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## **An Update on a Strategy for Work-related Asthma in Ontario**

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## **Introduction**

Occupational disease accounts for significant morbidity and mortality in Ontario workers. Despite this, occupational disease receives less attention than occupational injury in health and safety efforts. Work-related asthma (WRA) and other occupational respiratory diseases are of particular interest amongst occupational diseases. Approximately 10-25% of adult asthma is related to work (Kogevinas et al, 2007; Tarlo, 2014). Many Ontario workers are exposed to potential lung sensitizers and irritants. Thus there is potential for significant respiratory disease in the province. Despite this, it is known that there is underrecognition of work-relatedness of asthma (To 2011; Holness 2007). Given this, there is a clear need for an occupational lung disease strategy in Ontario.

In 2010, an Occupational Disease Strategy was developed for Ontario with a vision to eliminate occupational disease in the province. Immediate priorities included noise-induced hearing loss, hand-arm vibration syndrome, occupational respiratory conditions and occupational dermatitis. Strategy reports were prepared by various authors at that point addressing these 4 occupational diseases, including a report on work-related asthma (WRA) by this author.

## **Prior Work-Related Strategy (2012)**

This paper is an update on that previous strategy report addressing new and current needs of occupational respiratory disease in the province. This author previously prepared a strategic plan addressing WRA in Ontario in a report dated March 5, 2012. That report considered the current state, the gaps and needs and the short and long-term strategies for the six key objectives listed above. The development of that plan was conducted through a consultation meeting with various stakeholders. The meeting brought together stakeholders from across the health and safety landscape in Ontario to understand various perspectives on WRA. From this meeting, a strategic plan was developed to better address WRA in the province. There was representation from governmental organizations (Ministry of Labour, Ministry of Health and Long-Term Care), compensation (WSIB), health care providers (OHCOW, St. Michael's Occupational Health Clinic, respirologists, occupational medicine physicians, OOHNA), academia (Queen's University, University of Toronto, McMaster University), unions (OFL, ONA, OPSEU, UFCW, CEP), health and safety organizations (CCOHS, WSPS, WSN, IHSA, PSHSA), public Health (Ontario Agency for Health Protection and Promotion), and health organizations (Ontario Lung Association).

That process was useful in bringing together diverse health and safety stakeholders with unique perspectives and provided insight into this facet of occupational disease in the province. It was recognized that the effective management and eventual elimination of work-related asthma in Ontario would require the *collaborative effort of various stakeholders across the health and safety environment*. The solutions will not be found solely in the medical world or health and safety environment, but rather with all groups working together. Thus the strength of the previous consultative process was to bring together stakeholders with various perspectives and engage them in understanding and developing strategy objectives in WRA.

## **Methods**

This update builds on the prior strategy with incorporation of recent literature on WRA. There is considerable amount of material published in the medical literature on WRA. While there are many issues in WRA that have been explored, this review considered more recent literature

and new or novel aspects of WRA. This strategy update builds on the prior strategy of 2012 but does not re-articulate those prior findings. The reader is encouraged to refer back to the prior strategy report of 2012 for the outcomes from the consultative meeting.

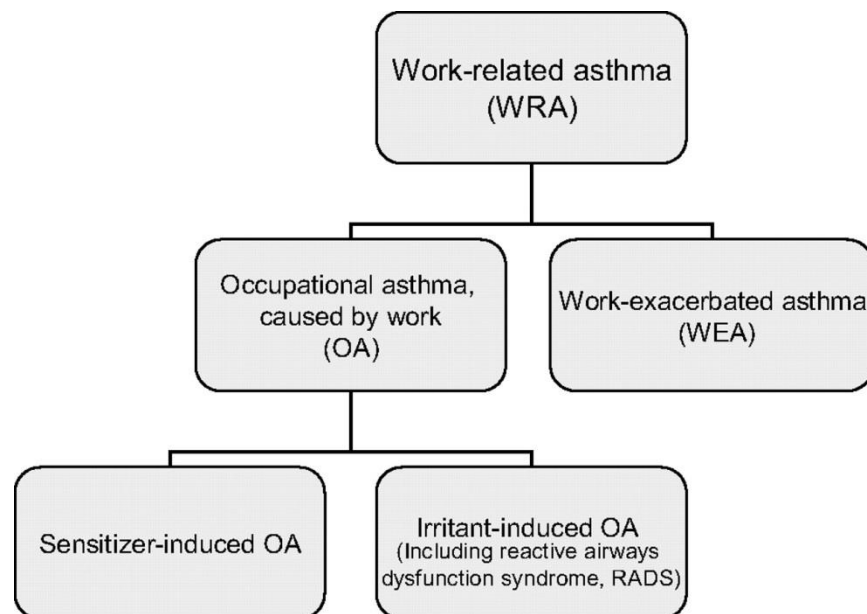
The strategy issues are considered in the conceptual framework developed by the Ontario Occupational Disease Strategy in 2010. This framework considers six key objectives in improving disease prevention:

1. Focus on reducing harmful exposures
2. Establish appropriate reporting and surveillance mechanism
3. Ensure maximum use of best evidence
4. Improve education and awareness
5. Target priority diseases, exposures, and industries
6. Promote ongoing engagement and strategic partnerships.

### Background

A significant proportion of adult asthma is related to work. Review articles suggest that the prevalence of WRA is approximately 10-25% (Kogevinas, 2007; Malo, 2007; Tarlo, 2011, Tarlo 2014).

WRA is a broad diagnostic classification that includes sensitizer-induced occupational asthma, irritant-induced asthma and work-exacerbated asthma. The following demonstrates a commonly used schematic for the classification of WRA (Tarlo et al, 2008):



These groupings are not mutually exclusive; e.g. OA can be followed by WEA

Sensitizer-induced occupational asthma is the new-onset of asthma due to a lung allergen/sensitizer in the work environment. It is type of WRA that is most often considered as the “classic presentation”. Sensitizer-induced asthma constitutes approximately 45% of WRA. Conventional high molecular weight (HMW) substances may cause OA, often by an IgE mechanism. However, there are even a number of low molecular weight (LMW) antigens that may similarly lead to OA, although the specific mechanism is not clearly understood (Tarlo, 2014).

Irritant-induced occupational asthma (IIA) is typically considered to be the development of asthma after a single, high level exposure to a respiratory irritant in the workplace. It is relatively rare, representing approximately 5% of WRA. The definition was initially based on the report by Brooks et al (1985) of reactive airways distress syndrome (RADS). However the case definition has expanded over time (see discussion below).

Work-exacerbated asthma considers those with pre-existing asthma who develop worsening of their symptoms in the work-place. This constitutes approximately 50% of work-related asthma.

Recognition of the appropriate subtype of WRA is vital as there are distinct differences in the epidemiology, pathophysiology, clinical course, management and prevention of the various types. For instance those with a clear sensitizer-induced asthma need complete avoidance of the offending agent. This often necessitates profound workplace restrictions, such as removal from work. However those with the other subtypes of asthma (e.g. IIA and WEA) may continue in the offending environment provided exposures are engineered down to manageable levels.

### **Reviews on WRA**

There are a number of position papers and reviews on WRA. Understanding of the basics of epidemiology, etiology, diagnosis, management and prevention of WRA. This paper will not explicitly articulate the basis of WRA that can be found in these papers. Important reviews on WRA can be found here:

#### Work-related asthma and occupational asthma

Tarlo SM, Balmes J, et al. Diagnosis and management of work-related asthma: ACCP Consensus Statement. *Chest* 2008; 134: 1S-41S.

Tarlo SM, Lemiere C. Occupational asthma. *N Engl J Med* 2014; 370: 640-9.

#### Irritant-induced occupational asthma

Tarlo SM. Irritant-induced asthma in the workplace. *Curr Allergy Asthma Rep* 2014; 14: 406.

