen presenting cells that are thought to activate T-cells during infection. Further we investigated the role of airway epithelial cells (AEC) in regulating DC and T-cell activation.

Using a mouse model, we observed increases in numbers of lung DC after the initial phase of RSV-infection. These seem to be triggered by an early release of GM-CSF from lung epithelial cells leading to an expansion of local DC-precursors in the lung which mature and become efficient T-cell activators. Early in infection DC preferentially induce Th1- and pro-inflammatory Th17-cells. The latter may contribute to excessive pulmonary inflammation in bronchiolitis and also during subsequent allergen sensitisation possibly facilitating the development of asthma symptoms which have been observed following RSV-bronchiolitis. The subset of plasmacytoid DC which are potent producers of interferon-alpha has a direct antiviral role during RSV-infection limiting maximum replication of RSV and contributing to its clearance. In addition they may have direct regulatory effects, reducing RSV-induced inflammation and lung function changes. Healthy AEC seem to prevent activation of mucosal T cells and DC. However this inhibition is lost after RSV infection of AEC.

We conclude that in the early phase of RSV-infection innate, epithelial cell dependent mechanisms dominate the antiviral response, releasing DC and T cells from inhibition, inducing expansion of lung DC and allowing activation of these immune cells. Subsequent innate and adaptive immune responses, including activation of DC and subsequently T-cell subsets contribute to the development and maintenance of pulmonary inflammation and associated lung function changes. Further, these virus-induced immune responses may also contribute to aberrant immune pulmonary responses after the resolution of RSV-bronchiolitis.

Non-invasive measurement of lung function in infants and young children

Dr Paul Seddon, Consultant Respiratory and Neonatal Paediatrician, Royal Alexandra Children's Hospital, Brighton

The last few decades have seen major progress in the development and standardisation of methods to measure lung function in infants. The use of these methods has started to yield answers to some of the important questions both about normal early lung development and the initial stages of lung disease in (for example) cystic fibrosis.

However, most of these methods require sedation in order to ensure deep enough sleep for measurements to be made. This limits their application in large epidemiological studies, because of reluctance by both parents and research ethics committees to allow sedation of healthy children for research. It also precludes using these methods to asses lung function in acute respiratory disease.

This presentation will review a range of 'non-invasive' techniques (methods not requiring sedation) to assess lung function, or surrogates of lung function – in infants and young children. The advantages and limitations will be discussed.

Neonatal sepsis - trials and tribulations

Dr Santosh Pattnayak, Consultant Neonatologist, Medway NHS Foundation Trust, Gillingham, Kent

Neonatal infection is an important cause of morbidity and mortality in the neonatal population especially in babies born preterm and with very low birth weight (VLBW). The aim in most of the sepsis trials is to reduce the adverse outcome by various interventions. But first of all, it is essential to monitor the epidemiology of neonatal infections.

The first UK based Neonatal infection surveillance network (NeonIn)[1] was established in 2004 collecting clinical and microbiological data on episodes of culture proven sepsis on a longitudinal basis. Currently 16 units are contributing data from across England representing 7% of the English birth cohort. This database can be used to monitor the epidemiology of neonatal infections, use of antibiotics for empiric therapy and will enable comparison over time and between the units.

In the year 2000 - 2007, both INIS (International Neonatal Immunotherapy Study) and PROGRAMS trials[2] intended to reduce the mortality and morbidity in this high risk neonatal population. INIS results are still awaiting but the latter trial concluded that early use of prophylactic GM-CSF corrected neutropenia but did not reduce sepsis, improved survival or short term outcome. This again brought out the complexity of immune system functions in prevention of neonatal sepsis.

In recent years many RCTs[3] have demonstrated the beneficial effects of probiotics in decreasing the incidence of necrotising enterocolitis and death. The PIPS (probiotic in preterm babies study) is trying to find out the effect on blood stream infection, stool microbiology with the use of a standardised single probiotic strain after careful stratification of the study population. Similarly Bovine Lactoferrin (BLF) has shown to reduce the incidence of late onset sepsis in VLBW babies[4]. There is a scope for further RCT for defining the dose and duration of treatment.

Both Coagulase negative Staphylococcus (CoNS) and Staph aureus are the predominant organisms responsible for late onset sepsis in the neonatal unit. A monoclonal antibody against the Lipoteichoic acid moiety (Pagibaximab) might be helpful in preventing Staphylococcal sepsis in VLBW neonates (MAB-N007 Trial). Use of Meropenem for treatment of neonatal meningitis (NeoMero2) is also under review, the study will aim at the safety, efficacy and pharmacokinetics of the drug.

These are the sepsis related trials that we are involved with. But the search for strategies to reduce neonatal sepsis continues.

References:

1. Vergnano S et al. Neonatal infections in England: the NeonIN surveillance network. *Arch Dis Child Fetal and Neonatal Edition*- in press.
2. Carr R et al. GM CSF administered as prophylaxis for reduction of sepsis in extremely preterm, small for gestational age neonates (the PROGRAMS trial): a single-blind, multicentre, randomised controlled trial. *Lancet*. 2009;373:226-33.
3. Deshpande G et al. Updated meta-analysis of Probiotics for preventing necrotising enterocolitis in preterm neonates. *Paediatrics* 2010;125:921-30
4. Manzoni P et al. Bovine Lactoferrin supplementation for prevention of late onset sepsis in very low birth weight neonates. *JAMA* 2009;302:1421-1428

Filaggrin gene mutations as major predisposing factors to promiscuous atopic disease

Professor Colin N.A. Palmer, Chair of Pharmacogenomics, Biomedical Research Centre, University of Dundee

We have demonstrated that a spectrum of null mutations in the gene encoding filaggrin predispose individuals to eczema in European and Asian populations, with the Asian populations containing distinct variants when compared to the European populations. These mutations promote severe eczema in very early childhood with 60% of individuals carrying the mutations showing symptoms within 6 months of life. We have also shown that early exposure to domestic animals, such as cats, may modulate the penetrance of eczema in these individuals. In addition we have found that this leads to an increased susceptibility to asthma, but this is clearly associated with the atopic status afforded by this genotype. The role of FLG mutations in allergic sensitization by both skin prick testing and RAST testing was examined and we have shown that FLG mutations confer a major risk for an individual's sensitization and allergy to multiple allergens, with many FLG mutation carriers being sensitized to all classes of allergens tested. Increased sensitization to both food and inhaled antigens was observed in FLG mutation carriers.

Filaggrin-related barrier defects in the skin but not the gut may increase peanut allergy risk in children

Dr Sarah Inglis, Senior Research Fellow, Biomedical Research Centre, University of Dundee

Authors: Sarah K. Inglis (Biomedical Research Centre, University of Dundee), Colin N.A. Palmer (Biomedical Research Centre, University of Dundee) and S. Mukhopadhyay (Brighton and Sussex Medical School).

Common mutations (carried by almost 10% of the UK population) in the gene encoding filaggrin, the skin barrier protein, increase the risk of children developing allergic disorders such as eczema. Until now, it has not been known whether these children are also at increased risk of developing food allergy. Previous work by Lack *et al* has suggested that peanut sensitisation may be triggered by entry of peanut allergen through the skin rather than the gut. This work implies that children with filaggrin-weakened skin may be more at risk of developing peanut sensitisation (PS).

We have studied the association between the presence of filaggrin gene mutations and PS in asthmatic children and young adults. In a cohort of children with asthma we found that there was a higher prevalence of PS in children heterozygous for filaggrin gene defects in comparison to those carrying the wild type filaggrin gene status. We then determined that although filaggrin is, as expected, expressed in the skin, it is not expressed in the intestinal wall. We subsequently measured the permeability of skin and intestinal epithelium, using transepidermal water loss (TEWL) and dual sugar tests respectively, in children with filaggrin gene mutations who also had asthma with wildtype children. We showed that whilst the skin permeability of children with asthma and with filaggrin mutations was significantly higher than that of wildtype children, the intestinal permeabilities of the two groups were similar.

In conclusion, filaggrin gene mutations increase the risk of PS. Filaggrin-related PS is likely to be related to altered allergen entry through the skin.

This is the first direct evidence of a skin barrier defect contributing to a food allergy and it points towards the need for further research on a number of different fronts.

References

G. Lack *et al*. Factors associated with the development of peanut allergy in childhood. *New England Journal of Medicine* 348:977-985, 2003.

Filaggrin gene defects and the atopic march: could a poor skin barrier worsen childhood asthma and allergy?

Professor Somnath Mukhopadhyay, Chair in Paediatrics, Brighton and Sussex Medical School and Consultant Paediatrician, Brighton and Sussex University Hospitals Trust

The protein filaggrin is mainly present in the skin. The role of any genetic defects altering filaggrin is thus likely to be restricted to the skin alone.

Previous work has suggested that filaggrin may play a role in maintaining the skin barrier.

We have found strong clinical evidence suggesting that filaggrin gene defects affect childhood asthma and allergy at various points.

We will present exemplar data from our studies to show how these defects adversely affect

- the risk of developing eczema in infancy
- the way the infant reacts to powerful allergens in the environment, like the cat allergen
- the amount of asthma medicines a child with asthma needs on a day-to-day basis
- the risk of developing asthma attacks as a child

This allows us to build a more composite picture of the role of this defect in increasing childhood morbidity.

It also leads us to the question of how the defective filaggrin in those with gene defects is actually failing, as – if we can remedy this – we may be able to make a difference to asthma and allergy management at a number of levels.

References:

1. Palmer CN, Ismail T, Lee SP, Terron-Kwiatkowski A, Zhao Y, Liao H, Smith FJ, McLean WH, **Mukhopadhyay S**. Filaggrin null mutations are associated with increased asthma severity in children and young adults. *Journal of Allergy and Clinical Immunology* 2007 Jul;120(1):64-68. Epub 2007 May 25.

