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European Respiratory Society

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The mission of the European Respiratory Society (ERS) is to advance respiratory medicine by stimulating and coordinating the actions of its members, in order to achieve the highest possible medical, paramedical and social standards in the treatment of respiratory disease in Europe. The society's 2005 congress had approximately 16 000 registered participants from 100 countries and with over 110 scientific and clinical sessions, the congress was Europe's largest annual scientific gathering in respiratory medicine.

1. All Governments Must Give More Funding to Lung Health

Respiratory disease is the third leading cause of death globally. Despite a rising burden of lung disease in Europe, the recent European Commission proposal for its next research programme[1] does not include lung diseases in its major disease funding category.

A recent ERS report estimated that the cost of lung disease in the European economy is 102 billion euro per year, largely because of the long-term treatment and support needed for patients with chronic lung disease. President of the ERS Professor Ronald Dahl commented that "rates of lung disease are rising throughout Europe and lives are being lost due to underfunding, while governments refuse to recognise the scale of the problem."

2. Stopping Smoking Benefits Everyone

At the end of 2004, the Irish republic made a revolutionary decision to implement a workplace smoking ban. The doomsayers predicted that the hospitality industry would suffer and many bars and restaurants would be forced to close because customers would refuse to visit nonsmoking establishments. However, over time customers have accepted the nonsmoking rule and are again going to these establishments.

Equally important, an Irish research team[1,2] demonstrated that 1 year after the smoking ban, there is a significant reduction in indoor particle level, indicating that the air inside these establishments is much cleaner. Additionally, lung function tests have shown that the lung health of service industry workers, both nonsmokers and ex-smokers, has already improved significantly. In contrast, the lung function of smokers continues to decline. Thus, the ground-breaking decision of the Irish republic has led to improved lung health in its citizens.

A Norwegian research team[3] reported similar results 5 months after the smoking ban in Norway. Service industry workers have experienced a significant decrease in respiratory symptoms, including morning cough, daytime cough, phlegm cough, and dyspnoea.

A Dutch research team[4] reported the results of a 25-year follow-up of smokers. It is well known that cigarette smoking is the most important risk factor for developing chronic obstructive pulmonary disease (COPD). Therefore, smoking cessation is regarded as the best preventive measure. The risk (odds ratio) of COPD development for smokers between the age of 50 and 60 years was 1.94 and 2.12 for smokers aged over 60 years. The researchers stated that to reduce COPD incidence, the greatest effort should be put into smoking cessation programmes.

German investigators[5] reported results from a large (n = 2936) prospective cohort study studying smoking and the incidence of asthma during adolescence. The study population was assessed as 9- to 11-year-olds in 1995–1996 and followed up in 2002–2003. Analysis showed that active smokers had a 2.6-fold increased risk of developing asthma in comparison with never-

1 The Seventh Framework Programme (2007–2013) of the European Commission for research, technological development and demonstration activities.

smokers. The authors concluded that active smoking is an important risk factor for developing asthma during adolescence.

As time goes on, there is increasing evidence to show that stopping smoking benefits both the smoker and people in the surrounding area. If people remain healthy, insurance schemes have fewer bills to pay, and the reduction in costs due to smoking will reduce insurance premiums for everyone.

Participants in the congress invited all governments to ban smoking in all public areas including trains, buses, bars, restaurants, offices and factories. Furthermore, governments should support extensive programmes to encourage and assist the cessation of smoking. Governments should be willing to cooperate with existing programmes that focus on smoking cessation.

3. Severe Persistent Allergic Asthma

Asthma is a chronic inflammatory disorder of the airways and is characterised by recurrent episodes of wheezing, coughing, and breathing difficulties. Currently, an estimated 300 million people worldwide have asthma and by 2025 that number is forecast to rise to 400 million. Of that number, approximately 18–25% have severe asthma that is inadequately controlled by currently available therapies. Severe asthma leads to increased hospitalisation, healthcare utilisation and death. There is a clear unmet need for an effective and safe treatment for inadequately controlled, severe, persistent asthma.

It is believed that a high proportion of asthma cases are triggered by allergens. In 1967, scientists discovered the immunoglobulin known as IgE. Later, scientists determined that IgE plays a central role in asthma, since IgE is responsible for initiating the cascade of inflammatory symptoms, such as airway constriction and shortness of breath. Based on these findings, scientists felt that IgE was a novel target for the development of new therapeutic agents. It is now possible to intervene early and interrupt the allergic cascade by targeting the IgE antibody.

Omalizumab was a first-in-class, recombinant humanised monoclonal antibody that binds to IgE antibodies, preventing the onset of the allergic inflammatory cascade. In addition to blocking the action of IgE, omalizumab has been shown to have an anti-inflammatory effect, which benefits the asthma patient.

