

# Respiratory Medicine Symposium

**Held on 4 March 2011 at the Royal College of Physicians of Edinburgh**

## DIFFICULT SLEEP PROBLEMS

**Dr Jacqueline Faccenda**, Consultant Physician, Borders General Hospital, Melrose, UK

Sleep disorders are wide and varied and whole textbooks have been written on the different classification of the diseases, one of the most common being sleep apnoea/hypopnoea syndrome, which, like many of the sleep disorders, is under-diagnosed. In the time constraints of the meeting, it is impossible to give an overview or to talk about all sleep disorders. Therefore I have decided to pick three different disorders: one which is very common but under-diagnosed; one which is less common but very debilitating; and one which is very rare but about which there is new research.

Restless leg syndrome is a common disorder and under-recognised but can be very debilitating if severe.

Narcolepsy is less common but a lifelong devastating illness, especially if it is associated with cataplexy.

Fatal familial insomnia has in recent years been recognised as one of a group of disorders called prion diseases. It has its onset in middle age and progresses to death in a relatively short period.

## TRAVELLING BY AIR WITH RESPIRATORY DISEASE

**Dr Robina Coker**, Consultant and Honorary Senior Lecturer, Respiratory Medicine, Imperial College Healthcare NHS Trust, London, UK

Nearly two billion passengers currently fly worldwide each year on commercial flights. Surveys suggest that at least 5% have health problems, and that many would welcome more medical advice before they travel. In 1998 Dr Coker and Professor Partridge conducted a nationwide survey of more than 400 British respiratory specialists to determine what advice they gave patients with lung disease planning air travel.<sup>1</sup>

Although the problem of altitude-related hypoxaemia was well recognised, there was no consensus on how to assess patients with lung disease before air travel, or indeed what criteria should be used for recommending supplementary in-flight oxygen. In the absence of clear evidence, many indicated they would welcome formal guidance. In response, the British Thoracic Society (BTS)

Air Travel Working Party, chaired by Dr Coker, published the first air travel recommendations in 2002,<sup>2</sup> and updated them in 2004.

This presentation will review the background to challenges faced by passengers with lung disease when they travel on commercial flights and will be supplemented by a short video from a 'frequent flier' with lung disease. It will briefly discuss the UK Flight Outcomes Study,<sup>3</sup> and the proposed 2011 BTS recommendations on air travel and lung disease. This latest advice will supersede earlier recommendations and addresses a wide variety of pulmonary conditions. It is expected that it will be published later this year.

### References

- 1 Coker RK, Partridge MR. Assessing the risk of hypoxia in flight: the need for more rational guidelines. *Eur Respir J* 2000; 15:128–30.
- 2 British Thoracic Society Standards of Care Committee. Managing passengers with respiratory disease planning air travel. BTS recommendations. *Thorax* 2002; 57:289–304.
- 3 Coker RK, Shiner RJ, Partridge MR. Is air travel safe for those with lung disease? *Eur Respir J* 2007; 30: 1057–63.

## MANAGING CHRONIC BREATHLESSNESS AT HOME

**Professor Scott Murray**, St Columba's Hospice Chair of Primary Palliative Care, University of Edinburgh, Edinburgh, UK

This presentation highlights two innovations that are currently being introduced throughout Scotland in primary care.

The first is the Supportive and Palliative Care Indicator Tool (SPICT) to help clinicians identify when a patient may benefit from a palliative approach.<sup>1</sup> It first asks the question 'Would you be surprised if your patient were to die in the next 6–12 months?' and if the answer is 'no' it invites you to consider adopting a palliative care approach if there is also a clinical indicator such as, in patients with chronic obstructive pulmonary disease (COPD), severe airways obstruction (forced expiratory volume in one second [FEV1] less than 30%), on long-term oxygen therapy, breathlessness at rest, or two recent admissions for an infective exacerbation of COPD.