2. Basu K., Palmer C.N.A., Lipworth B. J., McLean W.H. I., Terron-Kwiatkowski A., Zhao Y., Liao H., Smith F.D.J., Mitra A., **Mukhopadhyay S**. Filaggrin Null Mutations Are Associated With Increased Asthma Exacerbations In Children And Young Adults. *Allergy* 2008; 63(9):1211-1217. Epub 2008 Feb 25.

3. Bisgaard H., Simpson A., Palmer C.N.A., Bønnelykke K., Mclean I., **Mukhopadhyay S**., Pipper C.B., Halkjaer L.B., Lipworth B., Hankinson J., Woodcock A., Custovic A. Gene-Environment Interaction in the Penetrance of Eczema in Infancy Replicated in Two Birth-Cohort Studies: Filaggrin Loss-of-Function Mutations Triggered by Cat Exposure. *PLOS Medicine* 2008 Jun 24;5(6):e131.

4. Henderson J., Northstone K., Lee S., Liao H, Zhao Y., Pembrey M., **Mukhopadhyay S**., Davey Smith G., Palmer C.N.A., Irwin McLean W.H., Irvine A. D. The burden of disease associated with filaggrin mutations: a population based longitudinal birth cohort study. *Journal of Allergy and Clinical Immunology* 2008 Apr; 121(4):872-877.e9. Epub 2008 Mar 5.

5. Palmer CNA, Irvine AD, Terron-Kwiatkowski A, Zhao Y, Liao H, Lee SP, Goudie DR, Sandilands A, Campbell LE, Smith FJD, O'Regan GM, Watson RM, Cecil JE, Bale SJ, Compton JG, DiGiovanna JJ, Fleckman P, Lewis-Jones S, Arseculeratne G, Sergeant A, Munro CS, El Houate B, McElreavey K, Halkjaer LB, Bisgaard H, **Mukhopadhyay S**, McLean WH. Common loss-of-function variants of the epidermal barrier protein filaggrin are a major predisposing factor for atopic dermatitis. *Nature Genetics* 2006;38(4):441-446.

How should we feed preterm infants? – The ADEPT study

Dr Kenny McCormick, Consultant Neonatologist, John Radcliffe Hospital, Oxford on behalf of the ADEPT Study Group

Preterm babies who have intrauterine growth restriction and abnormal umbilical artery doppler studies have increased risks of adverse neonatal outcomes. These babies are already undernourished at birth and frequently demonstrate intolerance of milk feeds with an increased incidence of necrotising enterocolitis (NEC). There is no clear evidence to guide the timing of introduction of enteral feeds.

The Abnormal Doppler Enteral Prescription Trial (ADEPT) studied the effects of an early enteral feeding regimen (milk started day 2 of life) compared to a late regimen (milk started day 6) in a group of preterm babies (<35 weeks) identified antenatally as growth restricted with absent or reversed end diastolic flow velocities (AREDFV) in the umbilical artery. The rate of feed advancement was kept the same in both groups. Primary outcomes were age at which full enteral feeding was sustained for 3 days and incidence of NEC.

Characteristics & outcomes of analysed babies		
	Early	Late
No	189	183
Gestation (mean)	31.2w	31.1w
Birth weight (mean)	1042g	1018g
Received first feed within specified time	83%	77%
Received breast milk at first feed	82%	88%
Died before reaching primary endpoint	9 (5%)	8(4%)
Days to established feeds (median)	18d	21d*
NEC (% of babies)	13%	11%
Days of parenteral nutrition	18	21*

- p=0.001

In conclusion, growth restricted preterm babies with absent or reversed end diastolic flow in the umbilical artery who are fed from the second day of life tolerate and reach full feeds at an earlier age than babies fed from the sixth day of life. There were no differences in late onset sepsis between the groups; early fed babies had a significantly lower incidence of cholestatic jaundice. To date we have seen no overall increase in the incidence of NEC in babies fed early.

Although the trial was known to have relatively low power to detect differences in the incidence of NEC the results are encouraging and lend support to the growing practice of feeding high risk preterm infants early.

Randomised trial (RCT) on milking of the cord versus slight delay of cord clamping in preterms (VLBW)

PD Dr Heike Rabe, Honorary Clinical Senior Lecturer, Brighton and Sussex Medical School and Consultant Neonatologist, Brighton and Sussex University Hospitals Trust

Authors: Susan Ayers, Amanda Jewison, Ramon Fernandez Alvarez, Denise Stilton, Rob Bradley, Des Holden, on behalf of the Brighton Perinatal Study Group.

Background:
RCTs demonstrated a slight delay of 30s in clamping the cord benefits very low birth weight babies (VLBW) by reducing intraventricular haemorrhages and blood transfusion. Birth attendees hesitate to wait for 30s, therefore milking of the cord has been reported in one trial.

Aim:
To evaluate the circulatory effects of four times milking the cord (MilkG) versus a slight delay in clamping the cord of 30s (ClampG) in VLBW <33 weeks.

Method:
Prospective, single centre study, inborn singletons <33 weeks. Data analysis for significant differences was performed with Wilcoxon test. In addition parents' interviews were done to evaluate their perceptions on enrolling their preterm baby into a RCT before birth.

Results:
30 VLBW were randomised to the ClampG (median birth weight 1200g (525-1975), median gestational age 29w (24-32) and 28 to the MilkG (median birth weight 1170g (444-2245), median gestational age 30w (24-32). There were no significant difference found for postnatal adaptation and requirement for blood transfusion. There was trend towards less intraventricular haemorrhage in the MilkG. The parents expressed enthusiasm and altruism towards enrolling their babies into the trial.

Conclusion:
Our study demonstrates that MilkG could substitute ClampG in VLBW. The blood transfer from the placenta is similar with both approaches supporting postnatal circulatory adaptation. Very valuable lessons on how to improve informed consent for antenatal enrolment have been learned from the parents' interview study.

The study was supported by a Brighton and Sussex University Hospitals NHS Trust R&D grant.

The efficacy of treadmill training with partial body-weight support, or static cycling training for children and young people with GMFCS level IV and V cerebral palsy - a randomised controlled trial

Dr Terry Pountney, Head of Research, Chailey Heritage Clinical Services, Chailey Heritage School, East Sussex

Background:
Muscle weakness is common in children & young people (CYP) with cerebral palsy (CP), particularly if not walking independently (Gross Motor Function Classification System (GMFCS) Level IV -V). It contributes to deformity, pain, functional loss & is linked to contracture. Options for exercise in CYP are limited at GMFCS Levels IV to V and this may contribute to deterioration in functional ability.

There is evidence that strength training benefits CYP at GMFCS levels I-III (Darrah et al). Reviews on the efficacy of treadmill training have been reported (Damiano & Dejong 2009; Mutlu et al 2009) and 3 studies have included CYP with CP Level IV using a treadmill (Schindl et al 2000, Dodd & Foley 2006, Begnoche & Pitetti 2007). One study addressed CYP at Levels IV-V finding significant benefit using a static bike (Williams & Pountney 2007). This study builds on existing evidence to address the need for effective, acceptable interventions to improve/maintain functional ability for CYP with CP at GMFCS Levels IV -V.

Methodology:
A RCT with participants allocated to either to an adapted static bicycle bike, a partial body weight support treadmill or control group with a 6-week exercise graded exercise programme (3 sessions a week) and 6 and 12 week follow-up periods. Outcomes measures were Gross Motor Function Measure 66 and 88. A Graded Exercise Test for the bike and the Fastest Walking Speed on the treadmill were used to calculate the level at which each participant was exercised and overload was ensured by encouraging the participant to increase the duration and speed of exercise at each session.

Results:
Thirty-five children and young people completed the programme, 20 females and 15 males aged 9y 0m -17y 1m, mean 13y 1m, (SD 2.3) with bilateral CP. Twenty three were at GMFCS level IV and 12 were at level V and 14 were predominantly dyskinetic, and 21 spastic). At baseline there were no significant differences between the 3 intervention groups for the GMFM measures (66, 88D, 88E). On completion of the 6-week exercise period there were no significant differences between the groups for the GMFM 66, or the GMFM 88E (walking, running & jumping) scores (p=>0.05). However, significant differences were found for the GMFM 88D (standing) scores between the bike and control group (p=0.017), and between the treadmill & control group (p=0.046).

Discussion:
This study demonstrated that a relatively short, clinically feasible training programme on a static bicycle or treadmill can lead to CP. The static bicycle and treadmill provided a safe, effective means of exercise to a population with very limited opportunities for activity. The exercise was enjoyed, particularly by some participants with dyskinetic CP who appreciated the 'freedom' to exercise safely at speed. The exercise was designed to be feasible for the carers. Fitness bikes are readily available, the adaptations reasonably priced and bikes can be shared between children. The exercise period and sessions were relatively short and manageable in an already demanding lifestyle.

To do or not to do? Skin Prick Testing for children in general practice

Presented by: Professor Helen Smith, Chair in Primary Care, Division of Primary Care and Public Health, Brighton and Sussex Medical School

Background:

Atopic disorders are a common reason for consulting General Practitioners, allergies account for 6% of all consultations and 10% of primary care prescribing costs. Many children with asthma or rhinitis have allergies, but in primary care diagnostic and management decisions are usually made without a formal allergy history or testing. Failing to distinguish between allergic and non-allergic disease leads to empirical decisions on treatment. Advice regarding allergen avoidance is either not given, or if given, is non-specific to the child's problem and therefore futile. This trial will assess whether a formal allergy assessment (structured allergy history and skin prick testing) improves disease control. Descriptive studies in adults confirm the feasibility of the intervention and its potential to avoid inappropriate allergy avoidance advice.