#### Work exacerbated asthma

Henneberger PK, Redlich CA, et al. An official ATS statement: work-exacerbated asthma. *Am J Respir Crit Care Med* 2011; 184: 368-7.

Vandenplas O, Wiszniewska M, et al. EAACI position paper: irritant-induced asthma. *Allergy* 2014; 69: 1141-53.

## **Objective 1: Focus on reducing harmful exposures**

Once a patient has developed WRA and particularly sensitizer-induced OA, their prognosis is quite poor (Rachiotis et al, 2007). Tertiary prevention (i.e. medical treatment) of WRA is ineffective at properly managing this disease. As per well-known prevention dogma, there is significantly greater advantage in ameliorating exposures by primary prevention. Thus there needs to be an emphasis on reducing respiratory allergens and irritants in the workplace so that lung sensitization does not occur. Relevant exposures and how they are controlled depend greatly on the type of WRA. For sensitizer-induced OA in particular, it is imperative that identification, recognition and control of sensitizing agents be made.

### *Sensitizer-induced OA*

According to Tarlo and Liss (2005), “OA is potentially preventable”. In a review paper, they document primary, secondary and tertiary prevention efforts across various industries. There were relatively few studies that described prevention strategies in WRA. Primary prevention methods clearly focus on control of harmful exposures, including:

- Identification and relocation of highly susceptible workers from areas with exposure to known sensitizers;
- Use of engineering controls, such as elimination, substitution, ventilation, housekeeping or change in work practice;
- Administrative controls to reduce number of workers exposed or duration of exposure;
- use of personal protective equipment.

The authors cite examples in the literature whereby primary prevention was measured in healthcare, detergent enzyme, foam-making and dairy industries.

There are a myriad of exposures that may cause sensitizer-induced OA. Historically, these substances have been classified as high molecular weight and low molecular weight sensitizers (Tarlo, 2014). High molecular weight agents tend to be protein-based agents which may intuitively cause asthma or hypersensitivity. Examples include animal dander, latex, flour grains and enzymes. Most of these reactions are thought to involve an IgE-mediated sensitivity. The pathophysiology of low-molecular weight sensitizers in causing asthma is not clearly understood (Tarlo 2014). Low-molecular weight agents include isocyanates, metals (such as chromium and nickel), and formaldehyde. The distinction between high- and low-molecular weight allergens is important in assisting in recognition of causative agents.

Despite understanding of the importance of sensitizers, there can be issues with the proper identification of such agents in the workplace. Santos et al (2007) found that the lack of knowledge of the Workplace Hazardous Materials Information System and lack of awareness of sensitizing agents in the workplace contributed to delay in identifying work-relatedness of asthma.

Tarlo and Malo (2013) reported on ATS proceedings from the Fourth Jack Pepys Workshop on Asthma in the Workplace. Participants suggested that prediction of sensitization potential of different substances may be done by a “computerized quantitative structure-activity program”. MSDS sheets were felt to be “insufficient and inaccurate”. The authors cited high proportion of isocyanate sheets that did not mention asthma. There is a lack of safety education and training for workers. Further exploration into the mechanisms of irritants in causing OA should be explored.

While Canadian standards require clear identification of sensitizers on MSDS reporting systems, this does not always happen. Liss (private correspondence) found that even one of the most egregious sensitizers (isocyanates) was not always listed as a sensitizer on MSDS. Thus there should not be complete reliance on this system to identify sensitizers. It may take some sophistication to understand workplace exposures. In the diagnosis of WRA, health care providers may need to rely on additional resources such as occupational hygienists, health and safety specialists or workplace resources. Recognition of potential relatedness by temporal patterning with work or presence of potential sensitizers is helpful. However clinical history has a low positive predictive value.

While inhalation exposure is clearly the most important route of allergy induction, there is evidence that skin exposures may also be of significance. Arrandale et al (2012) reported on the association between occupational contact allergens and OA. Of the ten most common skin sensitizers, seven were found to be potential causes of OA. It is speculated that lung sensitization may occur from either dermal or respiratory exposure. The authors advocate for consideration of both dermal and inhalation exposures in evaluation of patients with OA. Nayak et al (2014) published an animal study on the toluene diisocyanate deposition and sensitization in dendritic cells of mice. This demonstrates the potential immune sensitization through skin exposures of TDI.

One of the success stories in exposure reduction has involved the mitigation of sensitization in health care workers due to latex exposures. Liss et al (2011) attribute low rates of OA in health care workers as being partially due to successful prevention efforts in this industry. Kelly et al (2011) report on the effectiveness of latex elimination in reducing risk of sensitization in health care workers.

*Irritant-induced asthma*

The pathogenesis of IIA is not completely understood. Takeda et al (2009) reported on bronchiolar lavage and bronchial biopsies of 10 patients with acute IIA. They found significant eosinophilic and neutrophilic inflammation many years after exposure. While a toxic exposure was responsible for initial presentation, there were persisting changes consistent with an allergic response.

There are a myriad of irritant agents that may cause IIA. Theoretically, the list of potential irritants may be long as occupational exposures in many industries include many irritants. However the literature includes preponderance of IIA in some industries. Such industries are more likely to expose patients to the clinical circumstances necessary to cause IIA, namely sudden, acute, high-level exposures. However more recently IIA has grown to also encompass those with lower-level, persistent exposures over time. As a result, it would be expected that more agents will be identified with this expanded clinical picture.

Important etiological agents include the following, as adapted from Vandenplas et al (2014).

Category	Examples
Gases	Chlorine (e.g. released by mixing sodium hypochlorite with acids), chloramines (released by mixing sodium hypochlorite with ammonia) sulfur dioxide, nitrogen oxides, dimethyl sulfate

Acids	Acetic, hydrochloric, hydrofluoric, and hydrobromic acids
Alkali	Ammonia, calcium oxide (lime), hydrazine
Biocides	Formalin, ethylene oxide, fumigating agents, insecticides (sodium methyldithiocarbamate, dichlorvos)
Halogenated derivatives	Bromochlorodifluoromethane (fire extinguisher), trifluoromethane, chlorofluorocarbons (CFC) (thermal degradation products of freons), orthochlorobenzylidene malonitrile (tear gas), uranium hexafluoride, hydrogen and carbonyl fluoride
Solvents	Perchloroethylene
Fumes	Diesel exhaust, paint fumes, urea fumes, fire smoke, fumes of iodine and aluminum iodide, diethylaminoethanol (corrosion inhibitor)
Sprays	Various paints (not specified), floor sealant (aromatic hydrocarbons)
Dusts	World Trade Centre alkaline dust, calcium oxide (lime)
Potential sensitizers	Isocyanates, phthalic anhydride

#### *Work-exacerbated asthma*

Work-exacerbated asthma is often caused by inhalation exposures. This may include a variety of irritant exposures and also respiratory allergens. Beyond inhalation exposures, WEA may be induced by environmental factors including heat, elevation and cardioaerobic activities (Henneberger, 2011). Many different agents may be associated with WEA, although few studies have been published on the matter. Exposures often include irritants, although sensitizers may also exacerbate an underlying asthma. Henneberger (2011) list studies on exposures that may cause WEA. They suggest the following themes: many different factors may contribute to WEA, exposure factors outside of work may also cause work-related worsening (such as second-hand smoke), and occupational health standards seem inadequate in preventing WEA.

There have been attempts to identify a link between work stress and asthma. Heikkila et al (2014) report on a meta-analysis of 11 studies examining the relationship between job strain and asthma exacerbations. They did not find a significant association between job strain (high demands plus low control at work) and severe asthma exacerbation. Lavoie et al (2014) performed psychiatric evaluations on 219 consecutive patients under investigation for OA. They applied the Primary Care Evaluation of Mental Disorders (PRIME-MD), the Whiteley Hypochondriasis Index (WI) to assess clinical levels of hypochondriasis, the Beck Depression (BDI-II) and Beck Anxiety (BAI) Inventories, and the Anxiety Sensitivity Index (ASI). Mood or anxiety disorders were 2 to 4 times greater in these patients than in the general population. Rates of psychiatric conditions were similar between those receiving and not receiving a diagnosis of OA. However hypochondriasis was more common in the undiagnosed group. The authors advocate for psychiatric considerations be made for patients undergoing work up for OA.

