

## Respiratory medicine in Saskatchewan: An historical perspective

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### EARLY DAYS: 1905 to 1957

Saskatchewan (capital Regina) was created out of the Northwest Territories on September 1, 1905, at the same time as Alberta, the second last provinces admitted to confederation. Its population has been relatively stable (one million  $\pm$  15%) since 1930. The University of Saskatchewan (U of S) was granted a provincial charter April 3, 1907, and, after considerable debate and controversy, Saskatoon was selected as the U of S site in April 1909; the first building was opened in 1912 and the first degree was also awarded in 1912. A two-year preclinical school of medical sciences (total faculty of five for many years) opened in 1926, initially with classes in converted greenhouses (1); clinical years were completed elsewhere. A university teaching hospital was conceived in 1911 (1), excavation began in 1948; the cornerstone was laid September 19, 1952, by Tommy Douglas, and the University Hospital (UH) opened May 14, 1955. The first class of MDs fully trained at the U of S graduated in 1957. The UH was renamed the 'Royal University Hospital' in 1990 (2).

### THE SASKATCHEWAN ANTI-TUBERCULOSIS LEAGUE (1911 to 1987)

The Saskatchewan Anti-Tuberculosis League (75-year history documented in reference 3) was founded in 1911 to coordinate the fight against tuberculosis (TB). Three TB sanatoria with >800 beds were established: Fort Qu'Appelle (also known as 'Fort San', 1917), Saskatoon (1925) and Prince Albert (1930), for hospitalized management of the disease. George Ferguson (1883 to 1964) came to Fort San in 1917 for six months and remained as Medical Superintendent of the League until his retirement in 1948. The League, under George Ferguson's direction, was the first in the Americas to offer free TB treatment (1920), to provide a mass Bacille Calmette-Guérin vaccination program (1930s) and to offer a mass TB screening program (1941). As drug therapy became available and successful, the three sanatoria were eventually closed in the 1960s and 1970s after a total of 10.5 million patient-days; the last patient was discharged from the Saskatoon San on June 26, 1978. In the 1960s, the League became progressively involved in other respiratory diseases and transitioned to the Saskatchewan Lung Association (SLA). The League continued to operate the TB control program until 1987. In 1987, the TB program was transferred to the Ministry of Health (provincial government) and the League was officially renamed the SLA, now the Lung Association of Saskatchewan (LAS) since 2000. In 1973, an historic agreement was signed between the Saskatchewan Anti-Tuberculosis League, the U of S and the UH to establish a respiratory disease unit in Saskatoon (3). The financial support for this unit continues to this day, and has allowed recruitment of an excellent group of clinicians and researchers.

### RESPIRATORY MEDICINE IN SASKATCHEWAN (1970s)

The first (nonphthysiologist) respirologist in Saskatoon was Clive Deutcher (MD, U of S 1967, postgraduate training University of Alberta, Edmonton, Alberta), recruited to the Department of Medicine in 1972; he left the university in 1976. Things were very

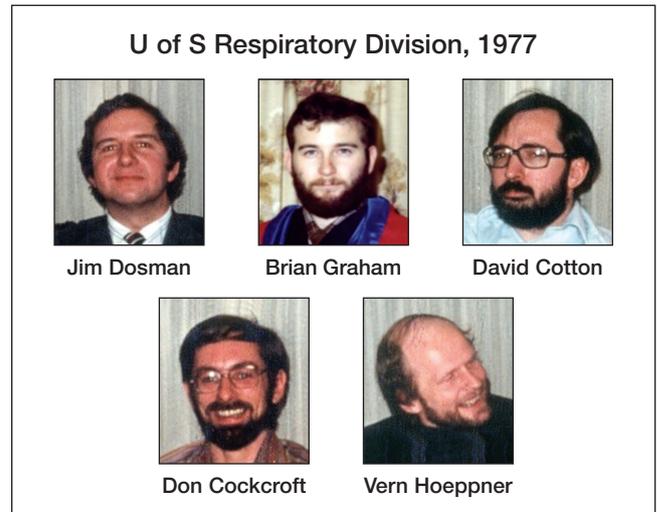


Figure 1) Members of the Division of Respiratory Medicine, University of Saskatchewan (U of S), 1977