This study, which is in the start up stage, is a pragmatic single-blinded randomised controlled trial (RCT) of allergy intervention (structured allergy history + skin prick testing (SPT) + appropriate advice on allergy avoidance). 300 children aged 6-16 years are being recruited from 10 general practices in Sussex identified through the Primary Care Research Network (PCRN-SE). After baseline assessment participants are randomised to receive the allergy intervention or usual care. The main outcome measures are a change in asthma and rhinitis symptoms and health related quality of life. The children will be reviewed by a blinded observer after 12 months. An economic assessment of the potential cost savings which could accrue to the NHS and to society through routine allergy assessment and SPT in General Practice will also be performed.

The growing lung and the early detection of lung disease

Dr Sarath Ranganathan, Senior Lecturer in Paediatrics, Brighton and Sussex Medical School and Consultant Respiratory Physician, Royal Alexandra Children's Hospital, Brighton, East Sussex

Respiratory diseases are responsible for approximately 50 percent of acute medical conditions in children, ranking second to cardiovascular disease in causing morbidity and mortality at a cost of well in excess of €100 billion to the European Union (1). A major driver in research over the last two decades has been to unlock the so-called 'silent period' in the preschool years where, until recently, there was a dearth of knowledge about early disease development, lung growth and physiology. As our knowledge increases it is becoming apparent that these early years of life are extremely important as it is the time during which many chronic respiratory diseases, such as asthma, appear to have their origin. In cystic fibrosis, lung disease appears to start soon after birth, with pulmonary inflammation and infection leading to the development of structural (2) and functional changes (3) within the first few months of life. Lung function in those born prematurely but without chronic lung disease appears to be lower than term-born infants and longitudinal studies suggest that 'catch-up' in lung function does not occur (4). This has been interpreted as suggesting that postnatal lung growth and development are affected in such infants, even in the absence of obvious direct insults to the lung. Our understanding of bronchopulmonary dysplasia has evolved as our understanding of lung development has evolved. In the era of exogenous surfactant therapy and improved medical management we still see the 'new' BPD, where the histology now represents less a pattern of lung injury and more a developmental arrest in alveolarisation and vascular growth (5).

Since common chronic respiratory conditions start in the early years of life better understanding of how the lung develops is essential. The last decade has seen significant research in this area, particularly in methods for assessing pulmonary function. Studies have investigated the influence of gender, age, premature birth and the influence of exposure to environmental tobacco smoke. There is now a need to integrate assessments of pulmonary structure and function, inflammation, infection, genetics and molecular biology into the study of the common respiratory diseases during the first years of life. As novel therapies to prevent, limit or even reverse the impact of insults on the growing lung are developed methods for monitoring the success of interventions in the first years of life are required.

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Pre-school wheeze: a problem for life

Professor Andrew Bush, Professor of Paediatric Respirology, Imperial College, and Consultant Paediatric Chest Physician, Royal Brompton Hospital

The aim of this presentation is to demonstrate that the fundamental genetic, epigenetic and environmental factors that interact to produce wheezing in the pre-school age do not abate over time, although they may be temporarily silenced, and return to cause significant respiratory disease in late adult life. The seminal observation by David Barker of the close link between prevalence rates of infant mortality from respiratory disease and subsequent standardised mortality rates in adults for chronic obstructive pulmonary disease (COPD) firmly put the roots of COPD in early life [1]. Subsequent work has established that early life events confer a risk at least equal to smoking for the development of COPD [2]. Epidemiological classification of pre-school wheeze [3] has suggested that transient wheezers (symptoms in the first 3 years of life only) have abnormal lung function at birth, with incomplete catch-up by age six, focussing attention on antenatal factors. These include in particular maternal smoking in pregnancy, maternal atopy, and also environmental pollution. Persistent wheezers (wheeze throughout the first six years of life) have normal lung function at birth, but have developed airflow obstruction at age six years, focussing attention on the post-natal period. Research has demonstrated that early sensitisation to aeroallergens is an important predictor of loss of lung function, bronchial responsiveness and asthma [4]. The natural experiment of immigration has also shown that the very early years are of key importance [5]. Pathological studies have defined a time window between 12 and 30 months during which the classical pathological changes of asthma develop [6, 7]. Over-lapping cohort studies have shown that after age six, in both normals [8] and wheezers [9, 10], there is no catch-up growth in lung function. However, an accelerated age-related rate of decline of lung function, a well known risk factor for COPD, is higher in those who in childhood had what we would now term episodic viral wheeze [11]. ADAM33, a gene important in lung development [12] and a determinant of pre-school lung function [13] is also important in COPD development [14, 15], and other genes have also been similarly implicated [16]. In the Melbourne asthma cohort [10], 44% of the severe asthmatics recruited at age 10 years have developed COPD [Tai A et al, data presented in abstract at ATS 2010] In conclusion, early life events determine lifelong lung health; after age 4 years, you can only go downhill, not improve! Prevention of COPD must start antenatally, and continue in the very early years of life.

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Respiratory function 'tracking' in adult survivors of prematurity and low birth weight

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Introduction:
It is well established that many survivors of low birth weight (LBW; <1500 g at birth) have impaired lung function. The aim of this study was to determine whether abnormal lung function at 25 years of age is established in childhood. A second aim was to see if abnormal lung function at 8 years of age tracks through the period of normal lung development to predict impaired maximal lung function and may be a precursor to COPD in adult years.

Methods:
A cohort of LBW (n=210; [VLBW n=124; ELBW n=86]) and normal birth weight (NBW; >2500 g at birth; n=60) has been followed for 25 years. Very Low Birthweight participants completed spirometry and lung volumes at 8, 11, 14, 18 and 25 years of age and NBW at 14, 18 and 25 years of age. Restricted maximum likelihood modeling was used for longitudinal FEV_1 z-score as it allows for analysis of data from different time points that are not necessarily evenly spaced, without being affected by missing data. Abnormal lung function was defined as those with an average z-score ≥ 2SD's below the mean for the study period. Small for gestational age (SGA) was defined as birth weight less than the 10th percentile of a population specific weight versus gestational age plot. Bronchopulmonary dysplasia (BPD) was defined as respiratory sequelae in an infant requiring oxygen at more than 28 days after birth.

Results:
167 LBW (SGA n=38; BPD n=47; SGA & BPD n=22) children completed lung function testing at 8 years, 119 at 11 years, 169 at 14 years, 147 at 18 years and 83 at 25 years of age. LBW was associated with reduced lung function when compared to NBW, especially in variables reflecting flow, FEV_1 z-score (14yrs -0.84, p=0.001; 18yrs -0.61, p=0.007; 25yrs -1.04, p=0.009), FEF_{25-75} z-score (14yrs -0.83, p=0.0002; 18yrs - 0.94, p=0.0001; 25yrs -1.13, p=0.009) and FEV_1/FVC z-score (14yrs -0.56, p=0.01; 18yrs -1.01, p<0.0001; 25yrs -0.51, p=0.1). Those participants who were SGA were ELBW. Those LBW individuals who were SGA had significantly reduced FEV_1 z-score (-0.51, p=0.006) and FVC z-score (-0.55, p=0.003) and these SGA individuals show evidence of 'catch-up' growth in terms of lung function (FEV_1 z-score slope 0.04, p<0.0001; FVC z-score slope 0.06, p<0.0001) , with the exception of FEV_1/FVC z-score (slope -0.03, p=0.0009) which falls further from their contemporaries. This effect on FEV_1 and FVC z-scores may suggest some protective element or compensatory mechanism of being born small for gestational age. Reassuringly, BPD as a neonate did not significantly affect lung function variables as these individuals as they age, with the exception of FEV_1/FVC z-score (-0.44, p=0.02).

Conclusions:
The reduced lung function in adult survivors of low birth weight is established in early childhood. ELBW especially those who were SGA have obstructive lung disease which is established in early childhood and 'tracks' through to adulthood, reassuringly these participants demonstrate significant 'catch-up' growth, suggesting some protective element or compensatory mechanism of being born small for gestational age.

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Evaluation of learning opportunities in a multidisciplinary, heterogeneous group in the morning handover meeting: do we need national guidelines?

Presented by: Dr Amit Saha, ST1, Paediatrics, Worthing Hospital, Western Sussex Hospitals NHS Trust

Authors: A Saha, U Pillai, A Garg

Institute: Department of Paediatrics, Worthing Hospital, Western Sussex Hospitals NHS Trust, Worthing.

Aim:
With the implementation of the European Working Time Directive in the UK, there is less training and teaching opportunities for junior doctors. In our hospital, we have a formal morning handover process, involving a multidisciplinary group. The aim of this study is to explore its effectiveness as a learning opportunity in its own right.

Method:
A cross-sectional paper questionnaire survey was undertaken, consisting of both closed and open ended questions. Data was collected over several handover sessions, with a total of 110 respondents.

Results:
Data was collected from various grades of doctors, medical students, nursing staff, matrons, midwife manager, mental health team etc. Both clinical and non-clinical topics were discussed. 91.6% of respondents felt it ensured good continuity of care, whereas 50% said it changed their practice in some way. Immediate feedback and multidisciplinary input were cited as the main advantages, and the main disadvantage perceived was the time constraint.

66.6% of respondents felt that the teaching opportunity, with real ward-based patients and immediate applicability, was better than other forms of formal, focus-group didactical teaching, whereas a further 25% felt both forms were equally important. Wide ranging comments were received on how to improve on this session further.

Conclusions:
This study demonstrates the role of the multidisciplinary morning handover as an alternative, high impact teaching session, especially with the work time restrictions in place. Larger, multicentre studies are needed to evaluate it further and the authors strongly advocate the need for national guidelines to make it widely applicable.