## Gaps/Needs

- A. New sensitizers are continually being recognized in the workplace
- B. Respiratory sensitizers are often unrecognized by workers, health care professionals and employers
- C. Material Safety Data Sheets (MSDS) may not provide a complete indication of the presence of sensitizers
- D. Potential etiologic agents of IIA are vast and likely under-characterized
- E. WEA may be caused by inhalation exposures, but also other environmental exposures such as heat, cold and cardioaerobic activity
- F. Psychological factors may contribute to WRA
- G. There is no clear resource that easily identifies asthma-causing agents
- H. Major sensitizers or high risk industries need to be clearly identified
- I. There is a need of improved engagement in the workplace in addressing WRA
- J. Need for better recognition of occupational hygienist in preventing WRA

## Strategies/Actions

### *Short Term:*

- Improve education of workplace stakeholders  
Workers, workplaces, unions, health and safety representatives and other workplace stakeholders need to understand the etiology and implications of a sensitizer-based condition such as WRA. As primary prevention is typically outside of the health care realm, education efforts should focus on workplace parties to make a difference in their work environment. Education of workplaces on asthma sensitizers requires up-to-date information on lung sensitizers. Thus there needs to be continual consideration of the medical literature to identify new allergens.
- Improve recognition of agents that may contribute to WEA  
As WEA is recognized under compensation in Ontario but work-relatedness of underlying asthma and potential exacerbating exposures are often neglected. There needs to be improved awareness of WEA and education on the myriad of potential agents that may worsen pre-existing asthma.
- Improve recognition of important exposures pertaining to IIA  
Regarding IIA, identification of important irritant exposures needs to be improved. In particular, there are high risk industries (e.g. cleaning industry) for which potential exposure circumstances should be addressed. Education on exposure mitigation in IIA should be a short-term goal.
- Ministry of Labour blitzes on asthmagens  
The Ministry of Labour (MOL) plays an important enforcement role in managing exposures in the workplace. Given the nature of WRA, causative agents and industries can be anticipated. These industries should be targeted for inspection and enforcement of allergen exposure control.
- Evaluate and improve MSDS system in identifying sensitizers  
Federal Hazardous Product legislation requires the clear identification of respiratory sensitizers in a product. Reports suggest that there are inadequacies in the identification of



sensitizers in MSDS. These gaps in MSDS accuracy must be addressed. Worker education should partially focus on this system in assisting in exposure identification.

- Collaboration in messaging  
The same agents that cause WRA are often associated with occupational dermatitis (Arrandale et al, 2012) and rhinitis. There should be collaboration across prevention efforts (regardless of disease state) in advocating for exposure reduction in the workplace.

*Longer term:*

- Further research into skin sensitization as a cause of WRA
- Further research of the role of psychological factors in contributing to WRA
- Enhance regulatory management of sensitizers in the workplace
- Co-ordinate prevention and education efforts with health and safety associations, clinics (such as OHCOW), Workers Health and Safety Centre to better develop education and management options
- Regulation requiring employers to review MSDS for the presence of allergens/asthmagens
- Ensure worker understanding, access and utilization of MSDS
- Improve regulatory standards
  - Look at other OELs/TLVs from other countries beyond ACGIH
  - Apply OELs to all workers/sectors
- Enhance resources that will assist in product substitution
  - Research on developing less toxic/hazardous substitutes
  - Develop a wiki/database of viable cost effective substitutions
  - Develop a “toolbox” for finding asthmagens in the workplace: directed at a JHSC level
- Promote the profession of industrial hygiene
  - Improve industrial hygiene access and utilization for industries
  - Provide industrial hygiene resources via resources such as OHCOW

## Objective 2: Establish appropriate reporting and surveillance mechanism

While definitive information on the incidence and prevalence of WRA remains elusive, there is clearly a measurable burden of this work-related disease worldwide. Given the large size of the worldwide workforce and the long duration of the illness, there will continue to be a considerable number of new (incident) and existing (prevalent) cases each year.

Reporting and surveillance of WRA can provide useful information on high risk industries, exposures and disease trends. Given the short latency of disease and the ability to impact the natural course of respiratory disease, preventive activities can be reactive and may be immediately directed in important directions. Surveillance mechanisms also provide longitudinal data to assess effectiveness of preventive strategies.

Surveillance systems have further attempted to estimate the incidence of WRA. Incidence data is helpful in understanding the occurrence of new cases. As opposed to prevalence data, the incidence is not affected by disease duration. Incidence is more difficult to measure and often requires effective surveillance systems to report new cases. The following table lists incidence estimates from various asthma surveillance system findings worldwide.

Study	Country	Incidence (cases/million-year)
Kwon et al (2015)	Korea	3.31
Mazurek et al (2013)	United States	179
Hannaford-Turner et al (2010)	Australia	5
Bakerly et al (2008)	UK	42
McDonald et al (2005)	UK	20-111
Ameille et al (2003)	France	24
Esterhuizen et al (2001)	South Africa	17.5
Karjalainen et al (2000)	Finland	174
Kogevinas et al (2007)	Europe	250-300

These data indicate considerable variability in the measured incidence of WRA. This may reflect actual variations in global burden of WRA based on industry or exposure. Certain regions may have more industry or more workplace exposures to sensitizers. However, it is likely that measuring issues (e.g. lack of reporting, diagnostic challenges, variability in asthma definitions) of such surveillance programs account for some variability in the measured incidence of asthma. It should be apparent that accurate measurement of the incidence of WRA is challenging.

Understanding the public health implications of WRA is difficult given the variability of data on disease occurrence around the world. Gender differences and willingness to report work-related conditions were cited as reasons for discrepancy of data (Tarlo and Malo, 2013).

Studies have indicated the difficulties in developing accurate reporting systems. Efforts were made in Ontario to develop a surveillance system for WRA. To et al (2011) describe the difficulty in instituting a surveillance/reporting system in the province. They describe the engagement of 49 physicians in Ontario to report this condition. There were 34 cases of OA and 49 cases of WEA reported. The authors suggest that it is feasible to implement a voluntary reporting system, but question its long-term sustainability. Tarlo (2013) discuss the difficulties

of using large population databases to measure the occurrence of WRA. They suggest a high propensity towards under-reporting due to lack of recording of occupation in such databases, making work linkages difficult.

Regarding WRA incidence in new workers, Kellberger et al (2014) studied work-related sensitization in early work life. They followed a cohort from childhood (9-11 years) to adulthood (19-24 years). They found that occupation in early adulthood had no effect on the development of asthma. Rather, sensitization in childhood, parental asthma, environmental tobacco smoke and gender were important factors in the incidence of asthma.

Many studies have tried to estimate prevalence of WRA. Review articles typically suggest a prevalence of 10 to 25% of asthma as being related to work. Given that asthma occurs in approximately 10% of the adult population, work-related disease represents a measurable fraction overall in this lung disease. The range of prevalence measures may be due to true geographic differences in WRA (due to varying density of industries, exposure to sensitizers, predilection to atopy, etc.) or may be due to systematic variation of measurement (differences in asthma definitions, diagnostic methods, etc.).