In previous studies, omalizumab improved control of severe allergic asthma during a 32-week core study and a 96-week extension phase. At the ERS congress, Chung et al.[6] reported results on long-term control in a further 52-week, open-label extension of the clinical trial evaluating omalizumab. Thus, patients completing the second extension had been taking omalizumab for 3 years. The study showed that omalizumab is both effective and safe. There was a persistent therapeutic effect in the current extension. The increases in forced expiratory volume at 1 second (FEV_1) from baseline seen in Extension 1 were maintained in Extension 2, indicating that lung function improved. The improvement was accompanied by sustained decreases in inhaled corticosteroid use. The study demonstrated that long-term use of omalizumab resulted in continued excellent or good asthma control, based on the physician's assessment.

Severe persistent allergic asthma impacts on patient quality of life. The physical, emotional and social aspects of the patients lives are seriously impaired. A meta-analysis[7] of six controlled clinical trials in patients with severe persistent allergic asthma showed that omalizumab significantly improves quality of life.

The dose of omalizumab should be adjusted for each individual based on bodyweight and their baseline total IgE concentration. In the study, the drug is given every 2 or 4 weeks as a subcutaneous injection. Professor Stephen Holgate from the University of Southampton, UK, stated that omalizumab addressed an unmet need in respiratory disease.

Omalizumab was launched in the US in July 2003 and since then it has been prescribed to more than 45 000 patients. In July 2005, the EU's Committee for Medicinal Products for Human Use (CHMP) gave a positive opinion on initial marketing authorisation for omalizumab.

4. Ongoing Threats from New Respiratory Infectious Agents

4.1 SARS Still a Concern

Specialists in lung disease and infectious diseases will remember 2003 as the year of the severe acute respiratory syndrome (SARS) epidemic. Unfortunately, the scientist who identified the causative agent died from SARS. At the time, SARS produced panic in the healthcare system and overwhelmed hospitals, it severely affected international trade, and it depressed the economy of many countries.

Today SARS remains a major health threat; recent cases in Singapore, Taiwan and China show that the risk continues to exist. Thus, it is necessary to maintain vigilance to detect new cases. The control of SARS requires early diagnosis and prompt isolation of all suspected cases because a single case could result in massive outbreaks. Diagnostic criteria proposed by the World Health Organization rely on microbiological testing for the presence of the specific anti-SARS-CoV immunoglobulin. Unfortunately, the presence of anti-SARS-CoV immunoglobulin

Table I. Results for the prediction rule

Parameter	Value (%)
Sensitivity to positively identify a SARS patient	97.7
Specificity to positively identify a SARS patient	81.3
Positive predictive value	47.8
Negative predictive value	99.5

usually occurs 10 days after symptom onset and most laboratories require 2 to 3 days to conduct the required analysis.

Scientists from Hong Kong have developed a prediction rule for the clinical diagnosis of SARS. The prediction rule will help clinicians in the initial diagnosis and management of potential SARS patients (table I).[8] The authors state that the prediction rule appears to be helpful in assessing suspected patients with SARS at the bedside and should be further validated in other SARS cohorts.

4.2 The Threat of 'Bird Flu'

During the past century, three pandemic outbreaks of influenza have killed more than 50 million people worldwide. Since 1997, we know that avian influenza viruses of different subtypes can be transmitted to humans directly, causing both disease and death.

Professor Albert Osterhaus from Erasmus Medical Centre, The Netherlands, warned that an early warning system and 'pandemic preparedness plans' must be developed so that governments can be ready for the emergence of a new pandemic virus. The question is not 'Will it happen?', but 'When will it happen?'

5. Improved Inhaler for Asthma and COPD

Studies have shown that many patients with asthma and COPD do not use their metered dose inhalers (MDI) correctly. One of the major problems of this method of delivery is the need to exactly coordinate actuation and inhalation.

Respimat® Soft Mist™ [2] is an improved inhaler that is actuated using the dose-release button in combination with a slow, deep inspiration. Additionally, the Soft Mist™ lasts approximately 4–10 times longer than conventional MDIs, which means that a patient using Respimat® Soft Mist™ does not need to be as coordinated when using a conventional MDI.

Kardos et al.[9] undertook an observational postmarketing cohort study in 4602 patients (mean age 57 years) with asthma, COPD, or both, who received add-on therapy with Berodual® Respimat® (ipratropium bromide/fenoterol) via the Soft Mist™ Inhaler. The investigators evaluated efficacy, tolerability and handling of the Berodual® Respimat® inhaler in a 4-week multicentre study conducted in 1506 general practices. Berodual® Respimat® improved dyspnoea in 83% of patients with asthma and 77% of patients with COPD, and reduced night-time waking in 64% and 60% of asthma and COPD patients, respectively (table II). Adverse events were reported by 0.8% of patients (n = 37).