Questionnaire survey: ward round based mini clinical examination (minicex) for paediatrics trainees in the Kent, Surrey & Sussex Deanery, UK

Presented by Dr Amit Saha, Department of Paediatrics, Worthing Hospital, Western Sussex Hospitals NHS Trust

Authors: A Saha, U Pillai, A Garg

Institute: Department of Paediatrics, Worthing Hospital, Western Sussex Hospitals NHS Trust, Worthing.

Aims:
MiniCEX is a structured, formative, workplace based assessment tool and is an integral part of the paediatric training portfolio in the UK. In our unit, instead of leading, consultants stand back for one or more patients and observe trainees conducting the examination and communication, giving them immediate feedback, both verbal and in the form of a miniCEX. We conducted this survey to obtain a wider trainee perspective on the applicability and feasibility of introducing this model to other units.

Methods:
A questionnaire survey was sent out via e-mail to all paediatric trainees (levels ST1 to ST3) in our Deanery. The results were collated and analysed online using a designated website on the internet.

Results:
The survey was sent to a total of 61 trainees of different grades, of whom 33 completed it. Among all trainees, 81.8% felt a formative assessment more accurately reflected their skills and competencies, and 93.8% trainees felt that this was a practical way of doing a miniCEX assessment. An overwhelming 94.4% of all paediatric trainees across the Deanery were in favour of formally introducing this model in their unit.

Conclusion:
The results clearly illustrate trainee enthusiasm for this model and identifies a need for change in which formative assessments are conducted. The authors recommend a pilot project for ward round based miniCEX be designed and introduced across all units in this Deanery. It is envisaged that after its successful regional implementation, this programme can then be formally rolled out across the United Kingdom.

Extracting respiratory data from pulse oximeter plethysmogram recordings in acutely wheezy preschool children

Presented by: Ms Catherine Olden, Paediatric Respiratory Research Nurse, Royal Alexandra Children's Hospital, Brighton, East Sussex

Authors: P. Seddon[1], C. Olden[1], D. Wertheim[2], E. Symes[1], H. Rabe[3]

Institution: [1]Royal Alexandra Children's Hospital - Brighton/UK, [2]Kingston University - Kingston/UK, [3]Royal Sussex County Hospital – Brighton.

Introduction:
Respiratory data can be derived from pulse oximeter plethysmogram (pleth) traces in healthy newborn infants (Wertheim, et al, Arch Dis Child 2009; 94: F301-F303). If such techniques could be applied in acutely wheezy preschool children, it could provide useful non-invasive respiratory monitoring in this difficult age group.

Aim:
To examine if respiratory data can be obtained from the pleth trace in acutely wheezy preschool children.

Method:
Children 1 to 5 years old attending hospital with an acute wheezy episode were studied. Pleth data were collected with a Nonin 4100 Digital Pulse Oximeter (Nonin Medical Inc., USA) connected via 'Bluetooth' to a notebook computer. Respiratory rate (by observation and breath counting) and heart rate were simultaneously assessed clinically. Sections of pleth data with little or no artefact from fifteen spontaneously breathing children were analysed using software that we developed with MATLAB (The MathWorks Inc., USA). Analysis included.

a) assessment of the main frequencies present in the pleth signal.

b) low-pass filtering to remove the heart rate frequency.

c) plotting of peak-to-peak amplitude of the pleth signal.

The median (range) age of the children was 31 (20 to 64) months.

Results:
In 24 of the 27 recordings, frequency analysis of the pleth signal showed clear peaks at a similar frequency to the respiratory rate obtained from clinical assessment. Low pass filtering of the pleth data yielded a signal with a similar frequency to the respiratory rate in 25 of the recordings, although in some sections the frequency was variable.

Conclusion:
These findings suggest that respiratory data can be obtained from the pleth waveform in acutely wheezy children.

***A fat lot of good*. An 8 year longitudinal investigation of fat intakes in a paediatric cystic fibrosis (CF) population**

Presented by: Mr Chris Smith, Senior Paediatric Dietitian, Nutrition and Dietetics, Royal Alexandra Childrens Hospital, Brighton, East Sussex

Authors: C. Smith[1], A. Winn[2], P. Seddon[3], S. Ranganathan[3]

Institution: [1]Royal Alexandra Children's Hospital, Nutrition and Dietetics, Brighton, United Kingdom; [2]University of Brighton, Computing, Mathematics and Information Sciences, Brighton, United Kingdom; [3]Royal Alexandra Children's Hospital, Respiratory Medicine, Brighton, United Kingdom.

Background:
Reducing total and saturated fat intake is recommended for the general population. UK population wide campaigns to reduce the sugar, total fat and specifically saturated fat in the UK paediatric populations diets has been in place since 2004. This has been designed to have maximum effect and exposure by targeting schools and industry through a variety of mediums such as television, advertisements campaigns and community projects. Early reports suggest this is now having a positive impact on intakes. High fat intakes however are still advised for those with CF and dietary advice has remained unchanged. We wanted to see if there was any suggestion these campaigns has independently influenced the diets of CF children. In addition, data from Italy has suggested the percentages of energy derived from saturated and monounsaturated fatty acids is significantly higher in CF compared with non CF controls, whereas the percentage of energy derived from polyunsaturated fatty acids (PUFA) is slightly lower. It has been suggested that quantity and quality of fat supplementation in CF need careful attention to balance the fat supply.

Aim:
To describe changes in macronutrient and fat intake over an 8 year period.

Method:
Three-day food diaries were completed by patients with CF during annual review and nutrient composition was analysed using Compeat (Nutrition Systems, UK). The influence of year on % energy by type (fat, CHO, protein) and % energy by fat component (SFA, MUFA, PUFA) was examined by linear regression (SPSS v17.0, Chicago, USA).

Results:
134 food diaries were reviewed in 28 CF subjects (10 males) age range 1 to 18 years. Over the study period % energy from fat decreased slightly and % energy from protein increased slightly but these trends were not significant (protein p= 0.06, CHO p=0.44, Fat p=0.07). The % of energy derived from SFA, MUFA and PUFA also remained statistically unchanged (SFA p=0.10, MUFA p=0.20, PUFA p= 0.15). Saturated fat consistently contributed the most: 13-18% of total energy (>120% of reference requirement), whilst MUFA contributed 10-13% and PUFA 4-6% (< 100% of reference requirement) of total energy respectively.

Conclusion: Macronutrients and fat source are not significantly changing in our population but there is an imbalance of fat-sources. With longer life expectancy more emphasis is needed on re-distributing fat sources to avoid the potential for hyperlipidaemia. Larger scale studies are needed to investigate fat intakes in CF patients to guide possible new approaches and clearer advice regarding appropriate sources of fat.

***The long and the short of it*. Experiences of a paediatric multi disciplinary short gut / intestinal failure team (RIFT)**

Presented by: Mr Chris Smith, Senior Paediatric Dietitian, Nutrition and Dietetics, Royal Alexandra Children's Hospital, Brighton, East Sussex

Authors: C Smith, Ms R Hallows, Dr A Butt, Prof D Candy

Background:
Parenteral Nutrition (PN) is life saving in patients with intestinal failure however it is associated with intestinal failure liver disease (IFLD) and results in high morbidity and mortality. Prevention and treatment is not well understood but when managed in an experienced centre 90% of affected children can be expected to survive. A recent national high profile enquiry into hospital patients requiring parenteral nutrition (NCEPOD) highlighted the need for a coordinated team approach for best practice. The RACH Intestinal Failure Team (RIFT), part of the RACH nutrition team, manages paediatric patients on PN and consists of 2 paediatric gastroenterologists, a paediatric/neonatal surgeon, a paediatric gastroenterology fellow, a specialist dietitian and speech therapist and a pharmacist. Establishing this group of patients on enteral nutrition (EN) and off PN support is the priority but this can be difficult due to many factors such as reduced absorptive capacity. This can often take time and balancing the treatments for these patients can be challenging.

Aim:
To report our experiences over the last 2 years.

Method:
In-patients with intestinal failure are seen by the full team once a week to review all the aspects of care and proforma review sheets are completed. Reviews begin with a sit down discussion meetings and cover all aspects of medical and social care. This is followed by a RIFT ward round. Patients are then reviewed by smaller teams throughout the week. Once they are established on EN or home PN and discharged they are followed up regularly by the team as out patient to monitor their progress. A dietetic data base records the teams activities and a surgical database records surgical procedures on these patients. A review of these databases and the medical notes was completed to describe our experiences.

Results:
There has been an increase in work load from 2008 (n=6) to 2009 (n=10) and the team has seen an increased proportion of their time spent in the inpatient setting suggesting an increased dependency. The majority of the teams referrals come from Trevor Mann Baby Unit, a high proportion of which are from outside Brighton and Hove PCT. At referral the majority of patients are on exclusive PN and this proportion hasn't changed in the last 2 years. When comparing end of year data it suggests increasing number of patients establishing exclusive EN. The surgical activity generated by intestinal failure patients over the last year period showed 8 CV line insertions, 9 CV line removals, 9 small bowel stomas (SBS), 15 closures of SBS and 3 repeat laparotomies. This data includes procedures performed as a direct result of nutritional care and excludes initial laparotomies.

Conclusion:
Increasing valuable experience gained from managing these patients ensures best practice for this small but highly vulnerable group. Maintaining excellent communication with the patients local hospital, the addition of out reach clinics and the development of our team could enable us to discharge these patients earlier using home PN which could be of great benefit to the patient, the families and the Trust.

