# Respiratory disease in Canadian First Nations and Inuit children

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First Nations and Inuit Children are disproportionately affected by respiratory infections such as viral bronchiolitis, pneumonia and tuberculosis. Rates of long-term lung disease following severe respiratory infections early in life, such as bronchiectasis, are also elevated. In contrast, rates of asthma may be somewhat less than in other Canadian children, although rates of poor asthma control are increased. Causes for the high rates of infections include poverty, overcrowding, housing in need of major repairs and better ventilation, and increased exposure to environmental tobacco smoke. Improving these issues will require addressing the social origins of health in First Nations and Inuit communities, including poverty and employment, building more and improving existing housing, and will likely require developing enhanced immunization and surveillance strategies.

**Key Words:** *Aboriginal; Asthma; Bronchiolitis; Indigenous; Inuits; North American; Pneumonia; Tuberculosis; Viral*

## Les maladies respiratoires chez les enfants inuits et des Premières nations du Canada

Le nombre d'enfants inuits et des Premières nations atteints d'infections respiratoires comme la bronchiolite virale, la pneumonie et la tuberculose est disproportionné. Le taux de maladies pulmonaires à long terme après de graves infections respiratoires contractées tôt dans la vie, telles que la bronchiectasie, est également élevé. Par contre, le taux d'asthme serait quelque peu inférieur à celui des autres enfants canadiens, même si le taux de mauvais contrôle de l'asthme est plus marqué. Ces forts taux d'infections s'expliquent, entre autres, par la pauvreté, les maisons surpeuplées, les habitations qui ont besoin de réparations majeures et d'une meilleure ventilation et par une exposition accrue à la fumée du tabac dans l'environnement. Pour atténuer ces problèmes, il faudra s'attaquer aux origines sociales de la santé dans les communautés inuites et des Premières nations, soit la pauvreté et l'emploi, la construction d'un plus grand nombre d'habitations et l'amélioration des habitations existantes, et il faudra probablement élaborer de meilleures stratégies de vaccination et de surveillance.

Along with depression, suicide, nonintentional trauma, childhood obesity and diabetes, respiratory diseases are among the medical conditions whose incidence are most strikingly increased in Canadian First Nations (FN) and Inuit (FN/I) infants, children and youth (1). Disproportionate rates of respiratory disease are not necessarily present for all respiratory illnesses; while rates of infection and their complications are markedly increased, asthma may be less prevalent (although rates of poor asthma control are increased). The present article will review the epidemiology and risk factors of the most important respiratory conditions affecting Canadian FN/I children.

Because a PubMed search (details available on request) returned no articles specifically reporting on the pharmacological management of respiratory conditions in Aboriginal children and youth, it was assumed that management is analogous to other paediatric populations and, therefore, will not be discussed in the present review. It is important to note that coverage of certain medications for FN/I individuals may require special approval from Health Canada.

## VIRAL BRONCHIOLITIS AND PNEUMONIA

Bronchiolitis is most commonly due to the respiratory syncytial virus (RSV) (2). Viral infection often involves the airways and interstitium; as a result, viral bronchiolitis and pneumonia are often considered together (3). Inuit children living in Baffin (Qikiqtani) Region, Nunavut, have the highest known rates of RSV bronchiolitis requiring hospitalization, with rates up to 484 per 1000 infants in the first year of life (4), versus 27 per 1000 infants in temperate Canada and the United States (5). Rates for young Navajo and White Mountain Apache are intermediate, at 64 per 1000 infants (6). Bronchiolitis is unusually severe in Inuit infants, with 12% of infants admitted to the Qikiqtani Region's hospital in Iqaluit (Nunavut) requiring air transport to a paediatric intensive care unit in southern Canada (4). Inuit and Alaska Native (AN) children often experience repeated, severe RSV infections in the same season, which is unusual elsewhere (7). FN children in Manitoba have also been reported to experience unusually severe bronchiolitis and pneumonia due to adenovirus (8). Most recently, FN/I children and adults were disproportionately affected by the 2009 Influenza A/H1N1 pandemic, including increased admissions to paediatric intensive care units (9).

