HISTORY OF THE MEAKINS-CHRISTIE LABORATORIES

Peter T. Macklem

The first quarter of the twentieth century marks the beginning of the history of the Meakins-Christie Laboratories for Respiratory Research. Shortly before his death in 1919, Sir William Osler, then Regius Professor of Medicine at Oxford University, the world's most renowned physician and McGill University's most distinguished graduate, wrote to the dean of the faculty of medicine recommending that McGill appoint a full-time chairman of the Department of Medicine who would establish research in the hospital as an essential part of academic medical activities. Until that time the teachers at McGill's medical school were all part-time physicians who had private practices outside the teaching hospitals.

It took the dean some time to act on Sir William's recommendation, but in 1924 Dr. Jonathan Meakins arrived from the University of Edinburgh to take up his appointment as physician-in-chief of the Royal Victoria Hospital (RVH) and the first full-time chairman of medicine in Canada. Dr. Meakins more than fulfilled his mandate to establish clinical research at the RVH. He wrested control of clinical laboratory services away from the Department of Pathology, so the clinical biochemistry and hematology laboratories became part of the Department of Medicine and provided the department with an extremely valuable research infrastructure. This extraordinary accomplishment made the RVH almost unique in the world. Traditionally, clinical laboratory services are supplied by clinical pathologists, but at the RVH they are supplied by internists. Although this organizational structure has frustrated hospital administrators, it is directly responsible for the tradition of hospital-based clinical research that has made the RVH such a renowned academic institution. Meakins' efforts to develop research in the RVH did not stop at biochemistry and hematology. In the early 1930s he recruited Ronald Christie for a postdoctoral fellowship at the RVH. Together they published a series of classic papers dealing with the mechanics of breathing in emphysema and mitral stenosis and with blood gas abnormalities in pulmonary edema.[1–3]

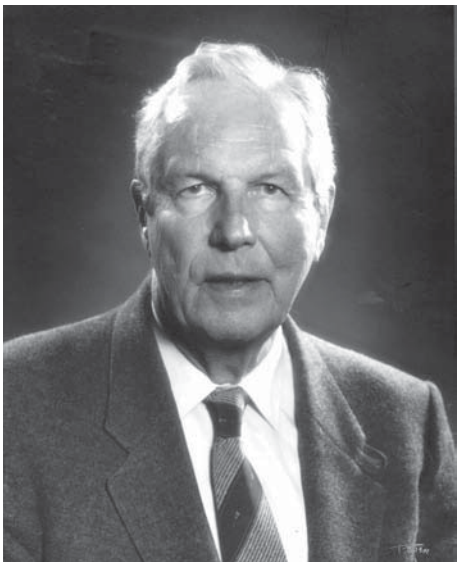
Dr. Jonathan Meakins

After 7 years in Montreal, Christie returned to England to take up an academic position at St. Bartholomew's Hospital Medical School, where he rose to the rank of professor and chairman. In the meantime, the Department of Medicine at the RVH had fallen into disarray with the appointment of one individual as physician-in-chief and another as departmental chairman. These two individuals did not see eye-to-eye on any issue, and the department was tainted by acrimony. An interim departmental head was chosen, while a search committee was established by the hospital's board of directors to find a permanent solution. The solution turned out to be Ronald Christie.

Christie had visited McGill at the request of the search committee and had been offered the job. He returned to London confident that the offer would be withdrawn because of the almost impossible conditions he had put on his acceptance, including a whole new wing for the Department of Medicine to match the one recently built for the Department of Surgery. He was therefore surprised to see Mr. David Muir, president of the Bank of Montreal and chairman of the RVH board, waiting outside his office in London one day. All of his conditions had been agreed to, and Christie accepted the job.

Ronald Christie returned to Montreal as physician-in-chief of the RVH and chairman of the McGill Department of Medicine in 1955, when I was a final year medical student. Shortly after he arrived, he gave a professional lecture to the faculty. Not many people can recall the details of a lecture delivered 50 years previously, but I remember Christie's well.

Dr. Ronald Christie



Dr. Peter Paré

He talked about lung compliance and resistance and how the two combined made up the work of ventilating the lung. He showed how these parameters changed systematically with changes in tidal volume and breathing frequency. He showed that in diseases affecting the mechanical properties of the lung, there was a particular tidal volume and frequency for a given minute ventilation that resulted in minimal work, and this was the breathing pattern.

I was entranced. While I understood diseases of other systems, I totally lacked a cohesive framework to understand diseases of the respiratory system. Although I had been taught about complemental air and supplemental air, these terms were never talked about during my clinical years, and classification of lung diseases into obstructive and resistive abnormalities was still in the future. Finally, someone had constructed a framework in which I could begin to understand respiratory function in disease.