Development of a functional classification system of eating and drinking for children and young people with cerebral palsy to improve quality of care

Presented by: Mrs Diane Sellers, Research Fellow, Chailey Heritage Clinical Services, Chailey Heritage School, East Sussex

Children with cerebral palsy (CP) cannot use the range of physical movement available to most of us. Difficulties may occur in the development of walking, speech and hand function. The movements involved in biting, chewing and swallowing are frequently affected. Children with CP who cannot move their mouth muscles to eat and drink efficiently, are likely to have problems eating enough food to grow and to stay healthy. Some of them will have problems with frequent chest infections because particles of food or drink enter their lungs when they swallow. These difficulties continue throughout their lives.

Currently there is no agreement about how to rate the severity of a child's eating and drinking difficulty, i.e. the child's ability to move muscles to bite, chew and swallow. The words "severe", "moderate", and "mild" are all used without an agreed definition. For some researchers, a "severe" difficulty is when a child cannot feed themselves. Others have mistakenly assumed that only children with more severe general movement difficulties have problems with eating and drinking.

Other scales have already been developed to rate a child's ability to walk and move (Gross Motor Function Classification System), and to use their hands (Manual Ability Classification System). These are both extremely useful and are increasingly widely used. We are currently seeking research funding to develop an eating and drinking classification system for children with CP by consulting with parents, children and experts both nationally and internationally.

Once developed, the system will be tested to see how easily and reliably it can be used. There are many benefits to children and families within the NHS that would come from such a rating system. They include:

- Increasing awareness of the mouth movements necessary for efficient and safe eating and drinking and distinguishing them from other types of movement.
- Enabling clear and efficient communication about a child's eating and drinking skills between professionals (e.g. children can fear hospital stays because of misunderstandings that have occurred at mealtimes).
- Providing a method by which limited resources can be directed (e.g. dietitian's time) to those children with the most severe difficulties, highest risk of malnutrition and therefore the greatest need.
- Increasing awareness and thereby reducing the risks to health whenever a child eats or drinks (e.g. particles of food and drink entering the lungs whenever a child eats, choking).
- Contributing to the identification of treatment needs of children with CP (alternative feeding methods, intensive movement therapy to improve skills etc).
- Facilitating research into this area.

There are four distinct phases of the project which will take place over approximately 3 years:

- Construct a draft of the initial eating and drinking classification system.
- Discuss the draft with a group of invited experts (speech and language therapists, parents, young people with CP, nurses, paediatricians, occupational therapists etc) using Nominal Group Process until consensus is reached about the classification system.
- Extend the discussion to a wider group of experts (including parents and young people with CP) using a Delphi Group Survey with questionnaires until a pre-defined consensus has been reached.
- Conduct inter-rater reliability studies for the system, comparing the ratings of individuals' eating and drinking abilities by different speech and language therapists.

Research for Patient Benefit Funding has been secured for three years for the study.

***'Feeding is a big thing, isn't it?'* Professional Support Networks: The support needs of carers of children with cerebral palsy fed by gastrostomy tube**

Presented by: Ms Hannah Pool, Medical Student, Brighton and Sussex Medical School

Background:
Children with cerebral palsy and related neurodisabilities frequently have difficulty eating and drinking. Gastrostomy is a procedure that can ensure adequate nutritional intake and reduce the risk of aspiration and is increasingly being used for children with disabilities. Qualitative research has informed our understanding of the complex needs and decisions made by families of children requiring gastrostomy feeding but this study aimed to research the parental experiences of the support networks available to them.

Methods:
The study used purposive sampling. A qualitative phenomenological design was used with semi-structured interviews which were tape recorded. Six parents of children with cerebral palsy or an associated neurodisability were recruited through local voluntary organisations supporting those with disabilities. The interviews were transcribed and analysed used Colaizzi's method of data analysis.

Results:
The parents were generally pleased with the support services available to them, particularly community and school nursing provision. There were problems identified with the coordination of care, educational provision, knowledge of gastrostomy feeding by GPs, training for respite carers and funding for equipment, as well as a lack of detailed information giving.

Conclusions:
Clinicians should consider the improved coordination of care, the encouragement of peer support groups, the formation of an education package for professionals managing gastrostomy feeding for the first time and a resource provision for training respite carers. The research has indicated the need for a larger study of similar design and specific research into mainstream educational provision and the introduction of key workers for children with complex disabilities.

Discrimination between neonates with and without lung disease using a volumetric vest system

Presented by: Catherine Olden, Research Nurse, Royal Alexandra Children's Hospital, Brighton, East Sussex

Authors: Dr Kerstin Walter, Catherine Olden, Dr Paul Seddon

Tidal breathing parameters are a non-invasive surrogate for infant lung function measurement, but their usefulness is limited by variability and the need to apply a facemask. We have recently validated a novel volumetric vest system (FloRight) for measuring a range of tidal breathing parameters; this also allows measurement of thoraco-abdominal asynchrony (TAA). Only T_{PTEF}/T_E (time to peak tidal flow/expiratory time) has been widely studied in infants: a variety of other parameters have been proposed.

In order to assess the potential of tidal breathing parameters and TAA, measured by volumetric vest, to detect lung disease in neonates, we measured both repeatability and ability to discriminate between healthy term newborns (N) and preterm infants with bronchopulmonary dysplasia (BPD).

We collected 2 periods of tidal breathing in 10 N and 11 BPD infants during quiet sleep, and analysed two 20-breath segments of stable tidal breathing for each baby. We measured T_{PTEF}/T_E, expiratory flow at (short name and initial for each) phase angle (ϕ). Repeatability coefficient was calculated, and parameters compared between N and BPD infants.

Results:

	N	BPD	p	CR%
T_{PTEF}/T_E	48.7	26.0	0.0005*	40.8
TEF50/PTEF	88.2	79.7	0.08	20.7
TEF25/PTEF	74.8	50.5	0.0005*	38.5
T_E/T_I	102.8	137.3	0.006*	37.9
FVg	0.51	0.45	0.001*	11.5
Phi	6.5	31.2	0.016*	151.5

* significant

We found significant differences in expiratory flow parameters: T_{PTEF}/T_E, Fe75 and FVg (centre of gravity along the flow-volume curve) were significantly lower in BPD babies while Te/Ti was significantly prolonged. There was also a significant difference in the breathing phase angle (6.5° vs 31.1°, $p < 0.05$) indicating a higher degree of thoraco-abdominal asynchrony in infants with BPD.

Conclusions:

The novel volumetric vest system not only allows to distinguish between infants with and without lung disease in several tidal breathing parameters but also allows to assess functional aspects such as thoraco-abdominal asynchrony.

How consistent is bronchodilator response by Rint in preschool wheezy children?

Presented by: Mrs Liz Symes, Paediatric Research Nurse, Royal Alexandra Children's Hospital, Brighton, East Sussex

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Body: Bronchodilator response (BDR) measured by interrupter resistance (Rint) distinguishes groups of preschool children with and without asthma (Am J Respir Crit Care Med 2003;168:640-4). However, to interpret an individual BDR for clinical use it is important to know its repeatability. To assess this we studied 26 preschool children with recurrent wheeze on no regular treatment, median age 48 (range 23-66) months, on 2 visits at least 28 days apart. At each visit we measured Rint before and 15 minutes after bronchodilator. Mouth pressure transients were recorded, and data analysed if at least 5 acceptable flow interruptions were achieved. Rint was calculated from transients using standard linear back extrapolation (LBE30/70), curvilinear back-extrapolation (CBE), end-interruption pressure (EI), mean plateau pressure (MP30/70) and mean oscillation pressure (MOP). BDR at the 2 visits was compared using Bland-Altman analysis to calculate coefficient of repeatability (CR). Data were excluded if at either visit the child had a respiratory infection (5 children) or insufficient acceptable interruptions (1 child).

Results					
n=20	LBE30/70	CBE	MP30/70	EI	MOP
mean BDR (kPa/L/s)	0.15	0.07	0.20	0.20	0.06
mean BDR%	11.0	6.4	12.7	12.0	6.5
CR of BDR%	37.5	50.0	37.4	41.1	33.2
CR of BDR% (42months+) n=13	27.5	54.1	23.5	33.1	30.8

Rint BDR shows considerable inter-occasion variability in wheezy preschool children, particularly under 42 months, and this varies depending on how Rint is calculated. A single BDR measurement should be interpreted with caution.

Loop diuretic inhibition of bone lengthening; concerns for paediatric administration?

Presented by Dr Peter Bush, Senior Lecturer, School of Pharmacy and Biomolecular Sciences, University of Brighton

Introduction:
Loop diuretics (e.g. furosemide and bumetanide) are one of the most commonly prescribed drugs in children,[1] but anecdotal evidence suggested that they may cause reduced bone lengthening. A study in newborn rats appeared to confirm this, however the mechanism of limb lengthening inhibition was not found and therefore remained speculative.[2]

Bone lengthening occurs at the growth plate, a layer of specialised chondrocytes arranged into columns, situated at the ends of growing bones. An increase in these cells volume is responsible for the majority of bone lengthening.[3] The Na-K-2Cl co-transporter (NKCC) is responsible for regulatory volume increase in many cell types,[4] and may therefore drive the volume increase seen in growth plate chondrocytes. Loop diuretics specifically inhibit NKCC and consequently, may explain the short stature anecdotally reported children.

This study set out to identify if NKCC is implicated in bone lengthening using fluorescent-immunohistochemistry (FlIH) and a bone rudiment assay.

