Respiratory health and farming: An essay

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Farming, one of the oldest professions of mankind, is by far the one that employs the largest number of individuals worldwide. Although outdoor country work is supposedly healthy, farmers are at risk of respiratory diseases because of their work environment. This essay summarizes the major respiratory health risks to farmers in Canada.

Farming is a major industry in Canada. Prince Edward Island and New Brunswick have potatoes, Nova Scotia has apples, Quebec and Ontario have dairy, the Prairies have wheat and British Columbia has fruits. But then we all have pigs, lots of pigs. In Quebec, there are as many pigs as there are humans, and in Saskatchewan, there are three or four pigs per person. Canada exports hog products around the world, mostly to the United States and Asia.

Because of the importance of this industry and the potential associated health risks, most often respiratory-related, Canadian researchers have developed internationally recognized expertise in this area. As a respirologist born and raised in a small mixed farm in Prince Edward Island, research on the respiratory health impact of the farm environment was a natural choice for me. My background allowed me to communicate with farmers in their terms and to understand their interest and concerns. This connection gave me a privileged relationship with farmers in Quebec, especially dairy farmers and swine producers, and made most of my work on farmer’s lung (FL) and swine building environments possible.

Dr James Dosman from Saskatoon, Saskatchewan, is by far the champion of Canada’s research in respiratory health in farmers. He has led the way in defining the respiratory health impact of grain handling, and swine and poultry production. Besides his excellence as a researcher, he shines in his promotional and leadership role. Because of him, the research community in this field now holds a seven-year Canadian Institutes of Health Research training program, a multimillion dollar grant for the study of endotoxins in swine buildings, and recently, a large Canada Foundation for Innovation cross-Canada infrastructure grant. Dr James Dosman is what we say in French a ‘rassembleur’, one who brings people together for a cause. Researchers across Canada who work together largely because of his initiatives include Judy Guernsey from Halifax, Nova Scotia; Caroline Duchaine and myself from Quebec; Lynn Holness, Will Pickett and Bob Brison from Ontario; Drs Sentilisilvan and Kulig from Alberta; Martha McLeod and Helene Ward from British Columbia; and of course Dr James Dosman’s team in Saskatoon.

DUST AND PESTICIDES

Farmers can be exposed to harmful respiratory substances in the fields. In dry climates like in western Canada, high concentrations of silicate dust are produced during field work such as harrowing or harvesting. Fine particles of this dust can accumulate in the lung, leading to a silicosis-like interstitial fibrosis. Farmers need to be very careful when applying toxic pesticides, some of which are potent carcinogens, while others such as the herbicide paraquat induces interstitial fibrosis at very low doses. Anecdotally, the first lung transplant performed in Canada by Dr Joel Cooper in Toronto, Ontario, was such a case.

INFECTIOUS AGENTS

Soil can also be contaminated with pathogenic fungi, including Blastomyces dermatitidis, Histoplasma capsulatum and Cryptococcus neoformans. Blastomyces and Histoplasma are prevalent in Quebec, especially in the valley of the St Lawrence river. C neoformans are typically found in areas contaminated by pigeon droppings. Blastomycosis can be quite a severe infection and typically involves the lungs, the skin and the joints. It can be successfully treated with the appropriate antifungal medication. Histoplasmosis is usually a benign condition. In some areas, it is often the cause of solitary or multiple pulmonary nodules. C neoformans can also induce lung infections with subsequent nodules, but its major interest is its propensity to invade the central nervous system.

Mice are prevalent on farms. Feces of deer mice can be contaminated with the hantavirus, which can cause a devastating infection in humans, an influenza-like syndrome that often leads to respiratory failure. Farmers should wear protective respiratory equipment when cleaning building areas where mouse droppings are present.

Farms are the usual sources of influenza outbreaks. Influenza viruses infect pigs or poultry, and from these sources, mutant viruses become contagious to humans. These animal viruses can be transferred from animals to humans even without a mutation. This has so far been the case of the Influenza A virus subtype H5N1 that, to date, only infected farmers in close contact with birds.