primitive in 1972; however, over his four years, with what must have been hard work and perseverance, Clive kick-started clinical respirology in Saskatchewan. Blood gas analysis – until then exclusively performed by anesthesiology – came under respiratory medicine until it was transferred to the biochemistry laboratory in 1976. He inherited a fledgling pulmonary function laboratory from John Merriman (cardiology) and upgraded it to then current standards. There was no intensive care unit; ventilator patients were managed in the postoperative recovery room. New volume-cycled ventilators were purchased to better manage respiratory failure patients. As the sole respiratory specialist in Saskatoon, providing clinical care along with patient education, undergraduate education, postgraduate education and continuing medical education consumed much of his time. Clive laid the foundations for what has become a very successful division in a (very) small Department of Medicine.

The Ferguson Professorship, named after George Ferguson, was created, with financial support from the Saskatchewan Anti-Tuberculosis League; the first recipient was Jim Dosman, recruited as Division Head in July 1975. The pulmonary research laboratory at the UH, dedicated to the memory of George Ferguson, was opened in November 1975. Brian Graham, biomedical engineer, was recruited in April 1976 and, with assistance of the League, David Cotton joined the Division in July 1976. July 1977 witnessed the arrival of Vern Hoepfner and Don Cockcroft, both applicants for the single position to replace Clive Deutcher, and both recruited with the help of the League. Remarkably, all five members (Figure 1) recruited over that 24-month period, remained active at the university 37 years later, in mid-2014. All four clinicians have been the Division Head, all four have held the Ferguson Professorship, and three of the four have been the Head of the Department of Medicine. Despite the continuing major teaching and clinical demands, this small group proved to be highly productive.

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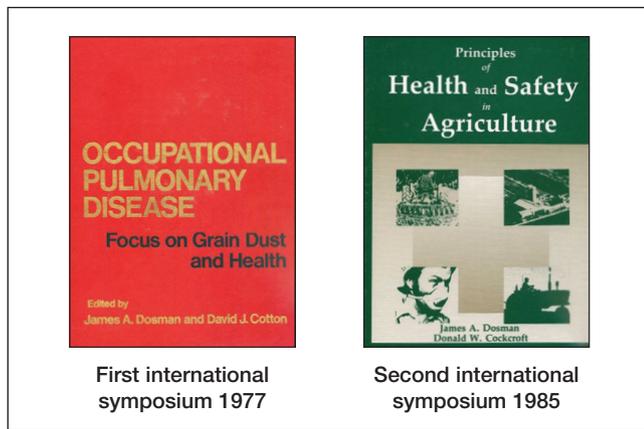


Figure 2) The first two international symposia publications

Jim Dosman pioneered studies of respiratory disease in agricultural workers (4-6). The first two (of seven) international symposia on grain dust/agriculture and health were held in Saskatoon in 1977 (7) and 1985 (8) (Figure 2) while he was still within our division. Jim was Division Head (Ferguson Professor) from 1975 to 1984, the Head of the Department of Medicine from 2002 to 2003 and President of the Canadian Thoracic Society (CTS) from 1984 to 1985. In 1986, Jim founded what is now the Canadian Centre for Health and Safety in Agriculture (CCHSA), a separate Division within the Department of Medicine. The CCHSA currently has nine full-time faculty including one clinician, seven PhD researchers with appointments in three different departments, and Jim Dosman as an Emeritus professor. In the past two years (2012 to 2014), the CCHA has hosted a successful seventh international symposium, has approximately 54 peer-reviewed publications and received in excess of \$15 million in peer-reviewed research funding. Jim continues to be heavily involved in the CCHSA research portfolio, and to do clinical work, self-described as 90% sleep medicine.

David Cotton and Brian Graham studied gas exchange and measurement of the diffusing capacity (9-11), resulting in the development of a three-equation (inspiration, breath-hold and expiration) method to more accurately calculate the diffusing capacity (10). The conventional method for measuring diffusing capacity relies on the breath-hold calculation, and requires rapid inhalation and exhalation to be accurate, which is not always possible in disease states. The availability of a rapidly responsive carbon monoxide detector enabled continuous monitoring of carbon monoxide and, thus, an accurate assessment of diffusion during inhalation and exhalation as well as breath-hold (Figure 3). The three-equation method is now commercially available on several pulmonary function systems. David was the Division Head from 1984 to 1994 (Ferguson Professor for nine of those 10 years), the Head of the Department of Medicine from 1994 to 2000 and CTS president from 1992 to 1993. For the last several years before retirement in 2014, David focused on sleep medicine, both clinical and research. Brian was seconded to the Saskatchewan Anti-Tuberculosis League/SLA as executive director while maintaining his academic post as an associate professor of medicine. This unique relationship enhanced the already very close links between the Lung Association and the Division. Brian was Director of the Canadian International Development Agency project to enhance TB control in Ecuador from 1999 to 2006, and is currently President and CEO of the LAS and was made an Emeritus professor in the Department of Medicine in 2014. The LAS has embarked on a project to establish the Lung Health Institute of Canada to provide respiratory education, clinical research, policy development and dissemination, health economic modelling and clinical services, particularly in underserved areas. The founding President is Brian Graham.

Vern Hoepfner showed that high-pressure nocturnal ventilation was *therapeutic* rather than just supportive in respiratory failure due

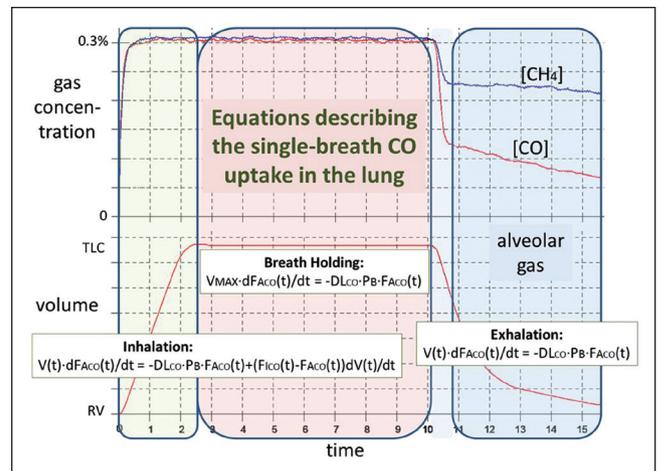


Figure 3) The three-equation diffusing capacity calculation (Graham, Cotton and Mink). There are separate equations for inhalation, breath-hold (standard calculation) and exhalation inspiration. Supplied by and reproduced with permission from Dr Brian Graham

to kyphoscoliosis (12). Vern was the director of TB Control for Saskatchewan from 1986 until 2011, and has published work in TB (13,14) including validation of directly observed TB therapy (DOT). Observations on directly observed prevention (DOP) are shown in Figure 4 (13). DOP for six weeks showed improved compliance over education and much improved compliance over standard treatment. Standard treatment was instituted at six weeks in all groups and, by 16 weeks, the compliance was dismal and no different in all three groups. This formed the basis for DOT instituted in Saskatchewan in 1989 (the first in Canada). DOT was implemented by the WHO in 1993. Vern was the Ferguson Professor (1986 to 1987, TB control), Head of the Department of Medicine from 2008 to 2013 and the Division Head from 2014 to 2015. He continues as a full-time professor in the Department of Medicine involved in TB epidemiology research.