A number of more recent studies continue to attempt to estimate the prevalence of WRA in medical practice. The prevalence of WRA was studied by Vila-Rigat et al (2014). They applied a WRA screening questionnaire to 368 asthmatic patients in a primary care setting in Spain. The prevalence of OA was 18.2% with a further 14.7% having work exacerbated asthma. Anderson et al (2014) examined a database of individuals in Washington State from 2006 to 2009, considering the relationship between occupation and asthma. The prevalence of asthma was 8.1%. Various occupations were associated asthma, notably teachers, administrative workers and health services. Few individuals discussed potential work-relatedness with their health care providers. Reeb-Whitaker et al (2013) evaluated isocyanate-related asthma in a database of WRA in Washington State. The majority (81%) were OA whereas the minority (19%) were WEA. 48% of cases occurred in the painting industry with 22% from foam manufacturing. Two cases seemed to be associated with dermatological exposure. Six cases seemed to occur from indirect exposure. Henneberger et al (2011) describe the prevalence of WEA to be 14 to 21.5% depending on the case definition of WEA.

Accurate reporting requires consistent and agreed-upon diagnostic criteria and case definitions for the different types of WRA. While the ability to diagnose sensitizer-induced OA may be challenging, the case definition is relatively well recognized. However, there is some inconsistency in the definition of IIA and WEA.

#### *Definition of IIA*

Irritant-induced occupational asthma generally consists of the development of reversible airway obstruction due to a single, high level of an irritant agent. This was generally consistent with the definition of reactive airways dysfunction syndrome (RADS) as described by Brooks (REF). Brooks described a condition with the following points:

1. sudden, high-level exposure to known irritant,
2. onset of symptoms within 24 hours,
3. new onset of reversible airflow obstruction,
4. persistence of symptoms beyond 3 months.

Generally, this RADS definition was considered to be the defining description of IIA. However, over time, there have been case reports of IIA inconsistent with this RADS definition. Notably, reports of IIA have been described for those with:

1. non-acute exposures. Asthma has been reported after repeated, low-level exposure to respiratory irritants.
2. latent disease. Notably, cases of IIA have occurred months after World Trade Centre exposures suggesting a prolonged latent period for development of airway obstruction (Banauch et al, 2005).

Thus the definition of IIA asthma has been expanded in recent times, although there remains disagreement as to recognition of atypical presentation of IIA. Most epidemiology is based on case reports, suggesting a lack of methodological rigour. It may be that other factors, such as pre-existing predilection, could be responsible for lung disease. Tarlo and Lemiere (2014) review these points, suggesting that a “spectrum” of irritant exposures may lead to asthma, while recognizing the difficulty and validity in assessing the various types of irritant exposures.

Vandenplas et al (2014) published a position paper on irritant induced asthma by the European Academy of Allergy and Clinical Immunology (EAACI). They identify the historical beginnings of the diagnosis from the definition by Brooks et al (1985) of reactive airway dysfunction syndrome (RADS). This definition originally considered an onset of asthma within a few hours of a single high-level exposure to irritating fumes. However, this position paper describes an important issue in the definition of IIA, namely the expanded definition of this clinical disorder. Most classically, IIA has been considered to occur from a single high-level irritant exposure, relatively consistent with the definition proposed by Brooks et al (1985). This remains the most common presentation of IIA, often termed “acute-onset IIA”.

Beyond this typical definition, case reports by Tarlo and Broder (1989) and Chan-Yeung et al indicate the development of asthma after repeated exposure to high-level irritants. There is repeated symptomatology with each exposure. However, diagnosis of asthma and fulminant symptoms are delayed. This EAACI position paper suggests the term “sub-acute IIA” for such presentations.

Further controversy stems from presentations of asthma after repeated, chronic exposure to more moderate levels of irritants. Six case studies were presented to describe asthma in those with repeated, often daily, exposure to moderate irritant exposures. Linking these conditions with causative occupational exposures can be difficult. Evidence of work-relatedness includes: i) adult onset of asthma, ii) chronic exposure to irritants; and iii) absence of a sensitizer in the environment.

Understanding these variable presentations of IIA, Vandenplas et al (2014) suggested that establishing a diagnosis of IIA varies across the clinical presentations of this entity. IIA from a single, high-level exposure to irritants (‘acute-onset IIA’) can be diagnosed with a high level of confidence and should be considered to be “definite IIA”. Those with a history of multiple, symptomatic, high-level exposures (‘sub-acute IIA’) should be considered to be “probable IIA”. Those with chronic, moderate irritant exposures should be considered to be “possible IIA”.

Diagnosis of IIA begins with identification of asthma by conventional means (e.g. reversible airflow limitation on spirometry, positive methacholine testing). Other conditions should be ruled out. A diagnostic algorithm is best depicted by Vandenplas et al (2014). Associating asthma with exposure requires careful occupational history and identifying temporal patterning of symptoms with exposures.

The following are important differentiating features of IIA and sensitizer-induced OA:

1. Those with IIA do not develop symptoms after re-exposure to low concentrations of the agent as they are not sensitized to the agent.
2. There is typically no latency period between exposure and disease with acute-onset IIA.

Differentiating sub-acute or chronic, moderate exposure IIA from WEA can be challenging. There are no specific diagnostic tests that might aid in this differentiation.

#### *Work-exacerbated asthma*

WEA should be considered for any asthmatic who has worsening of their symptoms. Initial step involves confirmation of a diagnosis of asthma. The next diagnostic step involves the identification of symptom patterning with work-place exposures. This may be done by symptom diary tracking, medication tracking or objective testing such as peak flow measurements. Concurrent with this is identification of non-work related factors. Occupational asthma should be ruled out.

However, the significant prevalence of asthma in society and the wide variety of potential exacerbating factors make the consistent identification of WEA challenging.

Henneberger et al (2011) propose the following case definition for work-exacerbated asthma:

#### Criterion 1:

Pre-existing or concurrent asthma. “Pre-existing asthma” is asthma with onset before entering the worksite of interest. The “worksite of interest” can be a new job or changes in exposures at an existing job due to the introduction of new processes or materials. “Concurrent asthma” or “co-incident asthma” is asthma with onset while employed in the worksite of interest but not due to exposures in that worksite.

#### Criterion 2:

Asthma–work temporal relationship. It is necessary to document that the exacerbation of asthma was temporally associated with work, based either on self reports of symptoms or medication use relative to work, or on more objective indicators like work-related patterns of serial PEFr.

#### Criterion 3:

Conditions exist at work that can exacerbate asthma.

#### Criterion 4:

Asthma caused by work (i.e., occupational asthma) is unlikely.

#### Gaps/Needs

- A. There is a lack of accurate disease registries in WRA in the province
- B. There are inconsistent mechanisms for measurement and reporting of all types of WRA
- C. There needs to be agreement on the classification and diagnostic criteria for IIA
- D. Similarly, there needs to be agreement on the classification and diagnostic criteria for WEA

## Strategies/Actions

### *Short Term:*

- Develop consistent case definitions of IIA and WEA  
Accurate and reliable surveillance of WRA requires a consistent recognition of all asthma subtypes in all regions. As described above, there is some inconsistency in the definition and diagnostic criteria for IIA and to a lesser extent WEA. There should be efforts to establish an agreed-upon case definition for these 2 important subtypes of WRA.
- Develop expertise from international experience  
There are a number of asthma surveillance programs around the world. These would provide a basis on which to develop a similar program in this province.
- Develop WRA surveillance in Ontario  
There should be a surveillance/reporting system for WRA in Ontario. This would require improved case-identification. While To et al (2011) describe the difficulty of establishing such a system in the province, they do identify some of the success in establishing such a system. Proper tracking of WRA requires reliable identification of disease status. While To's system depended on physicians to report cases, it may be more effective to improve database reporting and extraction to obtain this information. There is currently no standardized coding system that is consistently used to identify patients with WRA. It would be helpful to establish a usable method to ascertain disease status from existing reporting systems. This may involve integrating disease coding with OHIP/billing requirements or exploring the use of ICD 9/10 categorization in classifying this subset of asthma.
- Improve exposure and occupational coding deficiencies in medical reporting  
As well as disease identification, it is necessary to understand exposure or etiology of WRA. This would require coding of specific exposures, presumptive causative agents or occupation (as a surrogate of exposure). Exposure may be most simply integrated with current databases by improving occupation/exposure coding in current medical databases (e.g. EMR's).
- Shared expertise with existing occupational databases  
Exposure information is being developed for carcinogens by CAREX, a multidisciplinary team of researchers based out of UBC. Collaboration with this group may assist in the development of asthmagen tracking.