ANIMAL CONFINEMENT

Although farmers are at risk of developing respiratory diseases from outside exposure, the most frequent cause of respiratory problems comes from their work inside animal housing buildings. Farming evolved from a little bit of everything, from feeding a family and trading extras for other necessities to a specialized industry where animals were taken from the outdoors and densely confined in large buildings. A short drive to any Canadian farming region will provide you with multiple examples of huge building complexes, which can raise 1000 pigs, 100,000 hens or 1,000,000 barbecue chickens. Dairy barns have also grown; cows now seldom go outside to the pasture. Last year, I visited a dairy barn in northern Quebec, in...
an increased reaction to re-exposure as has been described in issue, and it seems that workers fortunately do not seem to lose advantages? We have just completed a study looking at this farmer. Are these days off long enough to lose the adaptation but the employees who spend 8 h a day, five days a week with longer the owner who works a few hours every day in his barns, ers have high levels of circulating soluble L-selectin. This environment (for eg, toll-like receptor mutation) or they adapt to from a few who are genetically equipped to tolerate this envi- ronment, doubles the number of circulating neutrophils, has a large neutrophilic influx into the nasal passages, and airways, and a transient increase in bronchial response to methacholine, frequently within the asthma range. He also and airways, and a transient increase in bronchial response to methacholine, frequently within the asthma range. He also may need a trigger, such as a viral infection, or coexposure with endotoxins or other microorganisms (bacteria or fungi). FL is a form of allergic or hyperimmune response to inhaled bacteria- or mould-containing dust found in poorly conserved hay, grain or straw. Moulding occurs when these farm products are stored at too high a humidity level (above 15%); humidity allows lactobacillus growth. This results in heating of the material, which in turn favours the growth of thermoactinomycetes. SR (formerly known as Micropolyspora faeni or Polyspora polys- spona), the bacteria most commonly associated with FL, is a thermoactinomycetes. This is the bug that Dr Jack Pepys described as the causative agent of FL. There is no doubt that this actinomycete (SR for short) is implicated in most cases of this disease. It is actually remarkable that humans, let alone pigs, can tolerate any prolonged exposure to some of these buildings. The air within contains as many as 10^9 viable bacteria identified by culture per cubic metre. A worker breathes and thus filters 12 times this volume in an 8 h workday. The norm for an office is less than 10^3. We now know that the number of bacteria recovered by culture represents only 10^-3 of the total number of bacteria present. This is explained by the fact that many bacteria are dead and that the milieu and cul- ture environment used is inappropriate for most of the airborne bacteria present.

It is not that these bacteria cause infections; the vast major- ity are not pathogens. What hits the lungs is their toxins: endotoxins, peptidoglycans and other potentially toxic or immunogenic substances. Until recently, it was believed that the ill effects of swine building exposure was caused by Gram- negative bacteria and their endotoxins. A recent study by Dr Caroline Duchaine and her colleagues confirmed that over 95% of bacteria in swine buildings are Gram-positive, mostly Archaeobacteria. Gram-positive bacteria do not produce endo- toxins, bu do produce peptidoglycans that could also be quite harmful.

When a normal, previously unexposed individual spends between 4 h and 6 h in a swine building, he develops an acute inflammatory response, doubles the number of circulating neutrophils, has a large neutrophilic influx into the nasal passages and airways, and a transient increase in bronchial response to methacholine, frequently within the asthma range. He also produces high levels of proinflammatory cytokines such as tumour necrosis factor, interleukin-6 and interleukin-8. Farmers who work in this environment also have increased numbers of neutrophils in their airways but of much lower magnitude, and most importantly, they seldom have an increase in their circulating neutrophil or cytokine levels, or airway hyper-responsiveness. Either farmers are selected out from a few who are genetically equipped to tolerate this envi- ronment (for eg, toll-like receptor mutation) or they adapt to it. The latter is the most likely. We have shown that pig farm- ers have high levels of circulating soluble L-selectin. This could block the signal to increase neutrophil recruitment. If tolerance is the result of an adaptation process, how long does the adaptation last? With ever larger operations, it is often no longer the owner who works a few hours every day in his barns, but the employees who spend 8 h a day, five days a week with off days and vacations, something unheard of for the traditional farmer. Are these days off long enough to lose the adaptation advantages? We have just completed a study looking at this issue, and it seems that workers fortunately do not seem to lose their adaptation after four days of nonexposure. We did not see an increased reaction to re-exposure as has been described in cotton workers, a rebound called ‘Monday morning fever’. Although farmers seem to adapt to the swine buildings, work- ers do have a high prevalence of chronic bronchitis and some have mild airflow obstruction and cross-shift decline in their forced expiratory volume in 1 s.