Don Cockcroft followed up on the observation that allergen challenge increased airway responsiveness to histamine and methacholine (15) and studied the effect of common asthma drugs on this feature (16). While studying the development of tolerance to the bronchoprotective effect of inhaled beta<sub>2</sub>-agonists, he made the serendipitous observation that regular use of these agents caused significant increase in the airway response to inhaled allergen (17). Salbutamol, 200 µg inhaled daily for 14 days, did not influence airway response to methacholine but caused an almost doubling of the airway response to inhaled allergen (Figure 5); in addition, there was tolerance to the bronchoprotective effect of salbutamol against both challenges. Follow-up studies documented that beta-agonist-induced increase in airway responsiveness to allergen is not only repeatable but also extends to increases in the allergen-induced late response (18) and allergen-induced airway inflammation (19). This is a plausible explanation for beta agonist-induced worsened asthma control (20). Don was Division Head and Ferguson Professor from 1996 to 2006, CTS president 1998 to 1999 and was a founding member of the Allergy Genes and Environment (AllerGen) National Centres of Excellence (NCE) Clinical Investigative Collaboration (CIC) in 2006. The AllerGen NCE CIC is a multicentre collaboration co-chaired by Paul O'Byrne and Louis-Philippe Boulet using identical methods of bronchoprovocation (developed mainly by Freddy Hargreave), primarily with allergen, to study early stage new pharmaceutical agents with both a view to potential new treatments as well as further understanding the pathophysiology of allergen-induced asthma (21). He continues to be a full-time academic professor at the U of S, 50% clinical/teaching and 50% research.

TABLE 1

**Academic members, Division of Respiriology, University of Saskatchewan (U of S) 1972–2015**

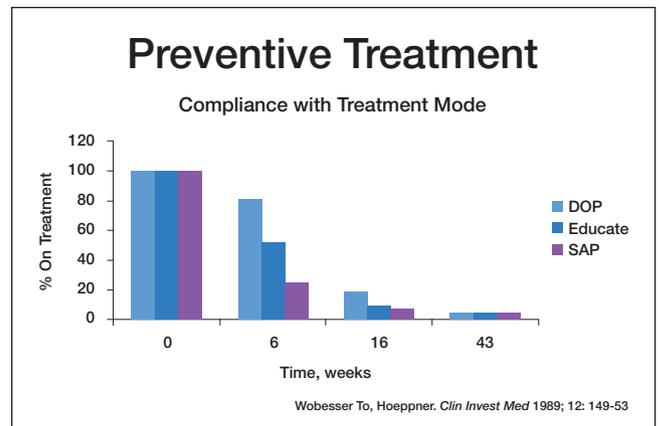
Member	Date	Expertise	2015
Clive Deutcher	1972–1976	Clinical respirology	Retired
Jim Dosman	1975–1986	Agricultural medicine	CCHSA
Brian Graham*	1976–2014	Gas exchange, diffusion	Emeritus
David Cotton	1976–2014	Gas exchange, diffusion, CF, sleep	Retired
Don Cockcroft*	1977–date	Asthma, CF	U of S
Vern Hoepfner*	1977–date	TB	U of S
Jeremy Road	1983–1985	COPD, home ventilation	UBC
Irv Mayers	1985–1995	ICU, Sleep	U of A
Charlie Gallagher	1987–1996	Exercise	Ireland
Tom Hurst*	1987–2007	Pulmonary function	Emeritus
Darcy Marciniuk*	1990–date	COPD, exercise	U of S
Mike Fitzpatrick	1992–1997	Sleep	Queen's <sup>†</sup>
Karen Laframboise*	1997–date	ICU, pulmonary hypertension, education	U of S
Anil Nagpal	1998–2000	Sleep	Kitchener
Robert Skomro*	1998–date	Sleep	U of S
Brian McNab	2000–2006	Education, clinical respirology	U of A
John Gjevre*	2002–date	ICU, sleep, CF	U of S
John Reid	2003–2014	ICU, sleep	Victoria
John Gordon*	2007–date	Immunology, inflammation	U of S
Mark Fenton*	2008–date	Transplantation, sleep	U of S
Chris Hergott	2009–2014	Interventional bronchoscopy	U of Calgary <sup>‡</sup>
Cam Pierce	2009–2011	Clinical respirology	Retired
Beth Davis*	2010–date	Asthma clinical research	U of S
Erika Penz*	2013–date	Health economics	U of S
Donna Goodridge*	2014–date	Health systems improvement	U of S

\*Current academic Respiriology Division Members; <sup>†</sup>Queen's University, Kingston, Ontario; <sup>‡</sup>University of Calgary, Calgary, Alberta. CCHSA Canadian Centre for Health and Safety in Agriculture; CF Cystic fibrosis; COPD Chronic obstructive pulmonary disease; ICU Intensive care unit; TB Tuberculosis; U of A University of Alberta, Edmonton, Alberta; UBC University of British Columbia, Vancouver, British Columbia