The second current innovation in primary care is the electronic palliative care summary (ePCS), which should be started on every patient who is identified for palliative care and placed on the practice palliative care register.<sup>2</sup> This is being introduced throughout Scotland to provide

out-of-hours staff with up-to-date records of medications, decisions regarding treatment and health status of patients requiring palliative care. Automatic twice-daily updates of information from GP records to a central electronic repository are available to out-of-hours services and some hospital units. This includes information about preferred place of care and resuscitation status.

Both these interventions have great potential to aid the early identification of patients for a palliative care approach, and to assist in communication with secondary care, especially out-of-hours. This should result in fewer emergency admissions, hospital admissions and futile resuscitation attempts.

#### References

- 1 Boyd K, Murray SA. Recognising and managing key transitions in end of life care. *BMJ* 2010; 341:c5897.
- 2 The Scottish Government. *The electronic Palliative Care Summary (ePCS) – update October 2009*. Available from [http://www.palliativecareguidelines.scot.nhs.uk/documents/ePCS%20Overview%20Oct%202009%20\\_PK.pdf](http://www.palliativecareguidelines.scot.nhs.uk/documents/ePCS%20Overview%20Oct%202009%20_PK.pdf)

## NOVEL THERAPEUTIC STRATEGIES FOR LUNG CANCER

**Professor Tariq Sethi**, Professor of Respiratory Medicine, King's College, London, UK

Lung cancer is the most common fatal malignancy in the developed world. Survival rates for lung cancer have not changed significantly over the past 30 years and new approaches to treatment are urgently required. A better understanding of the molecular and cellular biology of lung cancer will lead to the identification of earlier diagnostic markers and improved therapy. This lecture will focus on non-small cell lung cancer.

A concerted effort to reduce cigarette smoking and nicotine addiction is required. However, about 20% of patients with lung cancer were never smokers, highlighting a genetic predisposition. Genetic strategies provide new methods for predicting prognosis and response to treatment. While screening has not yet impacted on survival, understanding the mechanisms by which chronic inflammatory disorders such as COPD and lung fibrosis contribute to lung cancer development help identify high-risk patients and biomarkers of early disease as well as novel targets for therapeutic intervention. Current standard therapy for lung cancer has reached a plateau and novel biological agents to target lung cancer have been developed for clinical use, particularly tyrosine kinase/epidermal growth factor inhibitors and angiogenesis inhibitors.

It may be possible, with further validation of predictive biomarkers and tumour genetic signatures, to specifically tailor treatment decisions in individual lung cancer patients. Ultimately greater understanding of the

molecular events that drive lung cancer and the genetic mutations that determine sensitivity to conventional and targeted therapies may allow lung cancer to become a chronic disease with relapses and remissions with which patients can have prolonged survival.

## ROBERT W PHILIP LECTURE: 2011 UPDATE ON PULMONARY ARTERIAL HYPERTENSION

**Professor Marc Humbert**, Professor of Respiratory Medicine and Director, INSERM, South Paris University, Clamart, France

This lecture will summarise recent advances in the field of pulmonary arterial hypertension (PAH), a severe condition characterised by a progressive remodelling of small pulmonary arteries leading to elevated pulmonary vascular resistance and right ventricular failure. Epidemiology, genetics, pathophysiology and treatment will be the main focus of this lecture.

The prevalence of PAH in Europe ranges between 15 and 52 cases per million adult inhabitants, confirming that PAH is a rare but certainly underestimated condition. In the modern management era, PAH remains a progressive, fatal disease and is a condition that is notoriously difficult to diagnose. As a result, there is commonly a substantial delay of two or more years in the diagnosis and initiation of treatment of PAH. Thus, early detection is still inadequate. Screening programmes have been implemented in systemic sclerosis (SSc), based on cardiac echo-Doppler evaluation followed by right-heart catheterisation if PAH is suspected. When compared with SSc-PAH diagnosed on a daily practice basis, SSc-PAH screening identifies milder forms of the disease, allowing earlier management and better long-term survival.