The air in poultry houses can also contain large quantities of organic dusts composed of feed particles, dander, bacteria and gases. Dust levels and characteristics are different whether the animals are caged or whether the birds are free to move around. Fortunately, very few workers are exposed to this envi- ronment, but because of the small number of workers involved, little information is available on the short- and long-term effects of this exposure.

Of all farm animals, horses are probably the safest to house. Granted, one can be allergic to horses, but horse barns should be quite safe. The main reason for this is that horses them- selves are very sensitive to mouldy hay. They have a very high tendency to develop heaves, an asthma-like syndrome caused by an allergy to Saccharopolyspora rectivirgula (SR). Because of this, hay, grain and straw produced for horses have to be very clean. Horse breeders will only use hay that is produced late in season when drying conditions are usually much better than when hay is made for cows (mid-July versus mid-June). Basically, what is good for the horse is good for the farmer.

GRAIN HANDLERS

Grain handlers in western Canada show some cross-shift decrease in their forced expiratory volume in 1 s and forced vital capacity, but this usually does not lead to significant lung function loss over time.

SPECFIC DISEASES

FL

Hypersensitivity pneumonitis (HP) (also known as extrinsic allergic alveolitis), seen in dairy farmers, typically represents respiratory ailments of farmers and is simply called ‘farmer’s lung’. It is the earliest and best described respiratory health risk of the profession. Ramazzini described a lung disease that typi- cally defines FL as early as 1713. We owe to Dr Jack Pepys the scientific description of FL in the late 1950s. He and his col- leagues found that the cause of this disease was a bacterium that grows in mouldy hay. He may have been only partially right because we now believe that FL, like other forms of HP, may need a trigger, such as a viral infection, or coexposure with endotoxins or other microorganisms (bacteria or fungi).
response to multiple antigens than farmers without the disease. In a mice model, we have described an enhanced response to SR after a transient Sendai virus infection. The enhanced response persists long after the viral infection per se. Most farmers exposed to SR or other microorganisms, even those who develop serum antibodies to these microorganisms, have an immune tolerance and protects them from getting FL. This immune tolerance may be disrupted by one of these triggers, or by massive exposure to the antigen. Once the hypersensitization is achieved, the subject remains highly reactive to the antigen. In this condition, the subject develops FL, which manifests itself as recurrent bouts of fever and shortness of breath, 4 h to 8 h after the exposure, thus the term delayed immune response. The capacity of diagnosing HP has been greatly helped with the advent of high-resolution computed tomography and bronchoalveolar lavage (BAL). Geographical, patchy alveolar infiltrates that predominate in the lower lung fields on high-resolution computed tomography suggest the possibility of acute HP. Of all interstitial lung diseases associated with a lymphocytic alveolitis, BAL in HP patients yields by far the higher number of lymphocytes, up to 80% of all cells recovered while, for example, approximately 40% would be expected in sarcoidosis.

FL can recur after each exposure or have a more subacute presentation without the repeated bouts of fever and chills. In both conditions, if left un checked, permanent lung damage, either emphysema or fibrosis, or a combination of both, will likely occur. The only medical treatment for FL is oral corticosteroids. Although steroids do work in acute FL, their prolonged use is prohibited by side effects of the drug. We have recently found in a mouse model of FL that nicotinic receptor agonists may become a new class of drugs to replace corticosteroids. The idea to try these agonists came from a study by Peter Warren from Winnipeg, Manitoba, who showed years ago that smokers were less likely to develop serum antibodies to SR than nonsmokers. Subsequent studies confirmed that smokers were also less likely to develop FL than nonsmokers. The active ingredient in cigarette smoke may be nicotine. Although nicotine could not be used as a drug to treat FL, there are other nicotinic receptor agonists that may be considered because they do not cross the blood brain barrier and do not cause addiction.

Because of the major health and frequent financial impact of FL, prevention is of capital importance. Over the past 20 years, the prevalence of FL in industrialized countries has plummeted by 90%. When I started my studies on HP more than 25 years ago, FL was by far the most common type of the disease, and we saw between 13 and 20 cases each winter. Now HP accounts for only a small fraction of all HP cases, partly because other environments have been identified (eg, wood processing plants, peat moss factories, metal workers, etc) but mostly because of the decrease in its prevalence (two to three new cases per year). This decrease stems from two major factors: decrease in the number of family farms and improved methods of foliage preservation like switching from dry hay to silage or the use of better equipment to produce drier hay.