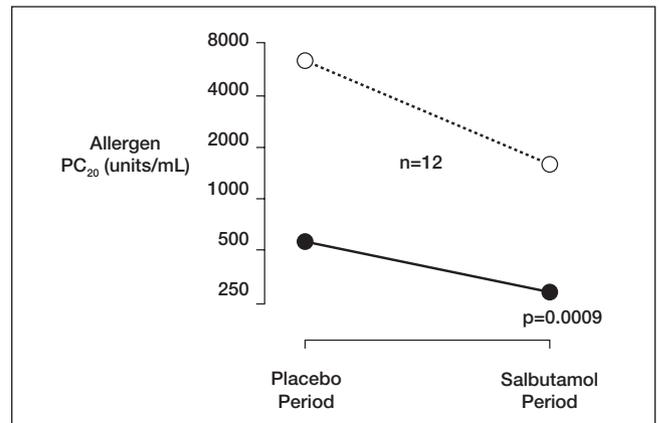
**RESPIRATORY MEDICINE IN SASKATCHEWAN:  
1980 to 2015**

In the years following the 1970s, our division has thrived and expanded with continued tremendous assistance from the LAS. The Lung Association has continued to provide salary support, both 41 years of Ferguson Professorships (eight individuals), and 135 person-years of additional Lung Association professorships (15 individuals). The John Moorhead Foundation funds research into asthma; these funds are administered by the LAS and have supported 18 research fellows (22 years). Table 1 outlines the academic members of the Division of Respiriology, Critical Care and Sleep Medicine from 1972 to date. The 19 members recruited since 1980 brought expertise in chronic obstructive pulmonary disease (COPD), exercise physiology, critical care, sleep, pulmonary hypertension, interventional bronchoscopy, health economics, basic allergy and immunology, and health services research (Table 1). In the last year for which statistics are available (2012 to 2013), the Division has co-authored 35 peer-reviewed publications, 30 conference abstracts and given 79 invited lectures; Division members are investigators or co-investigators on grants and contracts totaling in excess of \$5,000,000.

A Royal College certified training program in Respiratory Medicine was commenced in 1983, with program directors Hoepfner, Gallagher, Marciniuk, McNab, Reid and Fenton. We have successfully trained 39 respirologists. Thirteen of these currently work in Saskatchewan, 11 in respirology and two in general internal medicine. Six additional



**Figure 4)** Treatment adherence to tuberculosis prophylaxis. At six weeks, directly observed prophylaxis (DOP) was superior to education and standard treatment groups. Standard treatment was used from six weeks onward and adherence was dismal at 16 and 43 weeks in all groups. Modified from Wobeser, et al. The outcome of chemoprophylaxis on TB prevention in the Canadian plains Indians. *Clin Invest Med* 1989;12:149-53 and reproduced with the permission of Dr V Hoepfner and the journal. SAP Self-administered antituberculous prophylaxis



**Figure 5)** Allergen provocation concentration causing a 20% fall in forced expiratory volume in 1 s ( $PC_{20}$ ) following two-week treatment with placebo (two puffs four times daily) and salbutamol 100  $\mu$ g (two puffs four times daily). The solid circles are 12 h after the last dose of blinded medication: there is almost a twofold increase in airway response to allergen (fall in  $PC_{20}$ ) after the regular use of the beta-agonist ( $P=0.0009$ ). The open circles are repeat allergen  $PC_{20}$  measurements after a single dose of salbutamol 200  $\mu$ g; after regular use of salbutamol, there is a significant reduction in the bronchoprotective effect of the beta-agonist ( $P=0.025$ )

successful trainees have worked in Saskatchewan before moving elsewhere. Graduates from our program are practicing (or have practiced) from coast to coast across Canada, in the United States (including the Mayo Clinic) and internationally (Iran, Saudi Arabia and Kuwait).

