Proceedings of a workshop on near fatal asthma

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Concern has been expressed about rising asthma morbidity and mortality, although the latter appears to have declined recently. A reasonable surrogate for fatal asthma is an episode of near fatal asthma (NFA). The etiology of episodes of NFA appears to be multifactorial. Features that would characterize asthma patients at risk of NFA have been difficult to define but have included psychosocial barriers, environmental exposures, inadequate or inappropriate physician and/or patient responses to deteriorating asthma and, in particular, overreliance on symptomatic bronchodilator therapy. The association between fatal asthma and NFA with beta-agonist use has been controversial, with it being argued that high use of beta-agonists reflects severity of asthma as opposed to being causal. Studies in the laboratory and ambulatory care setting suggest that regular compared with as-required use of beta-agonists is associated with worsening in asthma control. Although a reduced perception of dyspnea has been identified in some asthma patients, it is not universally present in those with NFA. Retrospective data suggest that hyperinflation of the thorax, as judged by total lung capacity, may be a useful marker for subjects at risk of NFA. Future studies should better characterize these risk factors and develop management strategies (both therapeutic and educational) that might reduce the risk of subjects experiencing episodes of NFA and, by extension, reducing the continued unacceptable mortality associated with asthma.

Key Words: *Epidemiology, Near fatal asthma, Risk factors*

Compte-rendu d'un atelier sur l'asthme quasi fatal

RÉSUMÉ : Certaines préoccupations ont été exprimées au sujet de l'augmentation de la morbidité et de la mortalité liées à l'asthme quoi qu'il semble que la mortalité ait chuté récemment. Un substitut acceptable pour l'asthme fatal est un épisode d'asthme quasi fatal. L'étiologie des épisodes d'asthme quasi fatal semble multifactorielle. Les traits qui pourraient caractériser les patients asthmatiques à risque pour des épisodes d'asthme quasi fatal restent à être définis mais comptent parmi eux les barrières psychosociales, les expositions environnementales, les réponses inadéquates ou inadaptées de la part du médecin ou du patient, ou des deux, envers un asthme qui s'aggrave et, notamment, une confiance excessive dans les bronchodilatateurs pour traiter les symptômes. L'association entre l'asthme fatal et quasi fatal et l'utilisation des bêta-agonistes est controversée et certains affirment que l'utilisation excessive des bêta-agonistes ne serait pas responsable de l'aggravation de l'asthme mais refléterait plutôt sa gravité. Des études menées en laboratoire et dans des services de santé ambulatoires laissent croire que l'utilisation régulière de bêta-agonistes, comparée à leur utilisation au besoin, est associée à une plus grande difficulté à maîtriser l'asthme. Bien qu'une perception réduite de la dyspnée ait été observée chez certains patients asthmatiques, ce phénomène n'est pas toujours présent chez les patients ayant subi un épisode d'asthme quasi fatal. Des données rétrospectives laissent croire que l'hyperinflation du thorax, estimée à partir de la capacité pulmonaire totale, serait un marqueur utile pour les sujets à risque pour un épisode d'asthme quasi fatal. Les études futures devraient mieux caractériser ces facteurs de risque et mettre au point des stratégies de prise en charge (à la fois thérapeutiques et éducatives) qui pourraient réduire le risque d'épisodes d'asthme quasi fatal chez les patients ainsi que l'inacceptable mortalité qui reste associée à l'asthme.

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There is increasing concern over the rising rates of asthma mortality (1,2). Patients with near fatal asthma (NFA) represent an important group of subjects that can be evaluated to define risk factors for fatal asthma. To review the current data related to NFA, the Respiratory Health Network of Centres of Excellence and the Laboratory Centre for Disease Control (LCDC), with significant contributions from a number of pharmaceutical companies, hosted a workshop on NFA that was held in the Montreal Chest Institute on April 28 and 29, 1994. The objectives of this workshop were to review the current epidemiology of asthma in Canada, as well as global trends in asthma morbidity and mortality. In addition, the published literature on NFA was reviewed and specific risk factors were evaluated in more detail. The opportunity was also taken to present preliminary results from a number of studies on near fatal and fatal asthma from the Prairie provinces, New Zealand and Vancouver. It was also hoped that, following a review of the current knowledge with regard to NFA, future studies can be planned in Canada to evaluate the pathophysiological mechanisms associated with the final common pathway leading to near fatal and fatal asthma, to identify through prospective epidemiological surveillance studies risk factors for NFA and, finally, to develop interventions that might reduce the documented high risk of subjects who have an episode of NFA from progressing to a future NFA attack and, more particularly, death.

FATAL AND NEAR FATAL ASTHMA REVIEW

Dr J Mark FitzGerald reviewed the current literature and gave a synopsis of documented risk factors for NFA, usually defined as a severe life-threatening asthma attack requiring mechanical ventilation or intensive treatment in the presence of acute hypercapnic respiratory failure. The multifactorial aspects of an episode of NFA were highlighted with a complex interaction among the patient, therapeutic and environmental factors, and the intervention or lack of intervention of physicians (3). The documented high risk of a subsequent episode of NFA or death following an episode of mechanical ventilation for NFA was stressed (4,5). These and other issues were further developed in more detail by subsequent speakers.

CANADIAN ASTHMA MORTALITY AND MORBIDITY: AN EPIDEMIOLOGICAL REVIEW IN CANADA

Dr Felix Li reviewed the recent trends in asthma morbidity and mortality in Canada. The rising trend of asthma mortality and morbidity in Canada since the 1970s has raised much concern among health professionals, asthma patients and the general public (6,7). This trend is particularly worrying because it occurred despite continuing medical advances in the understanding and treatment of asthma. Studies have also shown that many asthma deaths and hospitalizations are potentially preventable (8,9).

This presentation reviewed the important epidemiological data on asthma mortality and morbidity in Canada from 1961 to 1991, and updated information provided in previous reports (6,7). Data on mortality and hospitalization for asthma (International Classification of Diseases [ICD] revisions 8 and 9, code 493) were obtained from the Health Statistics Division of Statistics Canada.

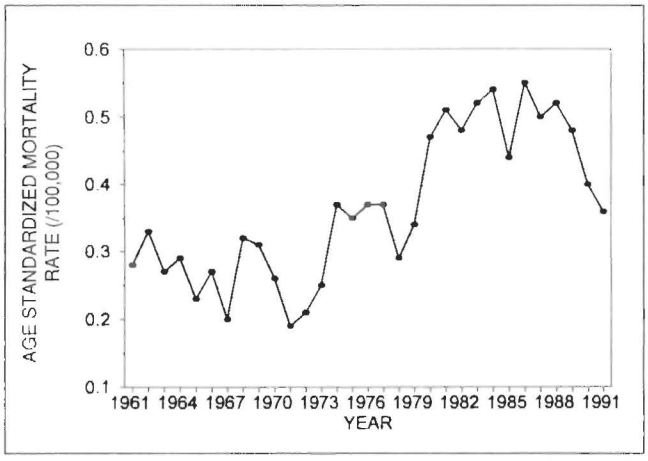

Figure 1) *Asthma mortality in Canada, ages 10 to 34 years, 1961 to 1991*

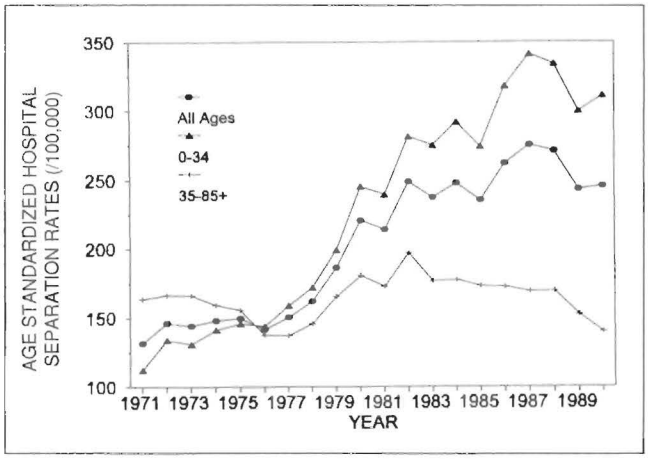

Figure 2) *Asthma hospital separations for all age groups, 1971 to 1990*

Mortality: A review of data from 1961 shows that a significant rise in asthma mortality in Canada occurred principally in the age group 10 to 34 years (Figure 1), in both sexes. In this age group, asthma mortality started to rise in 1971. By 1981, its age-standardized asthma mortality rate had risen to 2.7 times its 1971 level. There followed a plateau in rates that lasted most of the 1980s. In 1991, the age-standardized mortality rate for this age group was still 1.9 times its 1971 level. During the recent period of 1986 to 1991, asthma mortality in the 10 to 34 year age group was highest in Alberta and Saskatchewan.

Hospitalization: Hospital admission rates for asthma (Figure 2) in Canada started to rise sharply in the mid-1970s, and reached peak levels in 1986 to 1988. Thereafter, it has shown some small decline (latest available data are from 1990). The rising trend of asthma hospitalization was contributed mainly by the increase in the 0 to 34 year age group (Figure 2).

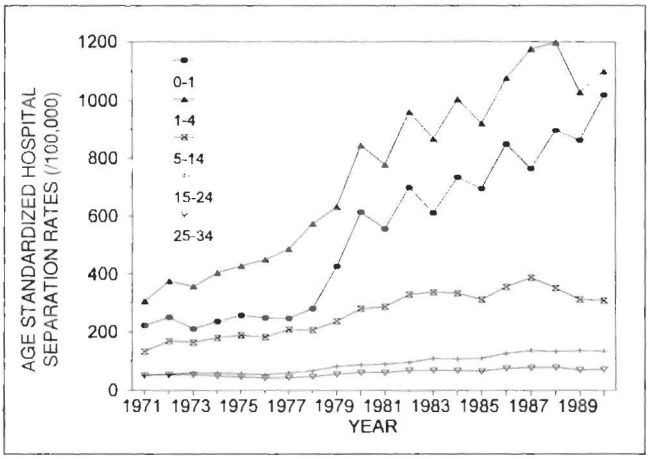

Figure 3) *Asthma hospital separations, ages 0 to 34 years, 1971 to 1990*

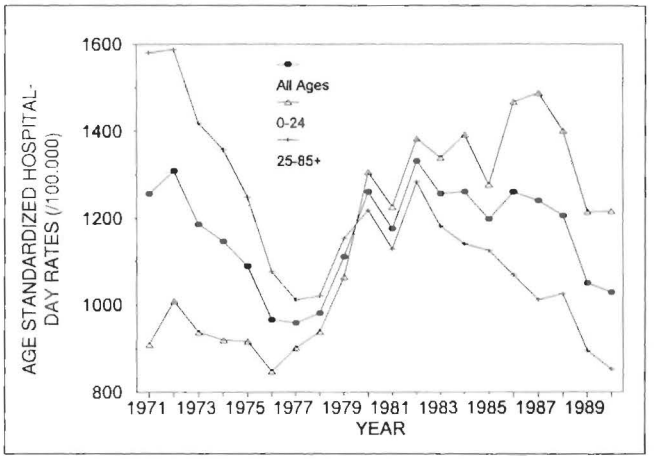

Figure 4) *Asthma hospital days for all age groups, 1971 to 1990*

Within this age group, the most marked increase occurred in the newborn to one year and the one to four year age groups (Figure 3), whose latest asthma hospital separation rates were 4.6 and 3.6 times their respective 1971 rates. In the under 35 year age group, males consistently have a higher (by 33%) hospital separation rate than their female counterparts, and Prince Edward Island, New Brunswick and Nova Scotia had the highest asthma separation rates in recent years (1986 to 1990).

Morbidity, in terms of annual hospital-days due to asthma, however, showed no net rising trend between 1971 and 1990. This is because the rise in asthma hospital-days in the younger (under 25 years) age group was offset by the decrease in the older (over 25 years) age groups (Figure 4). Prince Edward Island, New Brunswick and Nova Scotia again had the highest asthma hospital-days rates (1986 to 1990).

Prevalence: The Canada Health Survey (1978 to 1979) estimated asthma (self-reported) prevalence in Canada to be 2.4% (2.3% in the population over 15 years old). Subsequently, various provincial surveys yielded prevalence rates between 2.5% and 5.3%. Recently, results of the General Social Survey (1991) (10) showed an asthma prevalence of 6% among Canadians aged 15 years and above. Prevalence was equal in males and females; highest (9%) among 15- to 24-year-olds; and highest in Quebec (7%). However, it is unclear how much the apparent increase between 1978 and 1991 (from 2.3% to 6%) can be attributed to 'diagnostic transfer' from other obstructive pulmonary diseases.

Thus, over the past two decades, asthma mortality and hospitalization trends in Canada have generally undergone two phases – a rising phase in the 1970s, followed by a plateau phase in the 1980s. These changes affected mainly the population under 35 years old. Obviously, the increased asthma mortality and morbidity have had a significant adverse impact on the health and well-being of Canadians, as well as on the health care system. Although there was some decrease in asthma mortality and morbidity from 1989 to 1991, it would be premature to assume that this signifies the beginning of a decreasing trend.

GLOBAL TRENDS IN ASTHMA MORBIDITY AND MORTALITY

Dr Malcolm Sears reviewed the data related to global trends in asthma morbidity and mortality. Dr Sears cited a study by Bauman (11), who published an overview of studies in Australia from 1970 to 1990, showing the prevalence of diagnosed asthma in primary schoolchildren increased from less than 5% to over 20% during this period. Supporting data suggested this was at least in part a true increase in prevalence and not simply a change in diagnostic labelling. Similar data have been reported among 17-year-old males recruited into the Israel defence forces (12) as well as subjects recruited into the Finnish defence forces (13). In the United States, Gerstman et al (14) reported increased asthma hospitalizations in five- to 14-year-olds in the Michigan Medicaid population; increases occurred particularly in five- to nine-year-olds with a slight increase in 10- to 14-year-olds. In Australia, Kun et al (15) reported an increased proportion of emergency room visits or hospitalizations due to asthma. In the United Kingdom, hospital discharges and deaths from asthma increased approximately twofold from 1979 to 1985 (16), while most other respiratory diagnoses remained stable or decreased.

An examination of admissions and deaths from chronic bronchitis, bronchitis unspecified, emphysema and asthma data indicated that the increase in asthma deaths was not simply explained by diagnostic transfer between asthma and other diseases of airflow obstruction. Dr Sears outlined problems with mortality statistics, which include the true mortality from asthma together with effects from false positives and false negative certifications, and indicated that in the age group five to 34 years, the accuracy of diagnosis and certification of asthma deaths is nearly 100% (17,18). Within this age group, asthma mortality has increased over the past two decades in several countries, including England and Wales, western Germany, Australia, Japan, New Zealand and the United States. It was indicated again that the increase may have reached a plateau over the past few years and may now be decreasing. In the United States significant ethnic differ-

TABLE 1
Psychosocial problems complicating asthma

1. Lack of shared responsibility for asthma management
2. Delays in or absent communication
3. Lack of recognition of deterioration or failure to act on the deterioration
4. Poor self-efficacy
5. Failure to use peak flow meter
6. Failure to obtain and use recommended medications

TABLE 2
Factors complicating appropriate management of asthma

1. Prednisone phobia
2. Cigarette addiction
3. Substance abuse
4. Adolescent noncompliance
5. Patient will not accept seriousness of disease
6. Parental interference with management:
   - parental prednisone phobia
   - parental noncompliance with medical management
   - parental divorce or battling

ences, with higher mortality among blacks than whites and significant regional differences with higher mortality in urban compared with rural or outlying areas, have been documented (19).