Asthma
What about asthma? Three types of asthma have been described in farmers: occupational asthma, asthma-like syndrome and reactive airway dysfunction syndrome. Occupational asthma is generally of the high molecular weight type caused by an immediate type 1 allergic response to animal dander (cows and pigs), barn mites, or grain, feed or hay allergens. Asthma-like syndrome is caused by exposure to large quantities of organic dust, which contains bacteria and fungi. Endotoxins are usually blamed for this syndrome, although recent studies suggest that they may not be the sole cause. When mice tracheal smooth muscles are exposed to swine building dust, an increased response to methacholine is induced. When the endotoxin from this dust is removed, the hyper-responsiveness goes away, but when the dust only has pure endotoxin nothing happens. A hypothesis for this observation is that a combination of endotoxin and something else in the swine building dust act synergistically; what that other substance(s) is (are) is currently unknown. Reactive airway dysfunction syndrome can occur after a massive exposure to toxic gases. An example of this is exposure to poorly ventilated swine building dunk pits.

However, the news about asthma is not all bad. Many studies with farm children support the ‘dirty baby’ hypothesis. Children exposed in early life to farm buildings have less atopy and asthma than nonexposed controls. Endotoxin exposure in early life may favour a Th1 lymphocyte phenotype profile, thus protecting from type 1 allergic responses. This information led some to suggest that Jesus in his wisdom had told us that exposure in early life in a manger was good for your health. It took us over 2000 years to understand that message.

Silo filler’s disease and organic dust toxic syndrome
Silo!: One cannot talk about respiratory health risks of farmers without talking about silos. Silos come in different sizes, shapes and forms, and are built to store grass, corn or other types of grain.

A silo can be a deadly place. Fortunately, farmers are now aware of this danger and only accidentally get caught. The most dangerous time to go into a silo that contains grass or green corn is within a month to six weeks after its filling. Silage contains large quantities of nitrogen, especially with the use of nitrogen-rich fertilizers to grow the grass or the corn. Shortly after harvest, some of this nitrogen is oxidized into the very toxic nitric oxide. This gas of brownish colour is denser than air and thus sits on top of the silage like a cloud. Exposure to this cloud can result in immediate death by asphyxiation due to a lack of oxygen or by toxic bronchoalveolitis known as silo filler’s disease. Approximately 20 years ago, five (or was it six?) members of the same family died in a silo in Ontario, one after the other trying to save a family member. Unfortunately, it took tragedies like that to solve the problem by education. Now, farmers who need to go into a silo will ensure proper ventilation or use appropriate respiratory protective equipment before entering. Silo filler’s disease is less dramatic but can lead to a slower death by respiratory failure. Usually, the patient will eventually recover; the only treatment is that of ventilatory support given as needed.

Silos are also places where moulds abound. Typically, moulding occurs on the top of the silage and in pockets of air that form within the silage, especially if stored too dry. Farmers are at risk of exposure to these moulds when they are volatized during silo unloading or cleaning before their refill. Decapping a mouldy silo can create a cloud of organic dust that will induce an acute toxic response known as organic dust toxic syndrome (ODTS) when inhaled. ODTS was formally known as mycotoxicosis, but the name was changed when it became
known that the mouldy material contained not only fungi but also different bacteria, including SR. ODTS can be quite dramatic with high fever and excruciating cough. Fortunately, the syndrome subsides over a few days without leaving significant sequelae. Bronchoscopy performed during the acute phase shows inflamed airways, and if BAL is performed, a large number of neutrophils is obtained. BAL performed a month later will reveal normal airways and a mild lymphocytic alveolitis, probably part of the healing process.

CONCLUSION
Despite the above-mentioned respiratory health risks, farmers generally have good lungs, perhaps because of their lifestyle. The prevalence of cigarette smokers in Canadian farmers is approximately one-half that of the general population.

In conclusion, I believe it is fair to say that when a farmer consults for respiratory problems, the context of his work environment need to be taken into account in establishing an accurate diagnosis. Most farmers with acute FL are treated with multiple antibiotics for what is initially taken as a respiratory infection before the diagnosis is even suspected. More often it is the farmer, not the doctor, who will come up with that hypothesis. A few years previously, I did a small survey of dairy farmers and family physicians in farming communities. I was astounded to find that farmers knew much more about FL then their doctors.

SUGGESTED READING: