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COMMENTARY

The Air We Breathe: From Cigarette Smoke to Environmental Air Pollutants

Bruce Urch[1], and Frances Silverman[1]

Abstract

This commentary highlights the important influence Dr. Roy Shephard has had upon establishing the clear health benefits associating with reducing the exposure to cigarette smoke and various other environmental air pollutants.

Introduction

My first contact with Dr. Roy Shephard came soon after I received my BSc from the University of Western Ontario. It was 1979 and I was gaining research experience in my first full-time job, after many months of job searching and interviews. I was hired as a pulmonary function technologist at the Gage Research Institute on College St, just south of the University of Toronto campus. My first responsibility was to learn about the ongoing controlled human inhalation studies, under the direction of Dr. Frances Silverman. Fran had received her PhD under the supervision of the renowned Dr. David Bates and had established an environmental inhalation facility at the Gage in the early 70s. She was joined almost immediately by Larry Folinsbee, a post doc who proceeded to a distinguished career at the US EPA. Regrettably, we lost Larry to cancer when he was quite young. Dr. Shephard was collaborating with Fran and others on our air pollution studies. He was an invaluable asset with his vast expertise on exercise physiology, respiratory physiology and air pollution.

A main focus of our research at that time was ground-level ozone— one of the major components of urban smog. Ozone (O_3) is a photochemical oxidant that is not directly emitted from sources; it is a secondary pollutant formed through a series of complex atmospheric reactions in the presence of sunlight. We were examining the respiratory effects of O_3 including pulmonary function changes (e.g. airway constriction) and exercise performance (e.g. oxygen consumption). Healthy subjects recruited from the university population and surrounding area read and signed an informed consent. Participants who met the inclusion criteria were allocated to the exposure study in which they sat at a desk for 2 hours inside an office-sized 2.4 x 2.4 x 2.3 metre plexiglass enclosure.

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From the [1]Gage Occupational and Environmental Health Unit, St. Michael's Hospital and the University of Toronto. 223 College Street, Toronto, ON M5T 1R4
Phone: 416 978-5883 Email: bruce.urch@utoronto.ca; frances.silverman@utoronto.ca

Inhalation studies were randomized (and blinded) such that each subject received a filtered air (FA) control exposure and one or more ozone exposures on separate occasions. Ozone was generated by passing oxygen through a high intensity electrical field. The O_3 was then delivered into the inhalation facility. For air exchange, the O_3 inhalation facility had an air inlet at ceiling-level for air/O_3 delivery and an exhaust at floor-level creating a diagonal cross-flow. Ozone levels were precisely controlled to (depending on the study) target levels of 0.25, 0.37, 0.50 and 0.75 parts per million (ppm) in order to examine dose-response associations with health outcomes. Subjects pedaled on a cycle ergometer for 15-minute periods alternating with 15 minutes of rest while inside. The loading of the ergometer was adjusted to increase respiratory minute ventilation (V_E) by 2.5-fold above resting V_E. Intermittent exercise is commonly used in controlled exposure studies as a means of increasing the effective dose of pollutant inhaled by the test subjects. The first published account of using intermittent exercise was when Fran was a PhD student with David Bates (Bates et al., 1970). The effective dose is the product of pollutant concentration x V_E x exposure duration. We observed a significant association between the effective O_3 dose and change (% of FA control) in the spirometry outcome measure (e.g. forced vital capacity, FVC) (Silverman et al., 1976). In other words, for a higher effective O_3 dose subjects had a greater decrease in FVC with O_3 relative to FA. Although post exposure sub-maximal exercise performance (VO_2) was not altered by prior O_3 inhalation, there was a significant association between respiratory frequency (% of FA control) at 75% of aerobic capacity and the effective O_3 dose. Ozone inhibits inspiration, thus reduces tidal volume (the volume of each breath) and in order to maintain V_E respiratory frequency must increase.

During the late 70s and early 80s, we were also collaborating with Dr. Shephard on studies of the health effects of environmental tobacco smoke (ETS) or passive cigarette smoke. In these studies, we used a cigarette-smoking machine to generate ETS. This was long before the current ban (in Canada) on smoking in public places and in airplanes. However, I was reminded of the smoking ban on a recent trip to Denver when I had to pass through the smoking area in the airport restaurant to get to the smaller non-smoking area. Study responses included measuring the effects of ETS on tear film break-up time, pulmonary function, symptoms, sub-maximal exercise performance, heart rate, V_E and respiratory frequency. The "magnitude of the changes was small and of questionable biological significance", even in subjects with asthma. In the early 80's I was working closely with Dr. Shephard on a controlled exposure study of O_3 and ETS, comparing individual and combined effects. This was my first experience at co-authoring a manuscript and my first publication. I was a bit intimidated, given Dr. Shephard's wealth of knowledge and my lack thereof, but was eager to learn from him. During this interactive process, my interest in advancing my education was stimulated.

There were many other collaborations with Dr. Shephard, showing the breadth of his work. Veli Niinimaa was a PhD candidate working with Dr. Philip Cole, Dr. Shephard and others on studies of the nasal work of breathing, nasal airflow resistance and the switching point from nasal to oronasal

breathing (Niinimaa et al., 1980). Few studies had focused on nasal physiology and aerodynamics to the extent of this work. The switching point studies and inter-individual variability findings were seminal work and filled a gap in the literature. I found the work fascinating, especially the "head-out" plethysmograph used to measure nasal airflow and unique software used to measure the sigmoidal shaped nasal airflow vs transnasal pressure curve in real-time.