Multiple factors are likely involved. Second-hand environmental tobacco smoke (ETS) exposure is a known risk factor for bronchiolitis (10). While 9% of Canadian children (overall) were exposed to ETS in their homes in 2006 (11), airborne nicotine was elevated in 95% of houses of Inuit infants (12). Undernutrition may also play a role (13). Overcrowding is common in both FN reserves and Inuit communities. Forty-nine per cent of Inuit children and 26% of FN children living on-reserve live in crowded homes (14), compared with 3% of Canadian children overall (15). Indoor ventilation rates are below recommended Canadian residential standards in approximately 80% of houses in Qikiqtani Region, Nunavut (16). Both overcrowding and reduced ventilation are important risk factors for bronchiolitis and pneumonia in Inuit infants (16). Houses on many FN reserves do not have fresh running water (17). In Alaska, lack of potable water has been associated with an increased risk of respiratory infections in children, probably because hand washing is reduced (18). In communities where wood-burning stoves are used, emissions may be associated with an increased risk of lower respiratory tract infection in Aboriginal children (19). Gas space heaters and kerosene heaters are associated with an increased risk of cough and wheeze in infants (20).

It has been hypothesized that reduced innate immunity may also be involved, with peoples in Asia, Europe and Africa 'sharing' and thus developing some immunity to prevalent pathogens for millennia. Meanwhile, indigenous peoples in the New World have been isolated, leading to severe epidemics following exposure to

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immunologically 'novel' pathogens, such as measles and smallpox in South American indigenous peoples in the 1500's (21), Spanish Influenza in the Inuit in Labrador in 1918 (22), and Influenza A/H1N1 in FN individuals in northern Manitoba in 2009 (23). Whether Aboriginal people in North America have a genetic predisposition to respiratory infections is controversial. Indigenous infants in the Pacific Ocean Islands (24) and North America (8) seem to have particular difficulty with adenovirus bronchiolitis and pneumonia, but this could be related to other factors. Detailed testing has not found specific immune defects or mucociliary transport disorders in these populations (25-27). One possible genetic condition, which may be present in Inuit infants on west Baffin Island and the east coast of the Northwest Territories, as well as FN children in Manitoba, is idiopathic swallowing dysfunction leading to recurrent aspiration of oral feeds (28). We have observed that some of these children also have a type 1 laryngeal cleft. Other factors that may increase the risk of aspiration and lower respiratory tract infection in FN/I children include bottle propping (28) and bottle caries (29).

When managing bronchiolitis in this population, the use of thickened feeds should be considered, because these children may be at increased risk of oral aspiration (28,30). Consideration should be given to early medical evaluation at a larger centre for children living in isolated settings. Infants with lobar atelectasis should be carefully followed to ensure re-expansion of the affected lobe. Inuit infants appear to have a particular predilection for right upper lobe atelectasis (31). If radiographical evidence of atelectasis persists for four to six weeks, consideration should be given to urgent bronchoscopy to remove any mucous plugs and re-expand the lobe, to prevent permanent fibrosis and/or bronchiectasis (32). FN/I infants with recurrent episodes should have their swallowing function evaluated with a video-fluoroscopic swallowing study performed by a radiologist and an occupational therapist (28).

Preventive measures include restricting smoking to outdoors (not in an enclosed porch or furnace room), ensuring that wood stoves are properly sealed and maintained, and the use, when feasible, of a heat recovery ventilator to improve indoor ventilation, which has been shown to reduce the risk of wheezing illnesses in young Inuit children (33). A detailed guide to optimal use of wood stoves is available from the Canada Mortgage and Housing Corporation web site (www03.cmhc-schl.gc.ca/catalog/productDetail.cfm?cat=3&itm=94&lang=en&fr=1332604751406). Breast feeding should be encouraged (34), and bottle propping should be discouraged. Palivizumab prophylaxis has been shown to be effective in AN infants with traditional risk factors for severe RSV infection, such as prematurity and bronchopulmonary dysplasia (35). The Canadian Paediatric Society has suggested that palivizumab should be considered for use in term Inuit infants (36). Reducing rates of severe bronchiolitis remains challenging for multiple reasons. Rates of severe RSV bronchiolitis vary significantly throughout Inuit Nunangat (Canadian Inuit lands) (37). Severe bronchiolitis may be caused by a variety of respiratory viruses, including influenza virus and adenovirus. Ultimately, controlling this problem will likely require multiple interventions, including enhanced immunization strategies, improvements in housing, reductions in ETS, and amelioration of current economic and social disparities (33).

## BACTERIAL, FUNGAL AND PARASITIC PNEUMONIAS

Bacterial pneumonia due to *Streptococcus pneumoniae* is more common in Aboriginal children in Alaska and the continental United States than among other American children, even after vaccination programs have been introduced (38-40). The risk factors are analogous to those for bronchiolitis. Severe bacterial pneumonia may follow viral infection, such as influenza (41). Tachypnea is a useful predictor of pneumonia and a chest radiograph, when available, should be obtained to confirm the diagnosis, because crackles are nonspecific (42). Aboriginal children should be monitored closely for the development of parapneumonic effusions and empyema, which are more common in this population (43). Prevention, using appropriate immunizations, is essential (39,44).

Giant hydatid lung cysts and pneumonitis due to *Echinococcus* species have been reported in FN children living in northwestern Canada (45). Dog exposure is likely an important risk factor. Blastomycosis in rural northwestern Ontario and the Eastern Prairies (46), histoplasmosis in the St Lawrence (47) and Ottawa River valleys, *Cryptococcus gattii* in rural Vancouver Island (48) and hantavirus in unused buildings contaminated by deer mice in western Canada (49) occasionally cause pneumonia in children, particularly in rural areas. Subclinical histoplasmosis is often followed by calcified hilar nodes and pulmonary nodules that are easily confused with previous tuberculosis (TB) infection (50).

## TB

TB rates remain distressingly elevated in FN/I children and adults – particularly among the Inuit. In 2005, TB rates were 5.0 per 100,000 among the general Canadian population and 26.8 per 100,000 in Aboriginal people (11). Rates are rising in the Inuit, and were 157.5 per 100,000 persons in 2008 (51). In Canada, 21% of TB cases in Aboriginal people occur in children 15 years of age and younger, in contrast to 6% in Canadian-born, non-Aboriginal people (52).

TB infection is closely related to poverty (52) and overcrowding (53). Reduced ventilation is a key risk factor for TB transmission (54). Canadian research in FN communities observed that the rate of TB was 18.9 per 100,000 in communities with 0.4 to 0.6 persons per room and 113 per 100,000 in communities with 1.0 to 1.2 persons per room. An increase of $10,000 in community household income was associated with one-quarter of the risk (53). Mycobacterial genotyping in Nunavik found that cases were clustered, although significant transmission between communities also occurred (55).

The Canadian National Advisory Committee on Immunization recommends Bacille Calmette-Guérin (BCG) vaccination for infants in FN/I communities or groups of people where the average annual rate of smear-positive pulmonary TB is more than 15 per 100,000 people (all ages) in the previous three years, or where the annual risk of TB infection is more than 0.1%, if early identification and treatment of TB infection is not available (52).

FN/I children are routinely vaccinated with BCG in the Northwest Territories and in Nunavut (52). Among FN/I youth, previous BCG vaccination may complicate Mantoux skin test interpretation, although large reactions are usually due to TB exposure or infection (52). Control of TB in these populations will require addressing poverty, overcrowding and inadequate home ventilation, as well as improved surveillance and treatment strategies.