Dr Sears briefly discussed the issue of beta-agonist treatment, and asthma mortality and the data relating to this issue were further expanded upon by Dr Pierre Ernst (see below) (20-22). A recent substantial decline in asthma mortality since 1989 in New Zealand was reported (personal communication). It was noted that the beta-agonist fenoterol was first linked with excess mortality in 1989 (20). Suissa et al (22) attributed the 1989 to 1991 decline in mortality to a steady downward trend that had been evident since the peak of the epidemic in 1981, but the initial downward trend was small and mortality reached a plateau from 1983 to 1988. The subsequent abrupt downward trend in 1989 through 1991 was associated with restriction and withdrawal of fenoterol from the drug tariff in New Zealand. In conjunction with this reduction in mortality, there has been a substantial reduction in morbidity from asthma as measured by almost a 50% decrease in hospital admissions in five- to 54-year-olds, and a 75% decrease in intensive care admissions (personal communication). The decline in both mortality and hospital admissions indicates that the former is not due to better hospital access or emergency care, but rather to decreased severity of disease. Trends away from frequent beta-agonist use towards more appropriate use of anti-inflammatory therapy were felt to be in part responsible for the slight downward trends seen recently in other countries.

PSYCHOSOCIAL FACTORS IN NFA

Dr Paul Greenberger outlined reasons for patient noncompliance, identifying psychiatric disorders, psychological conditions, environmental and social factors, cognitive overload such as in the geriatric patient with potentially fatal asthma, ineffective physician-patient communication or crisis planning, and poor patient acceptance of their asthma and the associated patient responsibilities required to prevent acute life-threatening asthma (23,24). Dr Greenberger noted that from a group of 21 patients, aged 45 years or less, who were intubated during acute life-threatening asthma, a third had left the allergy service within a year (23) indicating the poor compliance with care in this group. Three of these seven patients died from asthma in that year. Dr Greenberger outlined the effects of psychosocial problems as they related to the patient with severe asthma, and these are listed in Table 1. Specific psychological factors complicating appropriate management of asthma are summarized in Table 2.

Dr Greenberger outlined factors beyond physician control such as the effects of poverty (24). He noted that such factors can force a change in priorities such that the patient with chronic severe asthma does not accept achieving effective management of asthma as a personal priority. Practically, it may be difficult to obtain adequate amounts of medications, arrange transportation and follow-up with appropriate trained physicians to work to prevent the next hospitalization. Alternatively, physician factors have contributed to patients meeting criteria for potentially fatal asthma in that the physicians fail to understand ambulatory management of severe asthma, fail to understand the severity of individual cases or learn to practise bizarre forms of asthma management.

To test the hypothesis that many cases of fatal asthma were attributed to potentially preventable causes, an investigation of asthma deaths in 39 cases aged 45 years and less was carried out (25). The authors, surprisingly, found that 14 of 23 (60.8%) cases where toxicological determinations for illicit drugs were performed were positive, suggesting an unexpected confounding factor of substance abuse. In discussion it was felt that such levels of substance abuse that might be present in inner city areas in the United States may not be relevant to asthma care in Canada.

BETA-AGONIST AND ASTHMA MORTALITY – OUTSTANDING QUESTIONS AND IMPLICATIONS FOR FUTURE STUDIES

Dr Pierre Ernst reviewed the literature on the association between the use of inhaled beta-agonists and deaths from asthma. This association was originally described in the mid-1960s when a temporal relationship between increasing sales of isoproterenol and an excess of asthma deaths was found in young people in England and Wales (26). The association was ecological only; that is, there was no evidence that subjects dying from asthma were actually using beta-agonists. For this reason no conclusions could be made as to causality. A similar association between sales of fenoterol and asthma deaths in New Zealand was suggested in 1989 (27); however, the comparison group in this study comprised subjects prescribed salbutamol, and it was therefore impossible to discern whether an association with life-threatening

asthma was present for most drugs in this class or was restricted to fenoterol.