Methods:
Unless stated, materials were obtained from Invitrogen (UK). Eight Sprague-Dawley rat pups (P7) were killed by decapitation following Home Office guidelines. Tibia (n=4) and metatarsals (n=19) were dissected and underwent IH using standard techniques (T4 anti-NKCC monoclonal Ab; 1:100 and AlexaFluor488 donkey anti-mouse 1:50). NKCC associated fluorescence was imaged using confocal laser scanning microscopy (CLSM; LSM510; Carl Zeiss Ltd, UK) and localisation analysed using Zeiss Image Browser. Metatarsals were incubated in αMEM supplemented with Na glycerol-2phosphate (10mM), BSA (1mM; Sigma-Aldrich, UK), ascorbate (5mg.ml^{-1}; Sigma-Aldrich, UK), bovine calf serum (10%) at 37^{o}C for 24hrs in the presence of either bumetanide (100μM) or vehicle control (ethanol). Bone lengths were measured from images taken at 0 and 24hrs (ImageJ; NIH, US). Data were expressed as the means±sem. Comparisons were made using student's t-test with $P<0.05$ considered significant.

Results:
Quantification of Fl CLSM imaging of P7 rat proximal tibia growth plate indicated a significant ($P<0.05$; n=4) translocation of NKCC from intracellular regions to the plasma membrane of growth plate chondrocytes immediately preceding cell volume increase.
Bumetanide resulted in a significant reduction ($P<0.002$) of rat metatarsal lengthening by ~35%. To confirm the effect of bumetanide was by means of an inhibition of growth plate chondrocytes volume increase, four metatarsals were histologically examined. There was a significant reduction in the proportional height of the zone containing swelling growth plate chondrocytes from 33.8±1.57% to 22.7±0.81% ($P<0.1$).

Discussion:
The FlIH indicates that growth plate distribution and cellular localisation of NKCC is consistent with the membrane transporters involvement with cell volume increase associated bone lengthening. This was confirmed by the ability of bumetanide to reduce bone rudiment lengthening by ~35%. A reduction entirely accounted for by the decrease in the proportion of the growth plate containing expanding cells. The detrimental effect of bumetanide on bone lengthening via NKCC ought to initiate a discussion in to the efficacy of paediatric administration of loop diuretics.

References:
[1] Prandota J. *Am J Ther*. 2001;8:275–289. [2] Koo WW et al. *Pediatr Res*. 1986;20:74–78. [3] Wilsman et al. *J Orthop Res*. 1996;14:927-936 [4] Lang et al. *Physiol Rev*. 1998;78:247-306

Studies in Neonatology 2010

Presented by: Mr Robert Delacour, Paediatric Research Nurse, CIRU, Royal Sussex County Hospital, East Sussex

Neurodevelopmental follow-up of pre-term infants
Babies born before 29 weeks gestation with a birth weight less than 1000 grams are reviewed at 1 and 2 years of age for developmental assessment.

Slight delay in Clamping the Cord versus Milking of the Cord
This study looks into whether gently squeezing the blood from the cord into the babies less than 33 weeks would achieve the same amount of blood transfer into the baby as delayed clamping.

Non-invasive Lung Function Measurements in Babies on CPAP
We hope to be able to find out which CPAP device would be best for an individual baby in the future.

Opptimum
This study will determine whether, in women at high risk of preterm labour, prophylactic vaginal progesterone, 200 mg daily from 22-34 weeks gestation reduces incidence of preterm labour and improved neonatal outcomes

Joint transatlantic EU-US Project on the Neonate and the Application of the New Paediatric Medicines Legislations
The new European Paediatric Drug Regulation has come into force on 26th January 2007. The major aims of the new regulation are the reduction of unlicensed or off-label use of medicines in children and especially in neonates. In order to achieve this goal there needs to be a coordinated effort on an international level.

Nutrition, anaemia, growth and oxygen weaning in Low Birth Weight oxygen-dependent infants in a Kangaroo Clinic
This project is monitoring the nutritional status (including haemoglobin levels) of a cohort of Low Birth Weight infants discharged home with oxygen and cared for at high altitude (2600 m) in Bogota, Columbia.

Go-Child
Looking at the influence of genetic and environmental factors on childhood diseases from the antenatal period to 2 years old, with blood or saliva samples taken from the infant for genotyping at birth.

Viral Load Immunity In Congenital Cyomegalovirus Infection Study (VICC)
The clinical impact of CCMV has been widely recognised for decades but the reason that some babies become severely affected whereas others remain asymptomatic is unknown and under-researched. This study aims to address this.

EPICure 2 Follow-up study
Structured follow-up of all surviving EPICure babies of the 2006 cohort in Sussex.

Bilirubin Study
Comparison of Bilirubin measurements by laboratory with non-invasive white light spectroscopic method in preterm and term neonates.

Solid vs. breastfed
The association between the age of introduction of solid foods to breastfed infants, iron status and diet composition at ages 8 and 18 months.

Septicaemia
Evaluation of the spectroscopic method to diagnose septicaemia early and objectively using a new device called Haemospect. We aim to find if this device can objectively recognise newborns with infection.

Prechtl Movement Study
To compare the use of infant movements, cranial ultrasound and neurological examination in the prediction of motor outcome in a cohort of pre-term infants.

A case of hereditary folate malabsorption in an infant

Presented by Dr Siba Paul, Paediatric SpR, St Richard's Hospital, Chichester, West Sussex

Authors: Dr Siba Prosad Paul, Prof David Candy

Introduction:
Folic acid is one of the vital substrate for normal development of the foetus and the infant. Studies in the past have demonstrated the effect of folate deficiency on the CNS antenatally leading to spina bifida. This poster presentation highlights the importance of folate in children for cortical myelination. We describe the case of a 4 month old male infant who presented with a hereditary folate deficiency to the paediatric services and in whom the effect of the supplementary folic acid on cortical myelination was documented by serial MRI examinations.

Case Study:
DS, 4 month old male infant, previously well presented to the paediatric services with history of poor feeding and pallor. Physical examination was unremarkable and vitals were stable. Initial blood investigations revealed megaloblastic anaemia with a haemoglobin of 7.1gm/dl and a MCV of 96fL. He developed an oxygen requirement and on day 3 of presentation further results showed a folate deficient status. DS was started on IV folinic acid, however his respiratory status deteriorated and was transferred to PICU. CXR findings were indicative of PCP and Septrin® was started, later BAL confirmed PCP. He received immunoglobulins for a period of time and improved. Currently he is jointly managed with GOSH with IM folic acid. The serial MRI Brain scans showed delayed myelination pattern but currently doing well.

Discussion:
(i) HFM is pan-ethnic and inherited in autosomal recessive fashion.
(ii) SLC46A1 is the only gene known so far to be associated.
(iii) Folate may be absent in the CSF.
(iv) Clinically presents from 2 month onwards with anaemia, immune deficiency, neurologic manifestations.
(v) FBC, serum folate, Vitamin B12 level are useful initial investigations.
(vi) Transient immunodeficiency may be seen at the start of treatment.
(vii)Red cell folate and CSF folate are necessary.
(viii)Serial MRI scans necessary to demonstrate myelination pattern.
(ix) Lifelong folate replacement therapy necessary.
(x) Involvement of metabolic specialist, immunologist, gastroenterologist and developmental paediatrician is necessary.

Conclusion:
This poster highlights the importance of investigating rare causes of macrocytic anaemia in the infancy. A normal neurological and developmental outcome may be achieved by aggressive folate replacement therapy.

All in one versus two in one parenteral nutrition in extremely preterm infants ≤ 27 weeks gestation and < 1000g birthweight

Presented by: Ms Sinead Doyle, Medical Student, Brighton and Sussex Medical School

Project undertaken at the Department of Neonatology, Brighton & Sussex University Hospitals NHS Trust, under the supervision of Dr J.R. Fernandez-Alvarez, Consultant Neonatologist and Lead for Clinical Governance.

Background:
Evidence suggests standardized total parenteral nutrition (TPN) confers benefits over individualized TPN in terms of availability, nutritional intake, cost-effectiveness and maybe patient safety (e.g. infections). However, it is unclear whether all-in-one or two-compartment (lipid separate) standardised preparations are more beneficial. This study aims to specifically address this question in a group of ELBWI.

Methods:
A retrospective matched-pair cohort analysis was carried out of 25 ELBWI ≤ 27 weeks gestation, born at the Royal Sussex County Hospital, Brighton (UK), between January 2005-December 2006 and January - December 2008. The early cohort received all-in-one TPN, while the later received two-component. They were matched for gestation, birth weight, admission duration, age at initiation and duration of TPN, and additional enteral feeds. Small for gestational age infants and infants with congenital anomalies were excluded. Clinical outcomes were daily weight gain, infectious and metabolic complications, and oxygen requirement at discharge. Daily cost of treatment was also compared.

Results:
There was no statistically significant difference in daily growth, triglyceride and bilirubin levels, oxygen requirement at discharge or financial cost There was a statistically significant increase in episodes (5 [range 3-9] vs. 3 [range 1-6]; p = 0.016) and days of antibiotic treatment (33 [range 14-62] vs. 20 [range 5-51]; p = 0.017) in the all-in-one group.

Conclusion:
All-in-one TPN seems to increase the risk of infection without conferring any clinical or economic benefits. Its use in ELBWI should probably be abandoned.

Transient Pseudohypoaldosteronism due to Neonatal Urinary Tract infection

Presented by: Dr Tiraj Mendis, Consultant Paediatrician/Specialty Doctor in Paediatrics, Eastbourne District General Hospital, East Sussex

Hyponatraemia with hyperkalaemia in a neonate is a life threatening condition, often associated with aldosterone deficiency due to salt losing congenital adrenal hyperplasia. However, alternative diagnoses involving inadequate mineralocorticoid secretion or action must be considered in the differential diagnosis. We present a case of transient pseudohypoaldosteronism in a neonate secondary to urinary tract infection which is an uncommon condition.

A 17 days old male neonate was brought to casualty for poor feeding, lethargy and passing cloudy urine and then admitted to SCBU for further management. On examination he looked unwell, yet well perfused and systemic examination was unremarkable.