## BRONCHIECTASIS

AN populations have the highest rate of bronchiectasis in the world (24,26). The great majority of cases follow severe bronchiolitis or pneumonia occurring early in childhood (57) – most often due to RSV or adenovirus (24). Rates are likely similar in Canadian Inuit. In FN children, severe adenovirus infection may also lead to pulmonary fibrosis and bronchiolitis obliterans – a

condition characterized by permanent scarring of the bronchioles and distal airway obstruction, leading to chronic wheezing that is unresponsive to bronchodilators. Imaging typically demonstrates a hypolucent lung secondary to concurrent destruction of the pulmonary vasculature (24). As the child grows, the affected lung fails to grow well, and it remains small and hypolucent as a result (in contrast to hyperinflated lungs, which are hypolucent but large). This finding, known as Swyer-James syndrome, is closely associated with adenovirus infection in indigenous populations (58).

FN/I children with chronic productive cough or wheeze unresponsive to asthma therapy and/or persistent pulmonary abnormalities (increased bronchial markings, dilated bronchi, and/or permanent atelectasis and fibrosis) should be evaluated for these conditions using computed tomography scanning. Many patients will have a combination of bronchiectasis, fibrosis and/or adjacent areas of bronchiolitis obliterans (24,58). Patients with bronchiectasis should be evaluated for immune deficiency and aspiration (see Bronchiolitis, above). FN/I children with bronchiectasis are usually chronically infected with *S pneumoniae* and/or nontypable *Haemophilus influenzae* (57). Vaccination for *S pneumoniae* and influenza with the polysaccharide (23-valent) vaccine, are recommended.

## PROTRACTED BACTERIAL BRONCHITIS

Aboriginal Australian and AN children have been reported to have a high prevalence of chronic, wet cough due to protracted bacterial bronchitis. This condition has been postulated to be a predecessor of bronchiectasis in these populations (59). The prevalence in Canada is unknown. Bacteria associated with this condition have been reported to include *Streptococcus pneumoniae*, nontypable *Haemophilus influenzae* and *Moraxella catarrhalis* (59).This condition may be associated with first-hand cigarette smoking (60), which is disturbingly common among FN youth; 26% of FN children and 70% of young adults living on-reserve report smoking, compared with 15% of Canadian youth in general (11). Protracted bacterial bronchitis has been reported to respond to a two- to six-week course of antibiotics targeting the relevant bacteria, although some patients are reported to require several courses of therapy (59).

## ASTHMA

In contrast to respiratory infections, rates of asthma in FN/I children are not clearly higher when compared with other Canadian children and might possibly be lower. Current data, obtained using a variety of methods, are conflicting. The reported prevalence ranges from 5.7% (61) to 12% (62) in Alberta FN children, compared with approximately 10% of non-Aboriginal Canadian children (61). An older study, using an abbreviated exercise protocol, found that Inuit schoolchildren from Nunavik had a lower prevalence of exercise-induced bronchospasm than children living in Montreal, Quebec. Obstructive pulmonary defects were present in 7.7% of these children, but this may reflect the effects of previous respiratory infections and differing body habitus as well as asthma. Only 5.3% of the Inuit children were atopic (63) compared with approximately 34% of Canadian children in general (64). The lack of high rates of pulmonary dysfunction and asthma later in life, given the high rates of severe respiratory infection early in life (4), is difficult to fully explain. It may be partly related to body habitus – an anthropomorphic evaluation of Inuit and northern Manitoba FN children observed that they have disproportionately longer trunks and shorter legs (65); therefore, pulmonary function results using norms based on Caucasian children may be artificially high (66). Lower rates of asthma and allergies is congruent with the 'hygiene hypothesis', which suggests that increased microbial exposure early in life shifts the developing immune system toward a T-helper cell (Th1), cell-mediated bias, rather than a T-helper cell (Th2) humoral immune system bias, reducing production of immunoglobulin E antibodies (67). In support of this, as living conditions in Greenland have become more 'urban', rates of atopy have increased (68). While asthma may be less common, rates of poor asthma control requiring emergency department visits are elevated in FN children in Alberta (69). In general, asthma likely continues to be both over- and underdiagnosed in both non-Aboriginal and Aboriginal Canadians (70).