### *Longer term:*

- Use of GIS/Geomapping in developing surveillance mechanisms  
Alternative methods of surveillance may simplify surveillance of WRA. Exposure mapping through GIS may be coupled with asthma disease databases to track WRA trends.
- Encourage physician understanding and reporting of WRA to assist in improved case finding
- Continued reporting and review of WRA incidence and prevalence in the medical literature to better understand worldwide epidemiology of this disease
- Implement WRA tracking in electronic medical records, with reliance on improved diagnostic information and exposure information
  - integrate into existing EMR software
  - integrate within other asthma database tracking

### **Objective 3: Ensure maximum use of evidence**

There are many new and emerging issues in WRA. There is extensive research into this occupational disease, with particular expertise in Ontario. As with all medicine, an evidence-based approach to WRA should be the foundation of ongoing efforts to understand this condition. This allows for a valid, scientific approach towards identifying sensitizers, diagnosing and managing patients, and instituting prevention strategies in the workplace. We need to continue to foster the research agenda on WRA and apply that knowledge to the identification, management and prevention of this occupational disease.

New sensitizing agents are being identified all the time. These are continually being reported in the medical literature. As well, there are periodic publications of review documents and databases which collate the information on potential sensitizers. While it is beyond the scope of this document to thoroughly review the literature on new sensitizers, it is useful to identify important review articles, databases or other similar resources.

#### Resources on occupational respiratory sensitizers

Web-based databases may assist in identifying known respiratory allergens.

1. Baur and Bakehe (2014)  
This recent review provides an evidence-based listing of allergens that may cause OA. The authors list allergens, estimated strength of evidence and estimated number of asthma cases per agent.
2. [www.hse.gov.uk/asthma/asthmagen.pdf](http://www.hse.gov.uk/asthma/asthmagen.pdf)  
The Health and Safety Executive in the UK published this review of potential workplace sensitizers. The document was last updated in 2001. It provides an evidence-based listing of various exposures
3. [www.occupationalasthma.com](http://www.occupationalasthma.com)  
A UK group has assembled resources including a searchable database of WRA references. This site also includes OASYS, a program which assists in the analysis of serial peak flow measures.

#### *Effectiveness of asthma management in WRA*

Effectiveness of management strategies has been rarely studied. Meijster et al (2011) published a report on theoretical modeling of intervention strategies in baker's asthma. They compared the effectiveness of such programs as pre-employment screening, occupational surveillance and hygiene intervention. The authors found that most interventions had little effect on decreasing respiratory morbidity. Only a "rigorous health surveillance strategy" consisting of identifying sensitized workers and those with upper respiratory symptoms and decreasing their exposure by 90% had a substantial effect on disease burden.

Quirce et al (2013) examined the utility of an asthma control measurement tool (Asthma Control Test or ACT) in the setting of WRA. The ACT questionnaire was a self-administered 5-item measure. They applied this tool to 33 OA and 14 WEA patients. They found that this ACT tool could document work-related asthma control.

#### *Screening*

Evidence should be used to evaluate the effectiveness of medical surveillance to screen for WRA. Surveillance may also occur at a patient level: early identification of asthma is vital in

separating the worker from the sensitizing agent. Surveillance programs in the workplace facilitate secondary prevention and allow for early diagnosis of respiratory impairment in affected workers. Medical surveillance in WRA may be particularly effective as pulmonary function testing allows for objective evaluation of respiratory changes in asthma.

Tarlo and Liss (2005) reviewed the literature on primary, secondary and tertiary prevention of OA. With respect to secondary prevention efforts, they cite reports from the platinum, isocyanate and enzyme industries. The authors suggest that secondary prevention efforts may be successful in decreasing risk of OA. Surveillance methods typically included symptom questionnaire, skin prick testing and spirometry. An off-shoot of such surveillance programs would seem to include enhanced awareness and control of sensitizers, leading to primary prevention.

Wilken et al (2012) reviewed the effectiveness of medical screening and surveillance pertaining to work-related asthma. They found 72 papers which dealt with the issue. These studies considered both pre-employment screening and medical surveillance while working. Evaluation of effectiveness was limited as most studies considered the diagnostic approach of their programs rather than effectiveness. The authors make various recommendations including:

- use of a questionnaire-based tool for surveillance
- pre-placement screening for sensitization for those in higher risk jobs with HMW allergens
- utilization of specific IgE or SPT for surveillance of those regularly exposed to HMW allergens
- consideration of pre-employment investigations in atopic individuals or asthmatics
- risk stratification by diagnostic models may be used in surveillance to identify those needing further investigation

Redlich et al (2014) provide standards report on spirometry in the occupational setting. This provides an evidence-based consensus on the proper methods of airflow measurement occupational surveillance.

Vandenplas et al (2014) discuss basic principles of prevention of IIA. Identification, management and elimination of irritants remain the mainstays of prevention. Alarm systems may help to identify excessive exposures. Worker education empowers workers to understand and avoid harmful exposure situations. Regarding secondary prevention, medical surveillance is not useful in mitigating acute IIA, but may be helpful identifying sub-acute or chronic IIA.

There is a significant lack of understanding of the pathogenesis of IIA. Human and animal pathology studies are needed to describe the acute and chronic pathologic response. This would be useful for effective preventive strategies. Clarification of sub-acute and chronic presentations of IIA will assist in the proper identification of irritant-associated asthma. There is suggestion that predictive biomarkers may be helpful in identifying IIA (Vandenplas et al, 2014). Given the subjective nature of the diagnosis of this condition, there is a need for better tests for diagnosing IIA.

The use of newer methods of diagnosis remains sporadic and varies across centres, depending on availability of testing. Lemiere (2014) describes the use of nitric oxide and sputum induction in assisting in the diagnosis of WRA. While the availability and use of these novel diagnostic methods varies around the world, they remain potentially useful adjuncts to the



diagnosis of WRA. Merget et al (2015) report on the use of exhaled nitric oxide (eNO) as a serial measure (at home and at work) in assisting with the diagnosis of OA. They found that eNO showed patterning with work exposures whereas FEV1 and symptoms did not show such trends. Jonaid et al (2014) studied exhaled nitric oxide in spray painters exposed to isocyanates. They found a “marginally significant” dose-reponse relationship between isocyanate exposure and eNO. The authors suggest the eNO may indicate increased airway inflammation in those exposed to isocyanates.

### Gaps/Needs

- A. Need for ongoing research into all facets of WRA
- B. Need for the application of the precautionary principle
- C. Ongoing need for the identification of new and emerging allergens in WRA
- D. Evaluation of management strategies of WRA
- E. Evidence-based approach to medical surveillance of asthma
- F. Consideration of novel methods of asthma diagnosis
- G. There is a lack of understanding of pathogenesis of disease

### Strategies/Actions

#### *Short Term:*

- Support researchers in the province  
Ontario has world-class researchers in the field of WRA. There should be ongoing support of this research so that best evidence may be developed and disseminated in the province. There should be an attempt to extend the legacy of this research expertise by encouraging and engaging new researchers.
- Support of research and reporting of new and emerging respiratory sensitizers  
New sensitizers and being continually identified and reported. Literature reports on new sensitizers allows for an evidence-based approach of the identification of causative agents. Given the volume of such issues, there needs to be reliance on the various review articles and databases of sensitizers. Dissemination of up-to-date information on sensitizers is of great importance to Ontario workplace stakeholders.
- Exploration of new methods to assist in diagnosis  
Novel diagnostic tests may assist in identification of WRA. Induced sputum and eNO have been studied in some centres as an adjunct to asthma diagnosis. There have been some developments on these methods in the province and this exploration should continue.

#### *Longer term:*

- When implementing best evidence, need to ensure outcomes /effectiveness are being measured
- Evaluation of management strategies should be encouraged to ensure that best evidence guides treatment decisions
- Medical surveillance can be effective in early identification of WRA. Appropriate surveillance strategies should be based on current evidence describing secondary prevention programs.

- Effectively disseminate information on sensitizers to all stakeholders, particularly workplace parties
  - Develop ways to be proactive – identification new/emerging sensitizers vs. reactive; action alerts
- Support research efforts to understand the pathogenesis of OA, IIA and WEA
- Develop resources on WRA:
  - Ontario-based repository of credible evidence that is sector or exposure based
  - Application of knowledge translation strategies/tools to get best practice asthma guidelines in practice
  - Develop resource/tool with common themes to guide workplace parties/practitioners – e.g. triggers that cut across sectors
  - Develop tools (e.g. questionnaires) for JHSCs to use to identify WRA: put the ability in the hands of the workers/workplaces to identify asthma
  - Translate scientific jargon into plain use of lay/language for use on shop floor

#### **Objective 4: Improve education and awareness**

Despite the high burden of morbidity associated with WRA, there is a relative lack of recognition and understanding of this condition (Holness 2007). Screening for potential work-relatedness is often lacking. Mazurek et al (2014) reported on patient-physician communication about WRA. Considering 50 433 adult, ever-employed asthmatic patients from an American surveillance system, only 14.7% had discussed the role work may have played in contributing to their asthma. This small proportion indicates that WRA is not adequately discussed/considered in asthmatic patients.

Poonai et al (2005) found that the mean time to diagnosis of WRA in an Ontario study was 4.9 years, despite a length of time from symptom onset to symptom reporting was only 0.61 years. They identified important barriers in the identification of work-relatedness. Parhar et al (2011) describe the barriers encountered by respirologists in recognizing or reporting work-relatedness. Important factors include time constraints and knowledge. Moscato et al (2014) performed a survey of occupational awareness amongst allergists in Italy. They found that reporting to workers' compensation, specific challenge testing and job modification recommendations were deficient. The authors concluded that WRA is neglected by allergists in Italy.

Further, there is often delay from consideration of work-relatedness to diagnosis. Lemiere et al (2015) looked at 434 patients with WRA at a specialty clinic in Quebec and 131 patients at a patient in Ontario. The delay from onset of symptoms to diagnosis was 4.3 years in Quebec versus 4.7 years in Ontario. There was a significant decrease in asthma-related health care utilization in both provinces.

Education efforts in WRA need to be improved for both health care providers and workplace stakeholders. Health care providers play a key role in the identification of WRA. There is a current underreporting of this disease and educational efforts need to focus on improving recognition and reporting. Further, health care providers need to be better equipped to diagnose and manage WRA. Workplace stakeholders need to be able to identify respiratory sensitizers in the workplace, understand the implications of workers with WRA and most importantly understand their role in preventing WRA by eliminating exposures.

Screening tools have been developed to improve recognition of the work-relatedness of asthma. Killorn et al (2014) reported on the utility of a WRA screening questionnaire (WRASQ(L)) in primary care in Canada. They compared this 14 item questionnaire with existing questions in the existing Asthma Care Map (ACM). The study sample (n=37) consisted of mainly females (73%) with a median age of 46.3 years. The WRASQ(L) questionnaire identified work-related symptoms in 38% patients and important exposures in 60% more than the ACM would have. The authors concluded that the WRASQ(L) provided additional information about potential WRA. The authors acknowledged limitations in incorporating the questionnaire into clinical practice.

Enabling patients to identify important work-related etiologies has also been explored. A web-based resource was developed to educate patients on work-related asthma. Ghajar-Khosravi et al (2013) describe the development and evaluation of this resource.

The Jack Pepys Workshop is a periodic gathering of respirologists, occupational physicians and other health care providers on WRA. It allows for the dissemination of new research and

discussion of emerging trends in WRA. Tarlo and Malo (2013) report ATS proceedings from the Fourth Jack Pepys Workshop on Asthma in the Workplace. This report considered 5 themes: public health considerations, environmental considerations, outcome after diagnosis of OA, prevention and surveillance, and other work-related obstructive airway disease. Main conclusions included: a) there is need for better comparative data on WRA between nations; b) improved preventive measures are possible but would require engagement of government for legislation in the workplace, c) need for more research on risks and benefits of reduction in exposure rather than complete elimination of exposure for subsets of WRA, d) WEA and other work-related airway diseases are underrecognized.

#### Gaps/Needs

- A. WRA is suboptimally recognized, diagnosed and managed in health care
- B. WRA is poorly recognized and prevented in the workplace
- C. Subtypes of WRA (ie. WRA, IIA) are often underrecognized
- D. There needs to be improved education efforts on WRA across the H&S sphere
- E. There is a lack of information for the most vulnerable workers (students, migrant workers, high risk industries)
- F. There is often no clear referral system or resource for patients with suspected WRA
- G. Marketing and dissemination of educational resources needs to be improved

#### Strategies/Actions

##### *Short Term:*

- Environmental scan of existing educational tools on WRA  
There is an abundance of educational tools on WRA. An environmental scan of existing tools/methods is needed to identify credible and effective resources that can be referenced.
- Development of an electronic resource on materials pertaining to WRA  
In this electronic age, there is a plethora and perhaps over-abundance of educational material on almost any topic. There are many educational materials on WRA. There needs to be an accessible, credible and sustainable resource, such as a website, that would collate the volumes of material on WRA. While there are multiple websites today, these tend to be fragmented and region specific. Resources, initiative and collaboration are required to develop such a resource.
- Dissemination/implementation of existing educational materials  
Dissemination efforts are clearly required to get tools into the hands of health care providers and workplace stakeholders. There is an immediate need to develop a marketing strategy for current programs/ resources, which may focus on few key target industries. Recognizing the evolving nature of information, the development of a media campaign on WRA should focus on social media (e.g. Twitter, Facebook communication, YouTube materials).
- Support of the WRA Project of the Asthma Plan of Action  
The MOHLTC funds the Asthma Plan of Action, a multifaceted program to address asthma in the province. Recognizing the role occupation may play in asthma, the program supports a WRA Project to educate workers, workplaces, health care providers, etc. on WRA. There should be continued support of this project to advance education on WRA in Ontario.
- Integrate EMR prompts for WRA

There are interesting efforts to incorporate automatic prompts into primary care EMR's. Given the relative ubiquity of EMR's in Ontario and the important role primary care physicians play in asthma recognition, an effective tool could heighten recognition of work-relatedness in asthmatic patients.

- Improve referral streams for health care providers  
Health care providers may be frustrated by a lack of expertise and referral resources on WRA. Providing the primary care physician with knowledge on WRA is of little use in the absence of respiratory referral sources or occupational clinics. There is a need to development of a management/referral algorithm that would provide practitioners with practical information on resources available in the province. This may include provincial support of less conventional health care resources such as nurse practitioners, certified respiratory educators or industrial hygienists
- Improve education of WRA subtypes  
While OA is traditionally considered to comprise most of WRA, there are other important subtypes that should be understood. Workers, employers, and health care providers should understand that WEA comprises almost half of WRA and that it is compensable in the province.