The Saskatchewan Asthma Epidemiology Project (SAEP) identified a cohort of 12,301 subjects aged five to 54 years dispensed 10 or more prescriptions for asthma drugs between 1980 and 1987 (28). Among a nested case control sample of 129 cases of life-threatening asthma and 655 control patients, there was a strong dose-response relationship between increasing use of inhaled beta-agonists and the risk of fatal and NFA, with a more than 20-fold increase in risk for subjects dispensed more than two canisters per month of either salbutamol or fenoterol. An analysis of the complete cohort, which allowed calculation of absolute rates of asthma death, strongly suggested that the excess in risk of NFA and death was largely confined to subjects dispensed more than 1.5 canisters per month (29,30).

The nonexperimental design of the SAEP makes it impossible to distinguish a causal association from one that results from the way in which asthma medications were prescribed. Dr Ernst noted that it seemed plausible that subjects who use large amounts of beta-agonists have more severe asthma, and that it is the severity of the disease rather than the exposure to these drugs that determined the excess in risk of life-threatening asthma. In an attempt to shed light on this matter, clinical indicators of asthma severity were examined in the case control sample from the SAEP (29). While several clinical elements were found to be associated with an excess risk of fatal and NFA, for example a history of loss of consciousness or of attacks precipitated by food, adjustments for such independent risks did not alter the association between beta-agonists and the risk of a life-threatening event. The available clinical data were sparse, however, so that disease severity was unlikely to have been accounted for completely. Uncertainty as to the nature of the association between life-threatening asthma and beta-agonist use does not prevent use of the Saskatchewan data to identify patients at risk of an adverse event based on their pattern of use of these medications. While it is readily apparent that users of more than two canisters per month are at greatest risk overall, a reanalysis of patterns of use among subjects using one or more canisters per month of beta-agonist found that the greatest increase in risk is seen among those with increasing use and that increasing use is a stronger marker of risk than the actual number of canisters dispensed (30).

There are various lines of evidence suggesting that beta-agonist use is more than just a marker of asthma severity. The seminal paper by Sears and colleagues (21) provided evidence that patients using beta-agonist bronchodilators on a regular basis had worse control of their asthma and a shorter time to exacerbation (31) than subjects who used their bronchodilator on an intermittent or as-needed basis. This work, which needs to be confirmed in other settings, suggests that beta-agonists used regularly may make asthma more severe and thus increase the risk of near fatal attacks. This increase in asthma severity may result from an increase in airways responsiveness (32). Use of beta-agonists has the potential to make attacks of asthma more precipitous. While delaying the bronchoconstrictive response, beta-agonists do not appear to limit the degree of bronchoconstriction once it starts and may actually make the fall in lung function more precipitous (33). Regular use of beta-agonists may be associated with a loss of their protective effect against induced bronchoconstriction to methacholine (34) or to AMP (35) and, more important, it appears to increase the bronchoconstrictive response to allergen (36). While beta-agonists certainly have detectable cardiac and metabolic effects (37), these have not been convincingly linked to life-threatening events. On the contrary, there is good evidence that NFA attacks are due to respiratory failure without significant cardiac phenomena (38).

Long-acting inhaled beta-agonist bronchodilators have been available for a number of years in other countries and became available in Canada in late 1994. Their role remains somewhat uncertain given the concerns expressed above about regular use of shorter-acting agents. The efficacy of the new long-acting preparations in reducing symptoms and improving lung function is impressive (39). No adverse effects on asthma control have been described as yet, despite close observation for up to a year (40). Life-threatening attacks of asthma are rare events, however, and studies of a large number of patients may be required to demonstrate safety. An attempt at such a study was recently published and found a threefold, though not statistically significant, excess of asthma deaths among approximately 15,000 patients dispensed the long-acting agent salmeterol compared with subjects taking the short-acting salbutamol four times a day (41). A more interesting comparison would be regular salmeterol versus a short-acting beta-agonist used on an as-needed basis.