At the end of the study, 94.4% of participants continued therapy with Berodual® Respimat®. Thus, this study demonstrated that asthma and COPD patients found this new soft mist inhaler effective and easy to use.

6. Can Patients Manage Their Asthma by Themselves?

The INSPIRE (International Asthma Patient Insight Research)[10,11] study is a global evaluation of asthma patients' perceptions. One objective was to assess asthma variability and its impact on management and patient attitudes to treatment. INSPIRE is the first study to highlight patient readiness for adjustable treatment. It shows that patients may be able to manage their own asthma by recognising and acting on the warning signs that occur prior to their asthma worsening.

One objective of INSPIRE was to assess asthma control and medication use. The organisers wanted to test the concept of warning time for asthma patients. The study was designed to answer the following questions:

- Do patients receive a warning?
- Do patients recognise the warning?
- Do patients know what to do when they receive the warning?

In the UK, previous studies have shown that 90% of patients say that their asthma is under control; however, 74% of these patients also say that they use rescue therapy daily. In INSPIRE, extensive telephone interviews were conducted with 1921 adults with moderate to severe asthma in 8 European Union countries.

Table II. The results at the end of 4 weeks of treatment from the Kardos et al.[9] observational postmarketing cohort study

Rated as good or very good	Patients (%)	General practitioners (%)
Overall efficacy	91	94
Tolerability	96.5	97.8
Handling	≥88[a]	≥88[a]
Ease of inhalation	≥90[a]	≥90[a]

a All types of patients, i.e. asthma, COPD or both, and physicians handling those patients.

2 The use of trade names is for product identification purposes only and does not imply endorsement.

Table III. Results from the INSPIRE (International Asthma Patient Insight Research) study telephone interviews in 1921 adults with asthma using inhaled corticosteroids

Level of disease control	Patients (%)	Exacerbations per year (average)
Well controlled	32	7
Not well controlled	21	7
Uncontrolled	47	14

A total of 66% of patients used a long-acting β_2-agonist, either in combination (51%) or with a separate inhaler (15%). All patients used inhaled corticosteroids (table III).

Overall, 47% of patients had at least one asthma exacerbation requiring medical intervention in the last year. Despite regular prescribed maintenance treatment, 68% of asthma patients were not well controlled. Even more shocking is that even well-controlled patients had an average of 7 exacerbations per year.

Many patients (88%) were very confident that they could self-manage their asthma without physician visits and 61% recognised the early warning signs of an exacerbation. The mean period from the early signs to the peak symptoms of an exacerbation was 5.7 days. Furthermore, the mean time to recovery was 5.6 days. The most common response to signs of an exacerbation was to increase short-acting β_2-agonist use. Inhaled corticosteroid use was increased only when the exacerbation reached its peak and patients increased the inhaled corticosteroid to a lesser extent than the short-acting β_2-agonist.

Professor Martyn Partridge from the Imperial College and Charing Cross Hospital, UK, discussed the fact that during an episode of worsening asthma symptoms, patients initially increase their airway opening reliever therapy and only increased their anti-inflammatory preventer treatments relatively late into the exacerbation.[11] While patients adjust their treatment during exacerbations, they adjust the wrong one. Professor Partridge emphasised that patients do not increase their inhaled corticosteroid sufficiently and they increase their inhaled corticosteroid relatively late into the exacerbation. He stressed that all of the published evidence shows that a prompt increase in both types of treatment is most likely to prevent the deterioration of asthma control and the need for unplanned healthcare.

The time from early warning to peak worsening offers a 6-day window of opportunity to assist the asthma patient. Professor Partridge stressed that potential advances in future treatment strategies would probably result from using the current effective treatments in a 'smarter' way. Patients must be taught to use their preventive treatment earlier. Education is the key since patients must be taught the methods and given the tools so they are able to effectively manage their own asthma. The healthcare profession has a responsibility to teach patients how to live better with asthma.

Often asthma is chronic rather than acute. Therefore, education must be a continuous process. In Finland and Norway, the governments are involved in the education of asthma patients; there is a good cost/benefit ratio for the healthcare system for this effort.

Acknowledgements

Dr Kitler is a consultant at Associates for Business and Research (ABR), which specialises in all issues relating to the pharmaceutical and biotechnology industry. She can be contacted at fredfifijdk@yahoo.com; phone +41 21 824 1419.

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