*Longer term:*

- Educational energies should be directed at workers. The individual patient will take particular interest in promoting their health. Tools (such as that mentioned above) that allow patients to identify work-relatedness themselves could greatly augment recognition of work-relatedness
- Integration of WRA in all relevant educational environments
  - Traditional groups = medical schools, residencies, nursing schools, occupational hygiene
  - Non-traditional groups = RT/RE education, H&S training, high risk professions
- Collaborate with educators to best understand adult education
- Consider all platforms of knowledge transfer: internet-based, didactic, telemedicine
- Consider resources for vulnerable groups:
  - Develop multilingual/simple hazard information materials
  - Young worker education
  - Small businesses, e.g. hair salons
- Educate employees/employers on rights and responsibilities

## **Objective 5: Target priority diseases, exposures, and industries**

### *High risk industries*

Given the nature of OA, high risk exposures and industries can be identified. There are clearly occupational exposures that are more likely to induce an asthmatic response than others. Understanding the causes of WRA and exposures in Ontario workplaces will allow us to anticipate those at risk and direct interventions accordingly. It is efficient use of resources to target high risk industries (e.g. painting, foam, baking, agriculture) and this will allow for rapid, effective and economical use of resources for those most in need.

Participants at the Fourth Jack Pepys Workshop on Asthma in the Workplace identified important themes in WRA (Tarlo and Malo, 2013). They suggested that strategies should concentrate on high risk industries, such as bakeries. Immunologic tests can play a role in secondary prevention in some circumstances. Prevention efforts should be focussed on young workers, including apprentices. Specific programs were discussed, including a web-based tool.

The literature on high-risk industries is voluminous. While it is beyond the scope of this report to review all important occupations, I will focus on two industries that provide interesting, important and representative illustrations of high-risk industries. Recent literature reports and personal experience suggest cleaners and bakers as being notable issues of WRA in the province.

Exposure to cleaning products may lead to sensitizing from a myriad of potential exposures, indicating propensity to sensitizer-induced OA. As well, it is well-regarded that cleaning agents are a common cause of IIA. There are many workers in the cleaning industry. Cleaners may have particular vulnerabilities as workers as they may be less educated, work for a small or underground employer and comprise an immigrant population with language challenges. Cleaners may be found in many industrial and commercial workforces and the issue of work-relatedness may be missed given the seemingly innocuous nature of their work. For these reasons, cleaners are an interesting and important group to focus efforts on.

There are a number of recent reports examining WRA in cleaners. Siracusa et al (2013) published a position paper of the European Academy of Allergy and Clinical Immunology on asthma and exposure to cleaning products. This consensus statement identifies high rates of asthma in this profession. Cleaners were found to experience high rates of OA, WEA and IIA. Important exposures were identified as cleaning sprays, bleach, ammonia and disinfectants (chloramine-T, quaternary ammonium products, ethanolamine). Prevention methods were emphasized.

Vandenplas et al (2013) studied asthma related to cleaning agents in a retrospective case series at a tertiary centre in Belgium. All patients had specific inhalation challenge (n=44). 39% of participants were found to have a significant reaction on SIC, indicating sensitivity. Quaternary ammonium compounds were the principal cause of reaction.

Lynde et al (2009) published on skin and respiratory symptoms in cleaners. They compared the rates of disease of these workers with other building workers. Respiratory symptoms in cleaners was related to dermatitis amongst the cleaners. The authors advocate for protective measures in this group of workers.

Liss et al (2011) examined compensation claims in Ontario for WRA. There were a total of 893 WRA claims across all industries during a 5 year period. Of these there were 645 for WEA, 99 for sensitizer-induced OA and 12 for IIA. There were only 5 claims for sensitizer-induced OA in the health care industry during that time: 2 for latex reaction and 3 for glutaraldehyde. The authors suggest that elimination of latex may be partially attributed to efforts to eliminate latex from the health care environment. There were 115 allowed claims for WEA and health care was the most frequent industry for WEA. No cases of IIA were identified in this database of compensation claims.

Gonzalez et al (2014) did a cross-sectional analysis on 543 health care workers. Risk of self-reported asthma correlated with cleaning tasks, particularly dilution of disinfectants such as quaternary compounds.

Identification of the specific sensitizing agent can be challenging. While it is intuitive that the baking industry would involve exposure to respiratory allergens, there are a number of potential culprits. This may include grains, enzymes and contaminants in the baking process (Brisman, 2002). Use of skin prick testing for such IgE-related exposures may isolate important allergens.

Wiszniewska (2013) evaluated WRA in 393 bakers who reported respiratory symptoms. 44.5% had OA; 16% had WEA. They found that specific challenge test was necessary to differentiate these two types of WRA as skin prick testing was not specific enough.

However the relationship between allergen and asthma may be complex. Baatjies et al (2014) examined the dose-response relationship between wheat allergen exposure and asthma. There was a bell-shaped response curve, with increasing allergic symptoms and probable OA increasing up to 10-15 ug/m<sup>3</sup>, after which there was a decrease.

### *Related conditions*

#### **Eosinophilic bronchitis**

Eosinophilic bronchitis is a recently recognized respiratory disorder that can mimic asthma (Brightling, 2006). It is characterized by chronic cough and eosinophilic airway inflammation. Unlike asthma, there is typically no variable airflow limitation or hyperresponsiveness. Clinically there is little response to bronchodilators. However, eosinophilic bronchitis typically responds well to corticosteroids. Sputum induction is predictably helpful in identifying airway eosinophilia.

A number of reports have identified eosinophilic bronchitis from occupational exposures. DiStefano et al (2007) describe eosinophilic bronchitis in a foundry worker and baker. The authors suggest causative agents to be isocyanates and flour, respectively. The authors suggest that induced sputum should be included as a tool in evaluating work-related respiratory disorders. Yacoub et al (2005) report on 2 workers with eosinophilic bronchitis. One worker worked at a metal part manufacturer. The other worked in a laboratory. Both had sputum eosinophilia that was worsened with specific inhalation challenge. Krakowiak et al (2005) reported on eosinophilic bronchitis in a nurse with exposure to a chloramine cleaner.

Lemiere et al (1997) reported on sputum eosinophilia in a 50 year worker exposed to acrylates. Symptoms consisted of cough and dyspnea and started within 3 months of beginning work.

Sputum induction results while at work indicate 13% eosinophils, dropping to 0% off work. A direct challenge test was done which showed increased sputum eosinophils developing 7 hours and 24 hours after inhalation test to glue. The authors conclude that “eosinophilic bronchitis without asthma needs to be considered when cough or symptoms of asthma occurring at work are not associated with evidence of variable airflow limitation”.

The role of induced sputum in occupational cohorts was reviewed by Lemiere in 2004. She suggested that airway inflammation with eosinophilia may be observed in exposed workers. While the availability of such testing is limited in many areas, such results may indicate important pathology in workers.

In a review article, Brightling (2006) suggests that “in patients with chronic cough who have normal chest radiograph findings, normal spirometry findings, and no evidence of variable airflow obstruction or airway hyperresponsiveness, the diagnosis of nonasthmatic eosinophilic bronchitis should be considered”. He further recognizes the potential importance of occupational factors, suggesting, “in patients with chronic cough due to nonasthmatic eosinophilic bronchitis, the possibility of an occupation-related cause needs to be considered”.

A review article on eosinophilic bronchitis by Gibson et al (2002) suggests that:

“Airway inflammation with eosinophils can be caused by exposure to allergens and occupational sensitizers. The triggers that cause EB without asthma are similar to the triggers of EB in asthma. Exposure to allergens, occupational chemicals and drugs are all reported to cause EB with cough.”

