**Research is the future, the future is……**

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**Abstract**

Over the past two decades, Professor Lenney has established the Paediatric Respiratory Department at the Royal Stoke University Hospital as a centre recognised for high quality research. A broad portfolio of clinical and laboratory based research is in progress. Four research areas are discussed that are likely to contribute to the continued academic output from the unit. These are the use of selected ion flow tube mass spectrometry for the detection of biomnarkers associated with pulmonary pathogens, the measurement of lung clearance index in preschool children, structured light plethysmography in children and the use of oral prednisolone for asthma exacerbations in children.

**Introduction**

Driven by Professor Warren Lenney, the academic output from the Paediatric Respiratory Department at the Royal Stoke University Hospital in the past 19 years has been formidable. To maintain this output in future years, the department plans to continue a broad portfolio of research. This presentation explores future research plans, focusing particularly on four established themes that Professor Lenney has been instrumental in developing. The caveat to discussing these plans is that predicting the future is challenging and any such plans are prone to tangential change, or even U-turns!

**Selected Ion Flow Tube Mass Spectrometry**

Professors Lenney and Smith have led an extensive programme of *in-vitro* and *iv-vivo* research investigating hydrogen cyanide (HCN) as a marker of Pseudomonas aeruginosa (PA) infection.1 This culminated in the SPACE study which collected regular breath samples from 233 children with cystic fibrosis (CF) over 2 years and demonstrated that HCN is a specific but not sensitive marker of early PA infection. A similar programme of research is planned with two other CF pathogens: Staphylococcus aureus (SA) and Aspergillus fumigatus (AF).

Initial in-vitro studies, using SIFT-MS have identified characteristic patterns of volatile organic compounds (VOCs) in the headspace of SA and AF cultures. High concentrations of 6 VOCs (mainly alcohols, ketones and aldehydes) were identified in the headspace of SA cultures and high concentrations of ammonia and 3 organosulphur compounds were identified above AF cultures.2 We plan to investigate how specific in-vitro factors affect the production of these VOCs. The factors that will be investigated include bacterial / fungal mass, genotype, phenotype, culture duration and culture conditions (planktonic / biofilm). The mass spectra from the initial SA and AF studies also revealed a number of compounds present at low concentrations that it was not possible to identify using SIFT-MS. We therefore plan to use Gas Chromotography Mass Spectrometry alongside SIFT-MS to allow identification of these compounds. In-vivo studies will then be undertaken to investigate if the same pattern of VOCs is seen in the breath of CF patients with chronic SA and AF infection and ultimately new SA and AF infection.

**Lung clearance index (LCI)**

Lung clearance index measured by multiple breath washout (MBW) tests has been shown to be a reproducible and a repeatable measure of ventilation inhomogeneity.3 LCI is more sensitive than standard spirometry in detecting early airways disease and demonstrating the clinical benefit of new interventions in patients with CF.4 The ease of performing MBW tests mean that unlike standard spirometry it can be performed in young children.5 The principle is based upon the washout of an inert tracer gas from the lungs, with no interference from gas exchange. There are three choices of inert gas (helium, sulphur hexafluoride and nitrogen) and various systems are available to perform MBW tests using these different gases. Irrespective of the inert gas used for the MBW test, LCI is defined as the number of volume turnovers of the lungs required to reduce the inert gas to 1/40th of its starting concentration.6 In healthy children LCI has a narrow normal range of 6 to 7 which is largely independent of age. Children with lung damage due to diseases such as CF will usually have a LCI above 7.

Using the InnocorTM Gas Analyser, The Royal Stoke University Hospital is becoming established as a centre for LCI in children. It will shortly be opening as the third centre for LCI SEARCH (Lung Clearance Index as a Sensitive measure of Early Airway Change in Cystic Fibrosis). This study aims to introduce LCI measurements into routine clinical monitoring in CF outpatient clinics and correlate LCI results with changes in infection status. In addition, a programme of research is planned in which LCI will be measured in healthy preschool as well as those with a number of respiratory illnesses.

**Structured Light Plethysmography (SLP)**

SLP is a novel, non-contact technique that measures chest and abdominal wall movement during tidal breathing. A structured light pattern (checkerboard) is projected onto the chest and abdomen and the movement of this pattern is reconstructed using stereo-photogrammetry. A number of tidal breathing parameters can be generated. In addition, breathing asymmetry and the relative contribution of the chest and abdomen can be quantified. At the Royal Stoke University Hospital SLP has been measured in 50 healthy children aged 2-16 years and in 60 children with asthma. Thirty of the children with asthma had been admitted with an acute exacerbation and thirty were attending a routine out-patient appointment and found to have reduced lung function. In all the children with asthma, SLP was measured before and after a dose of bronchodilator. Initial analysis of the data suggests the IE50 is the most useful tidal breathing parameter to distinguish between healthy and asthmatic children and to demonstrate an effect from the bronchodilator. IE50 is the ratio of inspiratory to expiratory flow at 50% of tidal volume. SLP uses movement of the thoraco-abdominal wall as this proportional to volume, and the first derivative of the movement signal as this is proportional to the flow.

**Oral Prednisolone in Acute Asthma**

Short courses of oral prednisolone are beneficial for children with acute exacerbations of asthma and are therefore included in all the relevant guidelines. Despite this there is a paucity of evidence to inform the optimal dose, course duration or formulation. Families also remain concerned about possible side effects. Working with the Pharmacy and Therapeutics department at University of Birmingham we are planning a number of studies to add to the evidence in this area. The first stage of this was national audit of prednisolone prescribing in the UK. This demonstrated that the majority of prescribers follow the British National Formulary for Children recommendations on dosage rather than those from the British Thoracic Society / Scottish Intercollegiate Guidelines Network. Despite this, we highlighted a four-fold variation in prednisolone dosages and very high usage of soluble formulations. The latter are 30 times more expensive than non-soluble tablets. Later this year we will be recruiting to a study looking at the prescription, dispensing and administration of prednisolone for children with asthma.

**Conclusions**

There is a broad portfolio of research taking place in the Paediatric Respiratory Department at the Royal Stoke University Hospital. It is hoped that the studies discussed above will enable the department to continue the high quality academic output that has been achieved in the past two decades under the guidance of Professor Lenney.

**References**

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