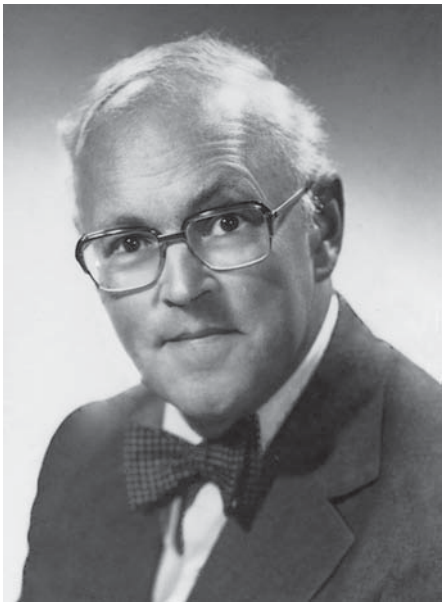
In retrospect, this lecture was to have an enormous influence on my future. It took some years before I chose to pursue the challenge of respirology, but there is no doubt that Christie's lecture engendered my interest in this field.

When Christie arrived in 1955, there was already a strong infrastructure in place at the RVH. Peter Paré was a young internist who had specialized in respiratory medicine and who had recently joined the attending staff. Darrell "Dag" Munro was an outstanding thoracic surgeon, and Bob Fraser was a young star of the radiology department.

Christie brought Dr. David Bates with him. In 1956 and he appointed him director of the newly created respiratory division. Bates and Christie went on to do an extraordinary job of recruiting: Maurice McGregor and his wife Margaret Becklake, from South Africa; William "Whitey" Thurlbeck, another South African pathologist, who was on the staff of the Massachusetts General Hospital; and Joseph Milic-Emili, from the Harvard School of Public Health. Nick Anthonisen, who came from the United States for residency training, stayed and joined the faculty. Charlie Bryan came from the RCAF to do his PhD degree under Bates. All of these people were to become world leaders in their respective fields.

Bates and Christie wrote *Respiratory Function in Disease*, which became a medical best seller. The title is a tribute to Meakins and Davies, who wrote a book of the same name in the 1920s, of which I have a copy, a treasured gift from Dr. Christie when the Meakins-Christie Laboratories opened. David Bates and Maurice McGregor formed the joint cardiorespiratory service of the RVH and the Montreal Children's Hospital (MCH). Margaret Becklake established excellence in respiratory epidemiology at McGill, a legacy that persists today and to which she is contributing as much as ever. Milic is world renowned for his contributions to respiratory physiology, particularly for his groundbreaking work on regional lung function using xenon 133 and his studies on the control of breathing. Thurlbeck established McGill as one of the leading centers of respiratory pathology and lung morphometry. Nick Anthonisen, a renowned physician, physiologist, and epidemiologist, went on to become dean of medicine at the University of Manitoba, and Charlie Bryan made many contributions to pediatric respirology, including the introduction of high-frequency oscillatory ventilation for the treatment of acute respiratory distress syndrome of infancy. Those who were already in place also made extraordinary contributions. Bob Fraser became the world's leading pulmonary radiologist. Peter Paré was renowned for his excellence as a clinician and teacher. He has been responsible for inspiring and instilling clinical excellence in a vast number of respirologists in Canada and around the world. Fraser and Pare wrote *Diagnosis of Diseases of the Chest*, the book by which all other clinical texts of respiratory disease were judged. Dag Munro performed the world's second lung transplant. It was a heady time.

David Bates deserves great credit for developing respiratory research at McGill in an inclusive multidisciplinary program including clinical, fundamental, and epidemiologic research in both the Royal Victoria and Montreal Children's Hospitals and spanning the disciplines of respiratory medicine, pathology,



Dr. David Bates

epidemiology, cardiology, and radiology. The joint cardiorespiratory service of the RVH and MCH rapidly became world famous. Respiratory research at McGill rivaled that of similar research centers at Harvard, Johns Hopkins, the State University of New York at Buffalo, the University of California, San Francisco, and elsewhere.

By 1962, following in Meakins' footsteps, Christie had become dean of the McGill Faculty of Medicine. In 1967 he retired. Maurice McGregor replaced him as dean, and David Bates became chairman of the Department of Physiology. I was appointed director of the Respiratory Division at the RVH.

Almost as soon as I was appointed, Peter Paré, my lifelong friend and professional colleague, told me that his brother, Paul Paré, then a vice president of Imperial Tobacco, was going to be made president. He suggested that we approach Paul to support respiratory research at the RVH. Our pitch was that the tobacco industry was causing lung disease and that since it was incapable of undertaking research into the diseases it was causing, it should support the research of scientists who could investigate how smoking led to disease. Paul, a man of great integrity, agreed. This led to negotiations with the Canadian Tobacco Manufacturer's Council, the consortium of Canadian tobacco companies. They agreed to donate $300,000 to McGill to build new laboratories for respiratory research and to provide overhead costs for the first 10 years of operation.

Today, this amount seems minuscule, but we were able to tap into federal resources to match those funds, so we had $600,000 to work with. After much discussion and some initial setbacks, we scaled our plans and settled on a two-storey addition to the Pathological Institute, conveniently located adjacent to Thurlbeck's lung morphometry laboratory. The plans were sent to tender, the contract was awarded, and work began. The egg was fertilized and the Meakins-Christie Laboratories were conceived.

