Barriers to Diagnosis of Occupational Asthma in Ontario

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Rationale: Occupational asthma (OA) prognosis has been related to the duration of symptoms before cessation of exposure to a relevant sensitizer. Delays in diagnosis can delay appropriate management. This study examines factors related to delays in OA diagnosis in Ontario.

Methods: 247 chart reviews were undertaken of patients referred to Toronto Western Hospital Occupational Lung Disease Clinic for evaluation of OA from 1997 - 2001. 42 patients fulfilling OA criteria answered a structured telephone questionnaire examining chronology of medical assessments and reasons for diagnostic delays. Results: The mean duration to diagnosis was 3.4 +/- 1.9 years (excluding 4 patients with delays >13y). On average, patients waited 8 months before discussing the work-relation of symptoms with a physician. Reasons given for this delay were failure of the primary care physician to inquire about work relatedness of symptoms (41.5%), patients were afraid of losing work time (37.5%) or job loss (33.3%) . Delays related to investigations (33.3%), included patients declining a trial of work exposure with peak flow / methacholine response monitoring, or inability to perform reproducible spirometry. 10.3% had lack of workplace exposure information, work closure or employer refusal to allow a work trial, associated with significant delay in diagnosis (11.3y vs 3.3y, P=0.05). Lower education [< secondary schooling](P=0.04) and lower household income (P=0.03) were significantly associated with an increased delay in diagnosis of OA.

Conclusions: Multiple factors related to delays in OA diagnosis. Some remediable factors may include increased primary physician awareness of OA, and earlier investigations before leaving the workplace.

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The Association between Workplace Exacerbation of Asthma and Quality of Life

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Rationale: Previous asthma quality of life research has indicated that adults with asthma are not only troubled by symptoms, but also by the physical and emotional impact on their lives. Preliminary data from the baseline phase of the Workplace Exacerbation of Asthma Study were analyzed in order to determine whether those that experience workplace exacerbation of asthma also report a worse quality of life than other adults with asthma. **Methods:** Adults who were enrolled in a health maintenance organization, aged 18-44 years and had prevalent asthma were asked to complete a telephone questionnaire. A work-related symptom score and exposure score were assigned to each participant in order to determine workplace exacerbation of asthma (WEA). A validated 20-item asthma quality of life questionnaire (AQLQ) was included. A total scale score and four subscale scores (breathlessness, mood, social, and health concerns) were created. **Results:** At the time of the interview, 332 participants were employed during the previous 12 months. Of these, 24% (n=79) had experienced workplace exacerbation of asthma. Internal consistency was high for the total AQLQ scale (Cronbach's alpha=.95). Those with WEA had worse quality of life scores, but the difference was not statistically significant (Wilcoxon rank sum test, Z=1.74, p=.08). The health concerns subscale was worse for those with WEA (Wilcoxon, Z=2.36, p=.02). **Conclusions:** These preliminary data suggest that a relationship might exist between WEA and a worse quality of life score. Future research will include analysis of the complete baseline phase data set. Also, the participants from the baseline phase will be re-interviewed in two years time to identify changes in their asthma as well as their quality of life.

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Is Metal Fume Fever a Determinant of Welding-Related Respiratory Symptoms and/or Bronchial Hyperresponsiveness ? A Longitudinal Study

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Our recent prevalence study among working welders has shown a strong association between metal fume fever (MFF) and welding-related respiratory symptoms suggestive of occupational asthma (OA).

The aim of this prospective cohort study was to investigate in 286 apprentice welders whether MFF is a predictor of symptomatic respiratory conditions suggestive of OA and/or bronchial hyperresponsiveness (BHR). The study consisted of a baseline and two follow-up assessments during an average period of 15 months. A respiratory and a systemic symptoms questionnaire, skin-prick tests to common allergens and metals, spirometry and methacholine challenge tests were administered.

The incidence of possible MFF (having at least one of fever, feelings of flu, general malaise, chills, dry cough, metallic taste, and/or shortness of breath occurring three to ten hours after exposure) was close to 40%. Around 12% developed immunological sensitisation (having at least one persistent positive skin prick test to a metallic solution). Welding-related respiratory symptoms suggestive of OA (having at least one of cough, wheezing, and/or chest-tightness) were reported by nearly 14%. Close to 12% had increased BHR with a 3.2-fold or greater decrease in PC20 by the end apprenticeship while 15% had increased BHR with a 2-fold or greater decrease in PC20. Apprentices with possible MFF and no welding-related respiratory symptoms suggestive of OA at first follow-up were at greater risk of developing the latter at the second follow-up visit (RR= 5.9, CI= 1.98-17.85). Our study did not identify MFF as a predictor for the development of BHR.