Urine dipsticks were positive for leukocytes and nitrites. Hence he was started on iv antibiotics after performing a full septic screen. Serum electrolytes revealed hyperkalaemia (8mmol/L) and hyponatraemia (123mmol/L), raising the possibility of congenital adrenal hyperplasia. Therefore, short synacthen test was performed and bloods were sent for androgen profile and baby was started on iv hydrocortisone and fludrocortisone pending results.

Ultrasound scan showed dilated right pelvic calyceal system and ureter filled with pus and subsequent MAG3 revealed delayed excretion. Short synacthen response was normal yet aldosterone and renin were high, 64000 pmol/L (100-800) and 240pmol/ml/h (0.5-3.1) respectively, suggestive of pseudohypoaldosteronism. Subsequent to this electrolytes normalised, steroids were stopped and discharged home with Trimethoprim prophylaxis.

Aldoesterone and renin were repeated and found to be normal. Repeat ultra sound scan done four months later too showed marked improvement with regard to pelvi calyceal and ureteric dilatation though it had not completely resolved. There was no evidence of reflux on MCUG.

This supports the idea that renal tubular resistance to aldosterone is due to urinary tract infection and the importance of considering this condition in an infant presenting with hyponatraemia and hyperkalaemia once congenital adrenal hyperplasia is excluded. This condition only requires fluid replacement, correction of electrolytes imbalance and treatment with antibiotics for urinary tract infection and looking for an underlying renal pathology.

Is massage therapy beneficial? An evaluation in two paediatric settings; cystic fibrosis and high dependency unit

Presented by: Ms Rachel Hill, Final Year Medical Student, Brighton and Sussex Medical School

Background:
In current society complementary medicine is rapidly progressing, with massage therapy being one of the most widely used alternative medicines. Due to this it has been involved in clinical trials to determine its efficacy. The effects of massage that have been demonstrated include; pain relief, decreased anxiety, improved sleep and changes to observations such as heart rate and blood pressure.
In a chronic disease setting, such as cystic fibrosis (CF), massage has been shown to have a positive outcome on the individual's anxiety levels. However, the data regarding pulmonary function is limited. In an acute setting massage can improve levels of anxiety and has been shown to reduce hospital stay.

Methods:
The study was divided into two arms:
1. Children with CF
All current CF patients aged between 5-18 years in the care of RACH were invited to take part in the study. On entrance they received 1 session or 8 weekly sessions of a 40 minute massage. Participants then completed a quality of life questionnaire before and after their first and last massage sessions. At this time objective measurements were also recorded (heart rate, blood pressure, respiratory rate, oxygen saturations and spirometry).

2. Children on the High Dependency Unit (HDU)
All eligible children on the HDU from ages 3 months -18 years were approached. On accepting they received one session in the case of long term HDU care it was possible to provide multiple sessions. Each session took 40 minutes and a quality of life questionnaire and observations were noted before and after; heart rate, blood pressure, respiratory rate, oxygen saturations, pain score and Brighton Paediatric Early Warning Score.

Results:
1. Children with CF
Results collected to date include 4 participants (M age = 12.03). The results demonstrate that a single dose of massage therapy is safe with no significant effect on the observations. The profile of mood and clinical states saw a trend towards improving mood.

2. Children on the HDU
Results collected to date include 11 participants (M age = 7.07). The results demonstrate that a single dose of massage is safe with no significant effect on the observations. An effect on the profile of mood and clinical states was seen with two factors, happy ($p=0.047$) and v. tired (0.016), significantly changing to indicate a trend towards improving mood.

Conclusion:
This study aimed to provide a service evaluation of massage therapy in two paediatric settings, children with CF and children on the HDU. From the results it has shown that in both populations a single massage has no significant effect on observations, with all observations staying within safe limits. From analysis of the profile of mood and clinical states it suggests a trend towards improving the mood in both populations following massage. Furthermore, the qualitative data demonstrates that patients find the massage enjoyable and beneficial.

These findings demonstrate that massage therapy is safe and feasible in both of paediatric settings. This study is on-going with the hope that it could be developed as part of holistic care at the Royal Alexandra Children's Hospital.

Increased albuterol use with salmeterol compared to montelukast in genetically susceptible children with asthma

Presented by: Dr Kaninika Basu, Clinical Research Fellow and Honorary SpR, Paediatrics, Royal Alexandra Children's Hospital, Brighton, East Sussex

Introduction:
Diminished efficacy of salmeterol for improving asthma control is increased in children with asthma homozygous for arginine-16(Arg16) allele of the adrenergic β_2 receptor gene (*ADRB2*). The US Food and Drug Administration have raised concerns regarding the efficacy and safety of long-term salmeterol use in patients with asthma. We investigated whether there is a genotype-specific difference in long-term asthma control with montelukast compared to salmeterol.

Methods:
In this pragmatic randomised controlled trial, 62 children with asthma, carrying Arg/Arg16 genotype and exacerbation of asthma at least once within the previous year, were randomly assigned by computer-generated randomisation sequence to receive fluticasone propionate plus oral montelukast, or salmeterol with fluticasone plus placebo. No effort was made to blind the prescribed inhaler. The primary end point was school absence, prospectively measured as individual events over the period of one year. This trial is registered with ClinicalTrials.gov, number NCT00655616.

Findings:
No significant difference was observed in school absences (p=0.097) between the treatment groups. The use of reliever medication was significantly decreased in the group receiving fluticasone propionate plus oral montelukast compared to the group receiving salmeterol with fluticasone plus placebo (p= 0.004). Self-reported symptoms were significantly improved in the group receiving fluticasone propionate plus oral montelukast compared to the group receiving salmeterol with fluticasone plus placebo (morning cough p=0.018; morning wheeze p=0.001; morning dyspnoea p=0.008; night wheeze: p=0.004; night dyspnoea: p=0.001). A significant improvement in quality of life as per the Juniper paediatric asthma quality of life questionnaire was observed in the group receiving fluticasone propionate plus oral montelukast compared to the group receiving salmeterol with fluticasone plus placebo (activity limitation score (p=0.004), symptom score (p=0.009), emotional function score (p=0.002).

Interpretation:
Montelukast, as an asthma controller added on to inhaled steroid, improved asthma symptoms and quality of life, while reducing the use of reliever medication, in comparison to salmeterol, in children with asthma homozygous for the Arg-16 mutation. A larger randomised controlled trial is required, comparing asthma control with salmeterol versus montelukast in the genotypic sub-groups in *ADRB2*, and to explore the cost-effectiveness of genotype-specific controller therapies in children with asthma.

Dopamine treatment in neonatal medicine with a focus on non-responder

Presented by: Dr Liam Mahoney, Academic F2, Acute Medicine, Royal Sussex County Hospital, Brighton, East Sussex

Background:
Haemodynamic adaptation in the first few days of life is a complex physiological process that often is disturbed in premature or sick infants. Systemic hypotension occurs in 20-50% of all infants admitted for neonatal intensive care and can have serious consequences including IVH, PVL and NEC. First line therapy involves expansion of the circulatory blood volume. If that is not sufficient, the neonate usually will be treated with inotropes. Dopamine is the most frequently used sympathomimetic amine for the treatment of hypotension in neonates. The common dosage for dopamine ranges from 3 -20 mg/kg/min. However, a significant proportion of neonates do not respond sufficiently to treatment with Dopamine.

Aim of the study:
We analyse the characteristics of dopamine-non-responders aiming to identify possible predictors of non-responsiveness to inotropes. *Materials and methods*: We analysed 95 premature and term babies born between 1/1/2008 and 31/12/2009 treated at the Trevor Mann Baby Unit, Brighton, UK who were treated with inotropes and/or steroids for systemic hypotension.

Results:
87 (91.6%) of our 95 patients received Dopamine as first line treatment. Out of these 33 infants (37.9%) received Dopamine only (classified as “Responder”, R). The remaining 54 infants (62.1%) required additional treatment with Dobutamine, Adrenaline and/or Hydrocortisone (classified as “Non-Responder”, NR). Mean gestational age in the R group was 28+4 weeks, with 6 babies (18%) being term, mean birth weight was 1304g (± 1048g) and mean duration of Dopamine-treatment was 2.9 days. In the NR group, mean gestational age was 31+5 days with 18 babies (33%) being term, mean birth weight was 1838g (± 1373g), and mean duration of Dopamine-treatment was 5.2 days. Additional hypotensive treatment in the NR group consisted of Adrenaline in 22 (40.7%), Dobutamine in 41 (75.9%) and Hydrocortisone in 23 (42,6%) babies.

Conclusion:
Dopamine is the most commonly used inotropic drug for treatment of systemic hypotension in neonates. However, only 1/3 of patients can be treated sufficiently with dopamine alone, nearly 2/3 of all patients require additional treatment with other inotropes or steroids. This is more likely in term babies of whom 75% required additional treatment than in preterm babies of whom 42.9% responded to Dopamine alone

Young GUM clinic patients: sexual health needs and care pathways

Presented by: Ms Catherine Aicken, Research Associate, Centre for Sexual Health & HIV Research, Research Department of Infection & Population Health, University College London

Authors: Ms Catherine Aicken[1], Professor Jackie Cassell[2], Dr Catherine Mercer[1]
[1] Centre for Sexual Health & HIV Research, Research Dept. of Infection & Population Health, University College London [2] Division of Primary Care and Public Health, Brighton and Sussex Medical School

Background:
Young people were identified by the National Strategy for Sexual Health and HIV and the National Chlamydia Screening Programme as a particular risk group for poor sexual health. For this reason, and as access to services may be a particular issue for the youngest patients, we examine the care pathways of genitourinary medicine (GUM) clinic attendees, comparing those aged<21 ('U21s' for brevity) with attendees aged>=21.