In 1981-82, I considered doing an MSc, but first wanted to "test the waters". I discussed this with Dr. Shephard and enrolled in a couple of graduate half-courses— "Physical Activity and Aging" and "The Child and Physical Activity". After graduating from Western in 1978, I had tried to get into the MSc Exercise Sciences program, headed by Dr. David Cunningham, but was not successful. Receiving an A- in both half courses, I felt confident to enrol in the MSc program in Exercise Sciences with Drs. Silverman and Shephard as supervisors (1982-86). The title of my thesis was "Physiological effects of passive cigarette smoke exposure and the influence of suggestibility on non-smoking intermittently exercising adults". One of the many things that I learned from Dr. Shephard was to be creative and think mechanistically— considering the pathways of response. For my thesis study design, I certainly had to be creative in designing the exposure system and psychological tests. I needed to design a system such that the subjects could see the cigarettes burning, but not know when or how much ETS that they were exposed to. Obviously, I was not able to mask the distinctive cigarette smoke odour. However, I was able to adjust the smoke levels pumped into the exposure room, set at low and high target levels on separate exposures. During "sham" exposures, subjects could see the burning cigarettes but clean air was pumped into the room. Exposures were randomized to minimize potential order effects. The premise was that in some "suggestible" subjects, just the sight of cigarettes burning would induce psychological and then physiological responses. A number of questionnaires were used to assess psychological outcomes. Perhaps the most interesting outcome measure I used was the psychogalvanometer, commonly used in "lie-detector" testing. Small electrodes were placed on the subjects' finger pads to measure skin conductance. Simply put, the test measured the sweat response due to arousal or excitement. Physiological responses were again smaller than anticipated and the suggestibility hypothesis failed to be fruitful. Writing never came easy to me, evidenced by the many drafts and re-writes. However, there was never any lack of suggestions or questions and edits in red/blue ink promptly returned by Dr. Shephard. Fran also noted how Roy was always challenging to his students. She remembered in thesis defences and other examples, when it appeared that all questions were put and comprehensively discussed, Roy would still find yet another insightful question or point of discussion. In a future manuscript (Urch et al., 2010), I thought back to those earlier days when trying to explain results that went against conventional thinking. A systemic response (blood interleukin-6, IL-6) to a combined particulate matter (PM) + O_3 exposure was diminished compared to the IL-6 response to PM alone. Further investigation demonstrated that in some subjects there was a (involuntary) reduction in tidal volume during PM + O_3 exposure, thus attenuating the pollutant

effect and resulting in an overall decrease in IL-6 response.

There was less contact with Dr. Shephard in the years that followed, as our studies on ozone and cigarette smoke ended. A new project from 1986-89 renewed our collaboration with Dr. Shephard. Given my interest in running and our studies of air pollution, I designed a study to examine the health effects of air pollution in a group of runners from the Longboat Runner's Club— a group that I was training with at that time. Each Wednesday evening we followed a group of about 10 runners downtown and out along the Martin Goodman Trail along Lake Ontario and back. We loaded bicycles with air pollution monitoring devices and rode alongside the runners to measure their "personal" exposure to air pollutants. Pulmonary function, carboxyhaemoglobin (COHb%) and symptoms were measured before and after runs. Probably due to their enhanced fitness levels, there were little changes in pulmonary function and no adverse responses. However, the symptom reports acted an integrator of the pollutant effects. Interestingly, because the carbon monoxide concentrations were lower along the lake, the COHb% levels improved over most runs! While the findings were never published, we are repeating the statistical analyses using current techniques and will publish the findings— a revival of the Shephard-Gage collaboration.

In the fall of 2010, I completed my PhD thesis entitled "Controlled human exposures to concentrated ambient fine particles and ozone: Individual and combined effects on cardiorespiratory outcomes". During this 6-year-period, we no longer had ties to Dr. Shephard, and my PhD co-supervisors were Drs (Paul) Corey and Silverman. The laborious thesis writing process brought me back to the days of my master's thesis and the insights and knowledge that I gained from Dr. Shephard in his classroom teachings and his manuscript and thesis edits/commentaries. Our current studies have expanded into the field of cardioelectrophysiology with our new collaboration with Dr. Nanthakumar at Toronto General Hospital. I am sure Dr. Shephard would be intrigued by this work in which we have demonstrated an alteration of spatial dispersion of myocardial repolarization following acute controlled exposure to fine particles and ozone (Sivagangabalan et al., 2011). My bonds to exercise are still strong, as I just completed the Boston marathon on April 18, 2011. It was a humbling and historic experience as I was hours behind the exhilarating run by Geoffrey Mutai of Kenya— the fastest time that anyone has completed the marathon distance, a time of 2:03:02! Thanks again to Dr. Shephard for his guidance and encouragement along my career path and for his collaborations with myself, Dr. Silverman and others at the Gage. Dr Silverman and I congratulate him on his illustrious career and wish him well in future endeavors.

Qualifications

The authors' qualifications are as follows: Bruce Urch Ph.D., Frances Silverman Ph.D.

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