HOW GENERALIZABLE ARE STUDIES IN NFA TO FATAL AND SEVERE ASTHMA?

Dr Nestor Molfino reviewed the studies of NFA, noting that the majority of studies on near fatal and fatal asthma have been epidemiological in nature, characterizing patients at risk of dying from asthma and investigating the measures being taken by patients, relatives and health care workers. The major conclusions of such studies are as follows:

- patients dying from fatal asthma and patients who suffer from NFA seem to come from the same population;
- the time elapsed to medical care, and the quality of such care, are crucial;
- there appeared to be improper therapeutic measures taken in emergency circumstances in general because of underestimation of the severity of the episode of acute asthma.

A review of the recent literature led to the conclusion that patients who die from asthma do so because they do not reach the emergency department expeditiously, and based on this hypothesis many authors have studied NFA episodes as a surrogate for fatal asthma (42). In this regard, Molfino et al (38) examined the mechanisms by which patients might die during acute exacerbations of asthma by studying 10 patients who arrived at the hospital in respiratory arrest or in whom it

developed within 20 mins after their admission. These patients had characteristics similar to those described earlier for patients at high risk of death from asthma. They were found to have marked hypercapnia (mean ± SD) 97.1±31.1 mmHg and acidosis pH 7.01±11 before mechanical ventilation was begun. In addition, four patients had hypokalemia on admission, although for the total group the mean potassium was in the low normal range (3.4±0.3 mmol/L). Despite the marked severe respiratory acidosis, no patient had a serious cardiac arrhythmia during resuscitation manoeuvres or during hospitalization. Although one patient had atrial fibrillation and another had relative sinus bradycardia, both arrhythmias reverted to sinus rhythm after the initiation of ventilation with hyperoxic gas mixtures. Based on these findings, it was concluded that, at least in this group of patients, the near-fatal nature of the exacerbations was the result of severe asphyxia rather than cardiac arrhythmias. Given the severity of their clinical and biochemical data on admission, these patients would probably have died if they had not been treated aggressively. Thus, they represent a subgroup of patients who die from asthma; this is true for other studies (38,43-51).

The mechanisms by which asphyxia develops in severe asthma are probably multifactorial: a combination of a certain degree of airway lability, the severity of the pre-existing obstruction, the magnitude of the stimulus applied, and the patient's ability to respond to the alterations of the airway geometry (52-55). Recently, Kikuchi et al (56) reported that patients suffering from NFA have reduced chemosensitivity to hypoxia and blunted perception of dyspnea.

It appears reasonable to conclude from the studies that patients suffering from NFA and fatal asthma are derived from the same population of individuals, and that a better understanding of near fatal events may lead to better prevention of fatal episodes of asthma.

ENVIRONMENTAL FACTORS RELATED TO ASTHMA MORBIDITY

Dr Sverre Vedal reviewed the association between asthma morbidity and the environment. Dr Vedal noted that air contaminants and asthma both exhibit a temporal variability, which suggests that environmental air contaminants and asthma may be linked. Aeroallergens also may be causes of asthma and factors that influence the course of asthma because of the marked differences in prevalence of aeroallergen sensitization between asthmatic and nonasthmatic subjects (57). Sensitivity to the house dust mite is in many settings the most common aeroallergen sensitivity in asthmatics, with sensitization to outdoor pollens and to cats also being common. However, based on data from the National Health and Nutrition Exam Survey in the United States, sensitization to fungal allergens, in particular alternaria, may be the most common aeroallergen sensitivity in asthmatics in many other settings (58).

