OBITUARY

Frederick E Hargreave

Frederick (Freddy) E Hargreave died unexpectedly on June 15, 2011. He was born in Hong Kong and completed his medical school training at the University of Leeds (Leeds, United Kingdom). After completing his initial clinical training, Freddy moved to London in 1964 to work as a house officer in respiratory medicine with Dr EJ Moran Campbell at the Hammersmith Hospital. Shortly afterward, he began his research training with Professor Jack Pepys at the Brompton Hospital. During this time, Freddy described a new clinical entity, "Bird fancier's lung disease" – a type of allergic alveolitis caused by the inhalation of bird antigens (1).

Freddy Hargreave joined the Department of Medicine at McMaster University (Hamilton, Ontario) in 1969, at the behest of Norman Jones (who was the first Division Director for Respiratory Medicine). He was based at the Firestone Institute for Respiratory Health (Hamilton), where he spent his entire career. Shortly after arriving in Hamilton, he started what was to become a lifelong collaboration and close friendship with Dr Jerry Dolovich, and their focus turned to understanding the mechanisms of, and the treatment of asthma. Within 10 years, the studies led by Freddy Hargreave had changed the way that asthma was diagnosed, and had paved the way to future studies that have revolutionized its treatment. In particular, Dr Don Cocker (who was Freddy's first clinical fellow) described the methodology for the measurement of airway hyper-responsiveness in asthma. Together, they demonstrated that this was a crucial component of the disease and present in all patients who had current symptoms. They also showed that the degree of airway hyper-responsiveness was related to the amount of treatment needed to manage asthma. The article describing this methodology is a citation classic, having been cited almost 1800 times (2).

In the early 1980s, the importance of persistent airway inflammation in the pathogenesis of asthma became apparent. The type of inflammatory response differed from patient to patient, and was difficult to measure because it required fiberoptic bronchoscopy and could not be performed routinely. The brilliance of Freddy Hargreave's research was that it was always focused at directly solving patient-related issues, and he recognized that the noninvasive measurement of airway inflammation was a critical step in the evaluation and treatment of patients with difficult-to-treat asthma. In 1989, this resulted in the development of the methodology for sputum induction and measurement of inflammatory cells in sputum (3). Almost immediately, this resulted in the identification of a new syndrome – persistent eosinophilic airway inflammation in the absence of asthma (4) – which accounts for approximately 20% of patient referrals with chronic persistent cough to respiratory clinics.

The methods that the Hargreave laboratory developed for sputum induction and processing are now considered the gold standard, and used as research tools in all laboratories that conduct clinical research in asthma. Moreover, based on extensive experience measuring sputum inflammatory cells in the clinical setting, Freddy became convinced of its added value in the everyday management of difficult-to-control asthma. Clinical trials comparing standard guideline-directed management of asthma with a management scheme that added the routine measurement of induced sputum showed a dramatic advantage of adding the sputum analysis in reducing the risks of severe asthma exacerbations, and also in determining the appropriate doses of inhaled and/or oral corticosteroids to manage these patients (5). In addition, using induced sputum allowed the identification of a group of patients (about 50% of those with difficult-to-treat asthma), who greatly benefit from the use of a monoclonal antibody directed against interleukin-5 (6). Some, but not all, tertiary level asthma clinics worldwide have embraced this methodology based on this evidence. Freddy's driving ambition, until his untimely death, was to extend the use of this method to benefit patients. His contribution to asthma care worldwide has been recognized by several honorary lectureships and an honorary degree from the University of Modena (Modena, Italy) in 2010.

Freddy Hargreave's brilliance as a clinical scientist was only eclipsed by his skills as a mentor. Almost all of the research leaders in asthma in Canada have trained at his laboratory at the Firestone Institute, and his previous fellows are research leaders in more than 20 countries. His honesty, integrity and precision in research were legendary, and he tried to impart these qualities to all of the trainees who flocked to train with him from all parts of the world. In addition to making landmark advancements in the diagnosis and treatment of asthma and other obstructive airway diseases, he mentored his trainees to being physicians first, and researchers and scientists secondarily. His research was entirely driven by the clinical needs of his patients and epitomized translational research. All of his many important discoveries led directly to the improved health of his patients. He rejoiced, not from his more than 300 publications in high-impact journals, but from the recognition of his grateful patients and the successes of his trainees.

McMaster University, the city of Hamilton, the Canadian respiratory community and the international scientific community have lost an extraordinary physician, humanitarian and clinician scientist. His untimely demise has deprived physicians and scientists across the world of a trusted colleague, friend and mentor. His wife, Alix, his children Clare, Erica and Peter, and his grandchildren have lost a devoted husband, a loving and caring father and an affectionate grandfather. Despite his world class accomplishments, he did not care for titles, accolades or his own advancement. To his patients, he was not Dr Hargreave, but Freddy – the doctor and friend who wore shorts, sandals and knee high socks, even in the depth of winter. There never has been – and probably never will be – a physician whose telephone line and home were always open to anyone in need. He cared genuinely and, in everything he did, he brought a level of decency that so many overlook.

Albert Einstein's tribute to Gandhi, "Generations to come will scarce believe that such a one as this ever in flesh and blood walked upon this earth" could easily describe the life and contributions of Professor Freddy Hargreave.

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REFERENCES
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