In young children, it is important to distinguish bronchiolitis from asthma. Thick oronasal secretions can cause transmitted upper airway sounds, which are often mistaken for 'wheezing' by families and health care professionals (71). Repeated episodes of wheezing that respond to asthma therapy supports a diagnosis of asthma.

FN/I children have increased exposure to a variety of contaminants that can increase the risk of developing asthma, which are asthma triggers in individuals with established asthma, including ETS exposure (12). Studies have shown that 29% of housing on Canadian FN reserves (72) and 32% of houses in Nunavut (73) are in need of major repair(s). Lower household income, houses in need of major repairs and older housing has been associated with a higher risk of asthma in Aboriginal children (74). Poorly constructed or maintained housing can lead to loss of the vapour barrier, allowing areas of dampness that are prone to contamination with mold (75,76). Problems with mold vary among communities due to differing local environmental conditions. Mold may be a particular problem in reserves where houses are prone to flooding and/or were built in damp, low-lying areas and is prevalent in coastal British Columbia, where high outdoor humidity levels promote mold growth (77). In contrast, mold appears to be uncommon in some other reserves, such as the Elsipogtog Reserve in New Brunswick (78), and in the Arctic, where indoor humidity levels are low (12), inhibiting mold growth. However, even in the Arctic, self-reported mold problems are common, affecting 20.8% of households with children in Inuit Nunangat and 33.6% in Nunatsiavut (79). Indoor mold can cause allergies and asthma in children allergic to mold. Mold also increases the risk of wheezing in young children, possibly by releasing various fungal toxins. Outdoor molds can also cause allergies and asthma in children allergic to these molds. *Alternaria* species grow in rotting leaves and can cause severe asthma attacks, especially in the fall (80). While pets such as dogs and cats and indoor dust mites can cause allergies, the Inuit and most FN families do not keep dogs indoors. In Nunavut, houses are usually not carpeted and indoor clutter levels and humidity levels are low, discouraging the growth of dust mites (12). In some communities, outdoor air pollution may also be a concern. Forest fires can cause serious asthma exacerbations and worsen asthma symptoms and lung function (81). Summer road dust is an annoyance in many communities, but its exact effects on lung function are not well understood.

Adherence, as in other populations where rates of poverty and depression are increased, is sometimes an issue. Families that are disorganized, impoverished or depressed may have difficulty giving medications regularly (82). One study involving members of an American Navajo tribe indicated that they can view asthma in a child as "a series of distinct, transient episodes" rather than a chronic disease with recurrent flares. This view could impede adherence to long-term, preventive therapies (83). Barriers should be approached with respect and sensitivity and education provided in a context relevant to the family.

## SUDDEN INFANT DEATH SYNDROME

Recent Canadian research found an RR of 7.15 for sudden infant death syndrome in Inuit-inhabited parts of Canada, compared with

the rest of Canada (84). FN/I infants may be more likely to be exposed to a variety of risk factors for sudden infant death syndrome (85), including bed sharing with a parent who smokes cigarettes or is intoxicated, and a higher bedroom temperature (12,85). Carnitine palmitoyltransferase 1A deficiency is more common in FN/I infants and is a known cause of hypoglycemia, hepatic encephalopathy and sudden, unexplained infant death (86).

## CONCLUSION

Respiratory morbidity and mortality remain unacceptably high among FN/I children. Improving the respiratory health of Canadian Aboriginal children will require enhanced disease surveillance and vaccination and, most importantly, addressing the social origins of health, such as income and employment, which in turn affect housing, rates of cigarette smoking and other determinants of respiratory disease.

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