The division of Respiriology, Critical Care and Sleep Medicine currently consists of 13 university-based faculty members (Figure 6): eight clinicians and five nonclinicians (two Emeritus). There are also 13 community-based clinicians, seven in Saskatoon (Kemp Gowda, Norm Joanis, Mandeep Ubhi, Rod Hafezi, Greg Peters, Nathan Janzen and Richard Nataraj) and six in Regina (Ram Abdulla, Prakash Patel, G Shridar, Abdalla Mufta, Shahbaz Sheikh and Zenon Belak). Jim Dosman is an Emeritus clinician in the CCHSA; this totals 22 clinical respirologists currently in the province. Individual highlights of division members recruited since 1980 are outlined below.

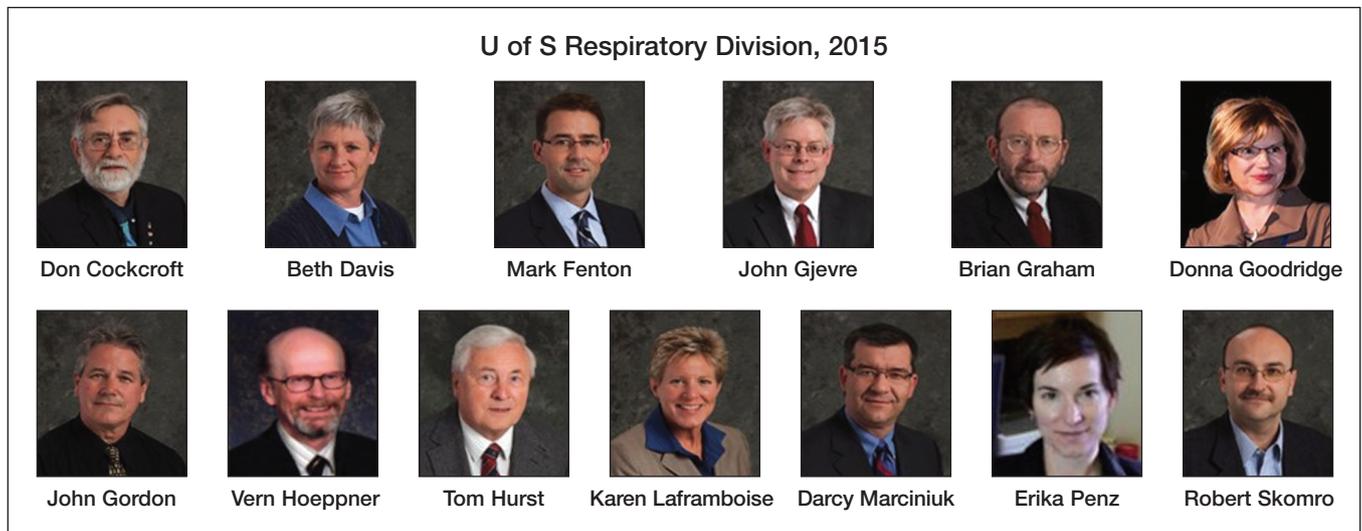


Figure 6) Current members of the academic division, University of Saskatchewan (U of S), Saskatoon, Saskatchewan, 2015

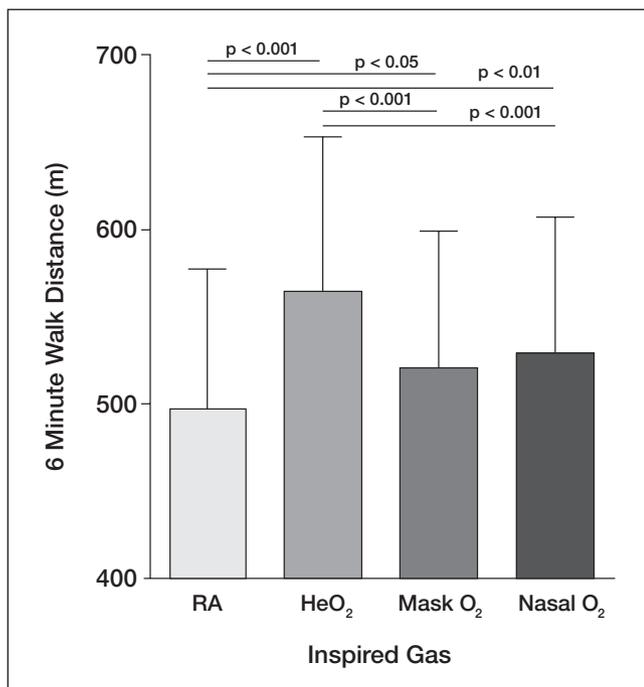


Figure 7) Improvement in 6 min walk distance with supplemental oxygen ( $P < 0.05$  to  $0.01$ ) compared with room air (RA) and greater improvement with 70% helium/30% oxygen (HeO<sub>2</sub>) mixture ( $P < 0.001$ ) in 16 subjects with chronic obstructive pulmonary disease. Reproduced from Marciniuk, et al. The effects of helium hyperoxia on 6-min walking distance in COPD. *Chest* 2007;131:1659-65, with permission of Dr D Marciniuk and the American College of Chest Physicians

Tom Hurst was a division member from 1987 to 2007. He upgraded and directed the clinical pulmonary function laboratory and provided valuable technical support for collaborative studies with David Cotton and Brian Graham, Jim Dosman, Don Cockcroft and, as a veterinarian, was particularly helpful in Irv Mayers' animal research program. Tom is currently a professor Emeritus in the division.

Darcy Marciniuk joined the division in 1990. He and Charlie Gallagher developed both research and clinical laboratories to study exercise physiology in health and disease. The exercise laboratory has yielded numerous publications and trainees. An example is shown in Figure 7. In 16 subjects with COPD and normal oxygenation at rest,

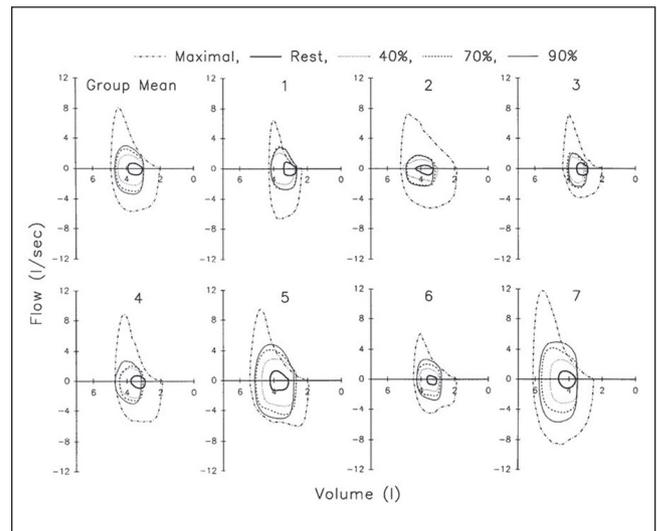


Figure 8) Individual and group mean ( $n=7$ ) at rest and at various exercise work rates; maximal flow volume curve is plotted for comparison. Expiratory flow limitation was evident in four (1, 5, 6 and 7). Reproduced from Marciniuk, et al. Lung volumes and expiratory flow limitation during exercise in interstitial lung disease. *J Appl Physiol* 1994;77:963-973, with permission from the author

supplemental oxygen by mask or nasal prongs significantly improved the 6 min walking distance. However helium/hyperoxia (70%/30%) produced a substantially greater increase (22). Darcy and Charlie were the first to fully investigate the behaviour of operational lung volumes in interstitial lung disease (Figure 8) (23). Darcy also worked to establish the *LiveWell* Chronic Disease Management program, and remains the medical director of the *LiveWell* COPD program in Saskatoon. Darcy was president of the CTS from 2006 to 2007, and the (first non-American) president of the American College of Chest Physicians from 2012 to 2013. He has been active in the CTS COPD committee and is lead author on several CTS COPD guidelines (eg, reference 24). Darcy is well respected in his field, with >270 invited national and international presentations. Darcy has currently taken on a new role as Special Advisor, Research and International with the U of S.

Karen Laframboise joined the division in 1997, bringing expertise in critical care, pulmonary hypertension and medical education. She is a member of the CTS pulmonary vascular disease committee (chronic thromboembolic pulmonary hypertension guidelines [25]) and recently

became program director for the Department of Medicine core internal medicine training program.