Quirce (2004) reviewed eosinophilic bronchitis in the workplace. He describes various case reports of occupationally related eosinophilic bronchitis. He proposes criteria for this condition, including:

- Isolated chronic cough (lasting more than 3 weeks) that worsens at work
- Sputum eosinophilia >2.5% in either spontaneous or induced sputum
- Increases in sputum eosinophilia are related to exposure to the offending agent (either at work or after specific inhalation challenge in the laboratory)
- Spirometric parameters are within normal limits and are not significantly affected by exposure to the offending agent
- Absence of airway hyperresponsiveness to methacholine (PC20 416 mg/ml) both at work and away from work
- Other causes of chronic cough are ruled out

This literature review confirms non-asthmatic eosinophilic bronchitis in working populations. Substances that cause occupational asthma seem to be able to cause eosinophilic bronchitis in exposed workers. Given the limited availability of sputum induction testing, there are only case reports in the current literature. Most authors advocate for expanded use of this sputum testing in examining workers with lung conditions.

### **Occupational rhinitis and RUDS**

While work-related asthma describes the lower pulmonary effects of occupational exposures, the upper respiratory tract may be similarly affected. Occupational rhinitis (OR) is relatively commonly encountered in clinical practice but there is little published on the matter. There are significant gaps in the understanding of identification, understanding, diagnosis, management and prevention of this condition.



There is little data on prevalence and incidence, although studies suggest that OR is 2 to 4 times more prevalent than OA (Ruoppi et al, 2004).

Moscato et al (2009) published an EAACI position paper on occupational rhinitis. Similar to WRA, occupational rhinitis may be rhinitis that is caused by occupational sensitizers or aggravated by occupational factors. A consensus diagnosis was proposed of,

“Occupational rhinitis is an inflammatory disease of the nose, which is characterized by intermittent or persistent symptoms (i.e., nasal congestion, sneezing, rhinorrhea, itching), and/or variable nasal airflow limitation and/or hypersecretion due to causes and conditions attributable to a particular work environment and not to stimuli encountered outside the workplace.”

Allergic occupational rhinitis may be due to an IgE mechanism, such as for high-molecular weight antigens or due to other, unknown mechanisms, such as for low-molecular weight substances. The authors also postulate non-allergic OR that may occur from irritant exposures. Most often this is due to single high-dose irritants with no latent period. Meggs (1994) described reactive upper airway dysfunction syndrome (RUDS), a disorder akin to IIA, but of the upper respiratory tract. Acute irritant exposure leads to a chronic rhinitis.

Many of the factors responsible for all types of WRA may similarly cause OR. The sameness of these disorders has led to consideration of “united airway disease”. This seems to hold most true for HMW agents for which there is sensitization (Vandenplas, 2005).

There is some inconsistency in diagnosing rhinitis. Documentation of nasal patency and parameters of inflammation varies considerably between centres. Diagnostic inconsistencies remain an important future need in the correct identification and management of OR. Temporal patterning with work and identification of causative agents remains a basic tenet in establishing work-relatedness.

The socio-economic cost of OR has rarely been investigated. It is likely that upper airway morbidity and cost is far less than that of lower respiratory conditions such as asthma. It is postulated that the burden of OR has its greatest impact on worsening of associated airway diseases, such as asthma and sinusitis, rather than its direct effect (Yawn 1999, Ray, 1996, Price, 2005). The ability to effectively grade the impairment and disability of OR for compensation purposes remains elusive.

Tarlo and Malo (2013) reported on discussions from the Fourth Jack Pepys Workshop on Asthma in the Workplace. It was recognized that COPD may be related to work in dusty trades. The authors suggest that there is a need for an occupational exposure history, not only a smoking history, for patients with COPD.

### Gaps/Needs

- A. Need to target high risk industries and exposures
- B. Lack of understanding, recognition, management and prevention of ancillary respiratory diagnoses, such as occupational rhinitis and eosinophilic bronchitis
- C. Lack of epidemiology on local rates of high risk industries

## Strategies/Actions

### *Short Term:*

- Ensure ongoing research, surveillance and reporting of new allergens and irritants  
Targeting high-risk industries requires an understanding of causative agents for WRA. There needs to be ongoing efforts to identify potential allergens and track industries in the province. This likely requires engagement of workplace parties and governmental agencies such as the MOL.
- Direct education, screening, diagnostic and preventive strategies at high risk industries
  - MOL inspections for at-risk industries
  - Education for workers entering high risk industries (e.g. workers entering baking industry)
  - Union and HSAs to target high risk occupations for educational opportunities
  - Develop medical surveillance strategies for those most at risk
- Educate health care workers as to high risk industries  
Health care workers need to be able to recognize potential work-relatedness in certain industries. There needs to be education of primary care physicians, respirologists, respiratory educators/therapists on important exposures and industries that may cause asthma
- Improve understanding of other related occupational respiratory diseases  
While WRA typically considers OA, IIA and WEA, there are other related respiratory diseases that should receive attention. There needs to be greater research and recognition of the role work-place exposures play in causing eosinophilic bronchitis. While it may mimic aspects of OA, eosinophilic bronchitis has distinct diagnostic and management principles. Occupational rhinitis is also similar to WRA. There may be both allergic and irritant (RUDS) etiologies of this condition. The prevalence of occupational rhinitis likely exceeds that of WRA, but it is often unrecognized. Despite the relatively low burden of disease, it is important to recognize the role occupation plays in causing rhinitis. COPD is another occupational lung disease that receives relatively little attention.

### *Longer term:*

- Develop industry-specific asthma epidemiology relevant to Ontario
- Use GIS to identify and respond to high-risk industries
- Consider multidisciplinary clinics that may service high risk industries
  - MOL inspects at-risk workplaces and activates education (WHSC) and clinical (OHCOW) interventions

## **Objective 6: Promote ongoing engagement and strategic partnerships**

Engagement of various stakeholders is necessary for effective management and prevention of WRA. The collaborative efforts of health care workers, health and safety workers, workers, employers, legislators and governmental agencies are needed to full address and prevent occupational diseases such as asthma. The prior strategic consultation meeting on WRA was a useful process in breaking down some of the barriers that separate the various stakeholders.

### Gaps/Needs

- A. Involvement of various governmental agencies: MOL, MOHLTC, MOE, WSIB
- B. Engagement of H&S agencies: Ontario HSO's, CCOHS
- C. Engagement of healthcare: specialists, primary care, occupational health nurses
- D. Engagement of workplace partners: employers, unions, workers
- E. Coordination of collaboration

### Strategies/Actions

#### *Short Term:*

- Recognition of importance of occupational disease  
Occupational disease receives less recognition than occupational injury. While it is often simple to understand the work-relatedness of acute injuries, there are many diseases that are not being identified as having an occupational association. It is likely that such diseases (e.g. asthma, dermatitis, cancers) contribute significantly to the health care burden in Ontario. There needs to be an increased effort to recognize the importance of occupational disease in the health and safety environment in the province.
- Coordination of stakeholder involvement  
Successful involvement of stakeholders requires energy, organization and resources to coordinate meetings, discussion and dialogue in bringing together the various groups. There needs to be a coordination role, perhaps housed in the MOL Prevention Office to ensure engagement by all relevant parties. Ongoing, multi-disciplinary dialogue is currently lacking and would be great stride forward in advancing the agenda of occupational disease.
- Stakeholder meetings  
It would be helpful to organize a periodic meeting of stakeholders on occupational diseases in Ontario. Face-to-face meeting of such groups is useful as they rarely have the opportunity to interact. Such meetings would help to maintain momentum in collaborative efforts to address occupational disease in Ontario.
- Develop partnerships across occupational diseases  
Work-related asthma is only one of a number of important occupational diseases. Sensitizer-induced diseases (e.g. WRA, occupational dermatitis) often affect the same industries. In order to prevent duplication of efforts for different disease states, a joint approach to occupational disease (rather than focusing on one disease at a time) would be most economical.

#### *Longer term:*

- Develop resources (e.g. websites) and communication methods (e.g. blogs, message boards) that will allow ongoing communication between stakeholders

- Consider legislative changes to develop a more collaborative approach to occupational disease: mandate multi-group involvement in dealing with important exposures
- Expand engagement to non-traditional groups: advocacy groups, education sources, vulnerable worker groups

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