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Respiratory Syncytial Virus RNA Persistence in Cam Hartley and Strain 2 Guinea Pigs

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A genetic predisposition to allergy has been implicated as a risk factor for development of post-bronchiolitis "asthma" in children (Sigurs et al., Pediatrics 1995;95: 500). In RSV-infected, "allergy susceptible", Cam Hartley guinea pigs, long-term, intrapulmonary RSV persistence is associated with chronic airway inflammation and bronchial hyperresponsiveness (Bramley et al., Eur Respir J 1999;14:1061). We hypothesized that the viral persistence observed in Cam Hartley guinea pigs reflects the allergic predisposition of this strain of animal. Lung specimens from RSV-inoculated Cam Hartley guinea pigs and "allergy resistant", Strain 2 guinea pigs underwent reverse transcription-polymerase chain reaction (RT-PCR) to test for evidence of RSV nucleic acid at Day 3 (acute) and Day 60 (chronic) post-inoculation. RT-PCR for a constitutively expressed host gene (glycerol-3-phosphate dehydrogenase [GAPDH]) was done as a positive control. On Day 3 post-inoculation, RSV and GAPDH were detected by RT-PCR in lung specimens from 2/2 Cam Hartley and 2/2 Strain 2 guinea pigs studied. On Day 60 post-inoculation, GAPDH was successfully amplified by RT-PCR in all lung specimens examined, and RSV nucleic acid was detected in 1/5 Cam Hartley guinea pigs and 2/6 Strain 2 animals. In conclusion, the lungs of a proportion of RSV-inoculated, "allergy-susceptible" and "allergy-resistant" guinea pigs show evidence of viral nucleic acid acutely and chronically. These findings indi
not a determinant of long-term

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Lymphopenia and Lymphocyte Apoptosis during Acute Respiratory Syncytial Virus Bronchiolitis in Children

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BACKGROUND: Respiratory syncytial virus (RSV) bronchiolitis is associated with lymphopenia. There is continuing debate about whether RSV can alter T cell memory responses to other environmental antigens. We hypothesized that during RSV bronchiolitis there is apoptosis of circulating lymphocytes. Apoptosis of mature lymphocytes is mediated through the Fas/Fas ligand or TRAIL pathways and involves intracellular proteolytic enzymes, including caspase-1. Caspase-1 also activates IL-18, which is associated with the up-regulation of Fas ligand expression and with allergic diseases. METHODS: Blood was taken from 32 infants during acute RSV bronchiolitis and after recovery. Membrane expression of Fas and TRAIL receptor were analysed using flow cytometry and serum caspase-1 and IL-18 by ELISA. The absolute lymphocyte count and clinical characteristics during acute infection and at convalescence were recorded. RESULTS: We found highly up-regulated cell surface expression both of Fas ($p<0.001$) and TRAIL receptor ($p<0.001$) during acute illness compared with convalescence. Lymphocyte counts were depressed at the time of the infection but normalised afterwards ($p=0.01$). Levels of caspase-1 were increased during bronchiolitis ($p=0.037$) but IL-18 levels remained unchanged between the paired samples. CONCLUSIONS: These data suggest that during acute RSV infection leading to lymphopenia circulating lymphocytes are primed for apoptosis. This may be a mechanism through which T cell memory is altered.

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Nebulized Epinephrine Versus Albuterol for Treatment of RSV Bronchiolitis

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Introduction: Respiratory syncytial virus (RSV) is a common cause of bronchiolitis in young infants. We used objective quantification of wheezing and crackles by computerized lung sounds recording and a detailed clinical score to compare the effect of inhaled β2-agonist (albuterol) to inhaled epinephrine in infants with RSV bronchiolitis. **Methods:** Double-blind randomized controlled study of infants aged less than 1 year with RSV bronchiolitis and dyspnea. Infants were randomized to receive a single dose of 1 mgr nebulized epinephrine or 2.5 mgr nebulized albuterol. Computerized lung sounds recording with quantification of wheezing and crackles (Pulmo Track) and a clinical score (heart rate, respiratory rate, retractions, oxygen saturation and wheezes) were performed before, 10 and 30 minutes after treatment. Analysis: Student t-test for independent samples, Mann-Whitney U test and Wilcoxon test. **Results:** 15 children received albuterol, 12 received epinephrine. The groups were identical at baseline . At 10 minutes there was a significant improvement in respiratory rate ($p<0.04$), and at 30 minutes also in heart rate ($p<0.02$) and clinical wheeze score ($p<0.03$) in the epinephrine group compared to the albuterol group. There was no difference in oxygen saturation, respiratory distress, total clinical score, and recorded breath sounds (wheezes and crackles by PulmoTrack). **Conclusion:** Nebulized epinephrine was superior to albuterol in some clinical parameters in infants with RSV bronchiolitis. Repeated dosing or a larger dose could augment this effect. Failure to show improvement by computerized wheeze quantification vs. stethoscope auscultation may be due to the high sensitivity of the recording device, or may be manifested in wheeze amplitude or frequency, which were not assessed.

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