Robert Skomro joined the Division in 1998 with a major clinical and research interest in sleep medicine. He assumed the position of Medical Director of the Sleep Disorder Centre in 2000 and oversaw expansion of the unit from eight to 30 studies per week. The sleep group has established the first publically funded home monitoring program for obstructive sleep apnea (OSA) in Canada. The sleep laboratory has investigated and treated >3000 OSA patients. Together with colleagues from the Division, Robert established a sleep medicine research program that focused on the diagnosis, management and comorbidities of sleep-disordered breathing (SDB). The group has published >50 articles. Robert and colleagues documented in a randomized controlled trial the comparable diagnostic efficacy of in-home level 3 sleep studies compared with in-laboratory level 1 studies (26). He became the Chair of CTS SDB Clinical Assembly in 2011 and a member of the CTS Home mechanical ventilation clinical assembly. These collaborations with colleagues from across the country have led to publication of four position papers and guidelines in the *Canadian Respiratory Journal*.

John Gjevre joined the Division in 2002 with expertise in critical care, cystic fibrosis and sleep medicine. He has been director of the adult cystic fibrosis clinic until recently and is currently the director of the sleep laboratory. His research interests are in the area of SDB particularly as related to patients with rheumatoid arthritis (27).

John Reid joined the Division in 2003 and relocated to British Columbia in 2014. He brought expertise in both critical care and sleep medicine. John was program chair from 2006 to 2013, and Division Head from 2013 to 2014. His research interests focused on SDB in pregnancy (28).

John Gordon joined the division in 2007 transferring from the Department of Microbiology in the College of Veterinary Medicine. He adds expertise in basic immunology especially as related to both allergic/asthmatic diseases (29) and neutrophilic inflammatory conditions (30).

Mark Fenton joined the division in 2008. He brings expertise in both transplantation and SDB and established the Saskatchewan Lung Transplant Clinic. Research interests are in the respiratory health of First Nations, physiology and clinical evaluation of OSA (31).

Beth Davis joined the division in 2010 as a research scientist. She documented the additive/synergistic effect of single dose H<sub>1</sub> blocker and leukotriene receptor antagonist inhibition of airway response to allergen (32). Beth runs the asthma (bronchoprovocation) laboratory with Don Cockcroft and is involved in numerous studies both within and outside the AllerGen CIC.

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Erika Penz joined the group in 2013, with expertise in applied health economics and cost-effectiveness trials (33). Current clinical research interests are in the areas of tobacco and e-cigarette use, lung cancer screening and prevention, COPD and palliative care.

Donna Goodridge moved from the college of nursing to our division in 2014. Her area of research examines interventions for health systems improvement, with a particular focus on health outcomes of populations with complex medical and social needs, such as individuals with COPD (34). She has been co-chair of the CTS COPD Assembly since 2011, and served on the executive of the ACCP/CTS that conducted a systematic review on prevention of acute exacerbations of COPD (35).

## REGINA

Howard Hopkins was the first respirologist in Saskatchewan (early 1970s) and has since retired. He established a pulmonary function laboratory in Regina. Ram Abdulla came to Regina in 1980 and established an intensive care unit at the Regina General Hospital. Ram is currently Head of the Department of Medicine in Regina. Five additional respirologists have joined the Regina group (Prakash Patel, G Shridar, Abdalla Mufta, Shahbaz Sheikh and Zenon Belak). Sridhar held a Lung Association professorship for many years. The current six respirologists in Regina are all clinical affiliates of the U of S and provide a valuable teaching resource for our respiratory training program as well as to the respiratory health of the southern part of Saskatchewan.

## SUMMARY

In a little over 40 years, the number of clinical respirologists in Saskatchewan has increased from two (one in Saskatoon and one in Regina) to 22. With immense help from the LAS, we have established and maintained a vibrant and successful Division of Respiratory Medicine at the U of S. This group has, arguably, performed beyond the relatively small numbers. The Division is proud of the graduates of the training program, which has supplied both academic and community-based respirologists in Saskatchewan, across Canada and internationally.

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