Guidelines have been published in the US and Europe, emphasising the major progresses made in the field. Among the novel strategies, combination therapy using drugs with different mechanisms of action to maximise clinical benefit is an accepted option in PAH. Nevertheless, novel therapies have to be developed in order to improve outcomes and survival in PAH patients. Safety and efficacy of novel agents such as tyrosine kinase inhibitors are currently being evaluated in multicentre randomised trials.

## ASTHMA: HOW MIGHT TODAY'S RESEARCH INFLUENCE FUTURE CLINICAL MANAGEMENT?

**Professor Neil Thomson**, Professor of Respiratory Medicine, University of Glasgow, Glasgow, UK

Despite instituting guideline recommendations for the management of asthma, a considerable proportion of patients have poorly controlled disease. Systematic evaluation should be undertaken to identify patients with refractory or treatment-resistant asthma from those with 'difficult to treat' asthma due to poor adherence, persistent allergen exposure, untreated co-morbidities, dysfunctional breathing or psychological problems.

Non-invasive biomarkers of airway inflammation may be of value in diagnosis, monitoring disease activity and predicting response to an intervention. Several biomarkers are under assessment using measurements made from induced sputum samples, exhaled nitric oxide and the electronic nose, as well as blood and urine samples.

Corticosteroids are the most effective treatment for asthma, although the therapeutic response varies considerably between individuals due to genetic, environmental and demographic factors. A better understanding of the mechanisms of corticosteroid resistance should lead to the development of drugs that restore corticosteroid sensitivity and/or reduce inflammatory processes in the lungs that are insensitive to corticosteroids.

Anti-immunoglobulin E (Anti-IgE) therapy is the only novel drug licensed for the treatment of asthma in the past ten years. Biological agents directed at blocking the effects of pro-inflammatory cytokines such as interleukin-5 and interleukin-13 as well anti-inflammatory cytokines such as interferon- $\beta$  are under development and these may prove useful for treating refractory asthma. Bronchial thermoplasty to the airways is a new treatment technique that involves the delivery of radio frequency energy to the airways with the aim of reducing airway smooth muscle mass and responsiveness in asthma. Clinical trials have shown that bronchial thermoplasty improves asthma control in patients with severe asthma.

### References

- 1 Bel E, Sousa A, Fleming L et al. Diagnosis and definition of severe refractory asthma: an international consensus statement from the Innovative Medicine Initiative (IMI). *Thorax* 2010 [Epub ahead of print]. Available from <http://thorax.bmj.com/content/early/2010/11/23/thx.2010.153643.full.pdf>
- 2 Spears M, Thomson NC. Factors influencing individual variability to the therapeutic response to corticosteroids. *Cur Res Med Reviews* 2006; 2:197–209.
- 3 Castro M, Rubin AS, Laviolette M et al. Effectiveness and safety of bronchial thermoplasty in the treatment of severe asthma: a multicenter, randomized, double-blind, sham-controlled clinical trial. *Am J Respir Crit Care Med* 2010; 181:116–24.

## GRANULOCYTE TRAFFICKING IN THE LUNG – NEW IN VIVO HUMAN DATA

**Professor Edwin Chilvers**, Professor of Respiratory Medicine, University of Cambridge School of Clinical Medicine, Cambridge, UK

Establishing the physiological transit time of neutrophils across the pulmonary circulation has been a source of much controversy, yet is of fundamental importance to our understanding of neutrophil-mediated lung diseases. It is widely believed that neutrophils transit the lung much more slowly than red cells, resulting in physiological pooling of these cells, as occurs in the spleen. The slow physiological transit of neutrophils has been attributed to their reduced deformability and hence difficulty negotiating the narrow and complex lattice of pulmonary capillaries. Mean transit times of 1–4 seconds have been proposed for red cells, while estimates for neutrophils range from 20 seconds to several minutes. However, previous transit data have almost certainly been compromised through inadvertent neutrophil injury sustained during cell purification and labelling, which results in major alterations in neutrophil behaviour when re-injected.