I had a pretty fair idea of how I wanted the laboratories to operate. I had spent an unforgettable year and a half with Jere Mead and Jim Whittenberger at the Harvard School of Public Health and had also spent time in Dick Reilly's department at the Johns Hopkins School of Hygiene working with Don Proctor and Sol Permutt. The attitude in both institutions was identical and wonderful—that work should be fun. In both places much of the day was spent exploring, discussing, and dissecting new ideas. The idea of change and innovation was not only welcomed, it was fostered. Almost daily, furious arguments (but neverquarrels) would break out, out of which spectacularly stupid and, more than occasionally, spectacularly brilliant ideas would emerge. And we had the academic freedom to pursue them. When I was in Boston, Jere Mead and I would drive to and from work every day. We would argue about the hot topic of the time and decide what we were going to play with that day. One such morning we were arguing hotly about the role of airway wall compliance in limiting expiratory flow, when Jere had an idea. He suggested that we push a catheter into the lung, push it right through the parenchyma and the visceral pleura, and then continue pulling it until the other end, which was widened into a bell shape, caught in a small airway. Then we could measure the pressure in small airways and partition the pressure drop and the resistance between central and peripheral airways. Such was the spirit of academic freedom in the laboratories that Jim Whittenberger directed, that we were able to start on this idea within half an hour, and within a week we had most of the methodologic problems solved.

This was science heaven. This was what I wanted for the Meakins-Christie Laboratories.

To achieve this, the laboratories were designed for procedures, not as individual private fiefdoms. There was a laboratory for animal mechanics, another for human mechanics, an exposure chamber, a gas exchange laboratory, and radioactive gas laboratories for both animals and humans. The sharing of laboratories, although it presented problems in scheduling and the setting up of equipment, promoted interactions among scientists with similar interests, which I hoped would stimulate new and exciting ideas. I was convinced that creative people interacting with other creative people with common interests would come up with more original ideas than they would conducting their science in isolation. One big room, the chief technician's domain, had tables and chairs and always fresh coffee. Everyone—technicians, secretaries, research fellows, and research directors—was encouraged to eat lunch in that room. One day, I arrived late; every seat was taken, but a junior research fellow from France immediately stood up and offered me his seat. One of the technicians piped up, "What are you doing that for?!" I was pleased. That was exactly the sort of atmosphere I had hoped to establish.

Large blackboards were put up in every room to encourage expression and discussion. The fellows' offices were adjacent to the research directors' offices. Doors were kept open, appointments unnecessary. Talking is one of the strongest stimuli to innovation. Thus, our weekly research seminar was the highlight of the week's activities. In order to embolden shy research trainees to comment and ask

Dr. Paul Paré

questions, beer was freely available to loosen their tongues. Although probably the research directors drank more than the trainees, this worked. The beer seminars were held in the evening and were open-ended. Many memorable ones went on past midnight. One visiting VIP said, "I'm told that here I won't get past my first slide, so I'm going to start with my second." This was a great compliment.

From the beginning, the laboratories were designed to be interdisciplinary, and physiologists, physicians, epidemiologists, pathologists, radiologists, and biomedical engineers were invited to participate. The laboratories were open in the sense that anyone who wanted to collaborate with one of the scientists working there was welcome to do so.

After a long gestation period, the Meakins-Christie Laboratories for Respiratory Research were born in August 1972. At the opening ceremonies we were tackled by the media about the propriety of accepting tainted tobacco money. When the reporters heard that the money was given carte blanche, with no strings attached, to investigate, among other things, how smoking damaged the lungs, this issue was resolved.

In creating the laboratories, we tried to make the concept that research should be fun, that secrecy was anti-innovative, and that free and open discussion was essential, the core of our philosopy. Judging from the list of distinguished scientists who have contributed to this book, I think we succeeded. I pay homage to some exceptional people with whom I collaborated, who were extraordinarily creative and who even after death command immense influence over their survivors. They stand as proof of the vitality of freedom, openness, and creativity in science. In particular, I am talking about Whitey Thurlbeck, Ann Woolcock, Harold Menkes, Fred Douglas, David Flenley, and Ludwig Engel. These people enriched my life extraordinarily and would have similarly enriched this book if they were still with us. During their time at McGill they promoted the vision of intellectual freedom and openness, so they deserve much credit for not only persistence of this vision in the Meakins-Christie Laboratories but also for promoting it in their own institutions. I cannot finish without pointing out that Jim Higg contributed hugely to the early years of the laboratories. He and Ann Woolcock were among my first research fellows. What a start that was!

I directed the Meakins-Christie Laboratories from 1972 until 1979, when I resigned to take up new challenges. The leadership of the Meakins-Christie Laboratories passed into the capable hands of Joseph Milic-Emili and then Jim Martin. It has continued to grow in size, influence, and contributions to new knowledge. Clearly, it is in wise and capable hands.

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