Methods:
As part of a broader study aiming to inform the appropriate configuration of sexual health services for local populations, we gathered patient survey data linked to clinical data, for patients aged>=14 attending four geographically and sociodemographically contrasting GUM clinics in England.

Results:
390/2203 of respondents were U21, of whom four-fifths were female. U21s were more likely to attend a GUM clinic in their PCT of residence than older patients (males: 84.1% *vs.* 53.6%; females: 80.1% *vs.* 65.9%, both $p<0.001$). One-fifth of males and one-third of female patients U21 reported previous STI diagnosis/es. Those U21 were more likely than older patients to report previous *Chlamydia* testing (males: 70.5% *vs.* 64.0%, $p=0.02$; females: 81.7% *vs.* 77.6%, $p=0.001$). There were no differences in the reasons reported for attendance (one exception: young males were more likely than older males to report attending because of referral from primary care).

Care pathways
Among patients attending for a new episode of care, there was no age difference in the proportion reporting symptoms (overall: 30.1% of males, 35.4% of females). However, among symptomatics, female U21s reported symptoms for longer than older women: medians of 14 days (IQR 21 days) *vs.* 7 days (IQR 17 days), $p<0.001$. Despite this delay, there was no evidence for delays in access once U21s sought care, as most received care the same day. Female U21s were no more likely than older women to seek care from other services first; however where they did, their care pathways were longer than for older women.

Sexual behaviour
U21s of both genders reported larger numbers of partners/past year than older patients: medians: males 4 (IQR 5) *vs.* 3 (IQR 5), $p= 0.04$; females: 2 (IQR 3) *vs.* 2 (IQR 2), $p<0.001$). U21s were also more likely to report larger numbers of *new* sexual partners/past year. Female U21s were more likely than older women to report sex since recognising the need to seek care: 50.7% *vs.* 39.9%, $p=0.002$, and with 1+ *new* partners. However, younger and older men were equally likely to have had (i) multiple partners and (ii) unprotected sex, since recognising a need to seek care.

STIs diagnosed at clinic
Female U21s were more likely to have 1+ acute STI diagnosis/es when they reached the clinic, than older women: 25.2% *vs.* 13.9%, $p<0.001$. There were no differences between younger and older male patients.

Conclusion:
U21s accessing GUM clinics form a significant minority of attendees. Given their numbers of recent sexual partners, time spent symptomatic, and the proportion having STIs diagnosed, young people need to be encouraged to seek sexual health care promptly when they have a suspected STI.

The influence of genetic and environmental factors on childhood diseases (Go-Child): process in the first year

Presented by: Ms Maureen Quin, Research Midwife, Royal Alexandra Children's Hospital, Brighton, East Sussex

Authors: Maureen Quin*, Shrabani Chakraborty*, Kaninika Basu, Ali Abd, Rebecca Allen, Robert Delacour, Somnath Mukhopadhyay.

Royal Alexandra Children's Hospital, Brighton and Sussex Medical School
**These authors contributed equally to the work*

Introduction:
Asthma, allergy and eczema are chronic conditions that affect millions of adults and children both in the UK and worldwide, and represent a major public health burden in children. The development of these conditions depend on environmental factors and certain inherited characteristics.

Early sensitisation to inhaled allergens constitutes a significant risk factor for asthma until the teenage years. This includes eosinophil response and effects of maternal smoking. The effects of polymorphic variations may be important from the pharmacogenetic perspective, and also may increase the risk of developing allergic disorders. We are exploring the natural history of atopic diseases from newborn period, and gene-environment interactions longitudinally, on a prospective basis, over a period of two years.

Method:
We are establishing a robust genotype-phenotype database and aim to maintain this database indefinitely in order to explore gene-environment interactions relevant to asthma and allergy and other childhood disease. The study was approved by the Tayside Committee on Medical Research Ethics. The pregnant mothers are approached at the antenatal clinics and an informed consent is obtained. A questionnaire regarding the child's environment, family history and clinical presentations is completed antenatally and at the first and second years of age. A dietary questionnaire is completed in the antenatal period, 3months and 9months of age. An infection and allergy questionnaire is completed at 6months of age. Cord blood is obtained at birth for genotyping. In absence of cord blood sample, saliva is collected by Oragene saliva collection kit. Currently we are recruiting from Sussex, Coventry, Tayside and Fife.

Findings:
We have recruited 1150 participants of which 800 are from Sussex, 237 from Scotland and 113from Coventry We have received 86% antenatal questionnaires back from the participants and 75% cord blood samples. 7% of recruited babies have a family history of asthma. Eczema is present in 15% fathers and 21% mothers. Allergic rhinitis was more common in mothers (38%) than fathers (12%). 20.7% of the fathers smoke while the smoking was less prevalent in mothers (7.4%).36% of the participants constituted the at risk population of children exposed to both smoking and a family history of maternal asthma. We also looked at the housing type of the participants and observed that 33% lived in a rented accommodation while 76% owned an accommodation themselves. A significant association between asthma and type of housing was observed. Amongst the participants with family history of asthma, 23% lived in a rented accommodation and 14% owned a property and the difference is significant (p=0.04).

Conclusion:
For the first time, we have created a database that will allow us understand the effect of gene-environment interactions that influence disease in childhood, thus allowing progress to future work, eventually enabling us to develop novel approaches for managing asthma, allergy among other atopic diseases in childhood. We have already recruited over half of the target within the first year. We hope to expand our study to many more sites in the UK and thus increase the variability in the cohort.

Parents perception of giving antenatal consent to include their preterm infant into a randomised controlled trial

Presented by: PD Dr Heike Rabe, Honorary Clinical Senior Lecturer, Brighton and Sussex Medical School and Consultant Neonatologist, Brighton and Sussex University Hospitals Trust

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Background:
Randomised trials have shown that a slight delay in clamping the cord enables placento-fetal transfusion, which benefits preterm infants greatly by reducing intraventricular haemorrhages and the need for blood transfusion. One ethical problem with performing such study is to obtain informed consent from parents at a time when they are very vulnerable and stressed by expecting a preterm baby.

Aim:
To evaluate parents' perception of including their unborn preterm infant < 33 weeks' gestation into a randomised trial on a slight delay in clamping the cord of 30 seconds or four times milking the cord.

Design/Method:
Prospective, single centre cohort studies. Parents, whose infants had been entered in to the randomised trial before delivery, were offered to take part in a structured interview either performed at the hospital or at home.

Methods:
Study design: Prospective single centre cohort study
Inclusion criteria: Parents, whose preterm babies were nerolled into the trial of comparing 30 seconds of cord clamping time to four times milking of the cord
Exclusion criteria: Not consenting to participate

Parents whose infants had been entered into the randomised trial before delivery (n=116), were asked to take part in a semi-structured interview either performed at the hospital or at home.
Thirty-seven parents took part in interviews:
22 females (mean age 29.9 years, range 19 - 41) and 15 males (mean age 33.12 years, range 21-46).
Results were correlated to infants CRIB scores after birth for both groups.

Analysis:
Transcripts were analysed using systematic thematic analysis and NVivo 8 software. In addition parents completed measures of current stress, anxiety and depression. Interview analysis was performed by a researcher who was blinded to the infant's allocation.

Results by identified topics:
1. Issues of recruitment
2. Reasons for participating in the trial
3. Implications of taking part
4. Professionalism of staff
5. Suggestions for improvement

Discussion:
The interviews gave us invaluable insight into parents perspectives:

- Inspite of the very difficult time before the delivery of their preterm babies, parents showed an altruistic attitude towards the study.
- The groups has similar outcomes with regard to intial adaptation after birth.
- Suggestions for improvement with regard to communications with parents have been taken up and all parents have been informed about the main outcomes of the study in writing.
- The results will help us in the design of future studies where informed consent is necessary before
- birth.

Comparison of clinical presentations of children and young adults with asthma between Scotland and Sussex

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Background:
Gene-environment interactions contributing to the development of asthma and its subsequent severity has been the focus of public health interventions during recent years. We have established a database of children and young adults with asthma across the UK to investigate the genetic markers of asthma susceptibility, severity, exacerbations, response to treatment and their interaction with environmental factors. Here we compare the clinical outcomes of asthma including exacerbations, between the two cohorts of similar number and data obtained between autumn and spring.

Methods:
A cross-sectional survey was undertaken in children and young adults with asthma (age 3-22 years) attending secondary care asthma clinics in Brighton (n=312) and Dundee (n=401)**.** Detailed clinical history was obtained including information on school absences, usage of oral steroids and hospital admissions over the previous 6months. Asthma severity and treatment stage were determined in accordance with the British Thoracic Society guidelines. Pulmonary function was measured and saliva was collected for genotyping.

Results:
In the Brighton cohort, mean patient age was 8.5years; 58.7% were boys. In the Dundee cohort, mean patient age was 8.4years;60.6% were boys. On logistic regression, asthma related school absences ($p<0.005$), hospital admissions ($p<0.005$), oral steroid intake ($p<0.005$), and total exacerbations ($p<0.005$) over the previous 6months were significantly increased in the Brighton cohort when compared to the Dundee cohort.

Conclusion:
We have characterised and compared clinical history, medication use and asthma exacerbations in two cohorts of children with asthma in two different parts of the UK. Patients attending secondary care clinics in Brighton had significantly increased asthma exacerbations in comparison to similar patients from Dundee. We need to further explore the roles of genotype, environmental variation and management policies on clinical outcomes in asthma in the two areas. This study may help to improve our understanding of the underlying mechanisms for asthma, identify at-risk populations for disease susceptibility and severity, and predict drug choice, thereby contributing to significantly improved asthma management strategies in the future.