This talk will present new data where we have studied the pulmonary transit of bolus injected <sup>111</sup>Indium or <sup>99m</sup>Techetium labelled autologous neutrophils in healthy adult human subjects using two independent methods, namely (i) rapid sequence radio-isotope imaging of the lungs and (ii) a novel arterial outflow detection technique; these studies suggest that the size of any lung granulocyte pool has been overestimated. In addition, we provide the first evidence that neutrophil priming alters dramatically the pulmonary transit of these cells in man and that depriming of neutrophils is an in vivo phenomenon. Finally, whole body counting and single photon emission computed tomography have been used to allow us to determine neutrophil migration specifically to the lungs of patients with COPD and quantify neutrophil loss from the airways.

## VENTILATORY SUPPORT IN THE ACUTE MEDICAL ADMISSION UNIT

**Dr Mark Elliott**, Consultant Physician, St James' University Hospital, Leeds, UK

Non-invasive ventilation (NIV) is well established as a treatment for acidotic exacerbations of COPD, with a meta-analysis showing better survival, more rapid improvements in physiology and a reduction in complication rate and hospital length of stay.

Initial studies were performed in intensive care units but a large multicentre trial from the UK showed that NIV could be delivered, with benefit, on general wards.

Outcome in patients with a pH < 7.3 was less good suggesting that more individually tailored ventilation, perhaps in a high dependency setting would be more appropriate. Most randomised controlled trials (RCT) excluded patients who were deemed to require intubation however an RCT from Italy comparing NIV head-to-head with intubation showed that the former was no worse, and that if it could be implemented, there were advantages in both the short and the longer term. These data suggest that in most cases there is little to be lost, and much to be gained, by a trial of NIV in the vast majority of patients with COPD, deemed to require ventilatory support.

However, a recent UK national audit yielded disturbing results. A significant proportion of patients for whom there is the best evidence base for NIV did not receive it and in those that did the outcome was worse than for patients with a similar degree of acidosis who did not receive ventilatory support. These data represent a significant challenge to the UK respiratory community.

Acute cardiogenic pulmonary oedema is another common reason for presentation to the acute medical unit. A number of meta-analyses showed that positive pressure ventilation is effective in reducing the need for intubation with continuous positive airway pressure (CPAP) probably being the preferred option. However, a large UK multicentre study, including more patients than all the other trials that contributed to the meta-analyses put together, did not show a survival advantage to positive pressure ventilation. It did, however, show that NIV was safe and there was more rapid physiological improvement and importantly quicker resolution of dyspnoea, which was very severe initially.

Most, but not all, patients with respiratory failure presenting to the acute medical admissions unit will be very dyspnoeic; they may be in a life-threatening

respiratory failure with little evidence of respiratory distress. There should be a high index of suspicion in patients with severe chest wall deformity or neuromuscular disease. Obese patients in respiratory failure present a particular problem. Again, there should be a high index of suspicion, particularly when there is significant oedema. There are no RCTs, but NIV has been shown to have a significant role. Particular attention should be paid to control of upper airway obstruction during sleep as there is a high prevalence of obstructive sleep apnoea. Obese patients with respiratory failure have a poor prognosis and all hypercapnic patients should be evaluated by a respiratory physician. For those who require ventilatory support their needs can change over time with a significant proportion who use bilevel ventilation initially being managed with CPAP once stable.

### **CURRENT MANAGEMENT OF PARAPNEUMONIC EFFUSION/EMPYEMA**

*Dr Mohammed Munavvar*, Clinical Director and Consultant Chest Physician, Lancashire Teaching Hospitals NHS Trust, Lancashire, UK

No abstract submitted. See handout.

### **CHEST RADIOLOGY IN ACUTE MEDICAL ADMISSIONS**

*Dr Sylvia Worthy*, Consultant Thoracic Radiologist, Newcastle upon Tyne Hospitals Foundation Trust, Newcastle upon Tyne, UK

The presentation will cover the radiographic appearance of several common medical emergency presentations, particularly focusing on the causes of a 'whiteout' of one hemithorax with demonstration of the key radiological features which enable accurate diagnosis.