Based on recent data showing that avoidance of allergens during the first year of life can reduce the incidence of asthma by the first year (59), and data showing an association between aeroallergen exposure at the first year and the likelihood of having asthma at age 10 years (60), allergens are likely to play a role in causing asthma. Several studies also provide strong evidence that continued exposure to allergens influences the course of asthma. Data from Barcelona, Spain (61) and from the American midwest (46) show that current aeroallergen exposure can also result in very severe adverse effects in asthmatics, including respiratory failure. Studies in which risk factors for adverse effects in asthmatics are studied using nonasthmatic control groups are less informative in implicating these risk factors in NFA than when an asthma control group is used. Another design problem that compromises the ability of a study to reach conclusive findings is the lack of statistical power. For example, in studying NFA, not only is it difficult to enrol enough subjects from one investigating centre, but if interest is in studying the risk of aeroallergen exposure in the subset who are specifically sensitized to that allergen, statistical power is even further compromised.

Meteorological factors clearly have an influence on asthmatics. Whereas the exercise-induced fall in level of lung function is exacerbated by low temperature and low humidity, it is less clear in clinical and epidemiological studies that low temperature and low humidity have similar associations with asthma exacerbations (62). In fact, in some instances both extremes of temperature are adversely associated with asthma course; humidity has variable effects depending on ambient temperature.

There is also a large body of data to support the notion that ambient and indoor concentrations of air pollution adversely affect asthma. The acute effect of ozone exposure on level of lung function has convincingly been shown to be due to a reduction in the ability to take a deep breath (that is, a reduction in inspiratory capacity) rather than being an effect on airways (63). It is not surprising, then, that the acute effect of ozone on lung function has not been shown to affect asthmatics more adversely than nonasthmatic subjects in exposure chamber studies (64). However, epidemiological studies have shown that subjects with asthma are adversely affected by ozone exposure, in terms of both asthma exacerbations and hospitalizations (65,66). Another aspect of ozone effects has recently been suggested by work showing that response to specific allergen exposure in sensitized asthmatics is aggravated by preceding ozone exposure (67).

The adverse effects of inhalable particles on asthmatics are causing great concern. A recent study from Seattle found an association between daily changes in inhalable particle concentration and emergency room visits for asthma at particle concentrations that are observable in any urban area in the United States or Canada (68). It appears that the adverse effects associated with inhalable particles are largely limited to particles generated by combustion (69). There has also been recent interest in the adverse effects associated with acid aerosols. A recent study of a panel of asthmatics in Denver found that the association between ambient air pollutants and asthma exacerbations was strongest for acid aerosols (70).

Given that the majority of our time is spent indoors, it is

likely that indoor concentrations of air pollutants can also adversely affect asthmatics. Exposure of asthmatic children to environmental tobacco smoke has been shown to result in reduced levels of lung function and increased bronchial hyperresponsiveness (71). Recently, exposure to environmental tobacco smoke in children as assessed by urinary cotinine concentrations has been shown to be associated with exacerbations of asthma (72).

It is likely that any exacerbation in an asthmatic is caused by several factors acting together. Environmental factors such as indoor and outdoor aeroallergens and indoor and outdoor air contaminants are among a group of factors that can help to trigger exacerbations of asthma.

VANCOUVER NFA STUDY

Dr Mark Turner outlined the preliminary data from a prospective evaluation of 99 patients admitted with acute asthma over a 20-month period to the Vancouver General Hospital and St Paul's Hospital (73), Vancouver. Subjects gave a detailed history of their asthma, recent exposures to possible triggers, treatment undertaken and compliance. Measurements of airflow obstruction were recorded, and while in hospital the patients had skin prick testing and blood drawn for serum immunoglobulin E. Following discharge a home visit was made, samples of bedroom and mattress dust were collected for house dust mite analysis, and air samples were collected for analysis of moulds. Subjects were defined as cases if they had respiratory failure (PCO_2 greater than 45 mmHg) or mechanical ventilation (controls were all other asthma patients admitted to hospital during the same period). Subjects were between the ages of 15 and 55 years.

There were 20 cases and 79 controls identified. There were no deaths. The cases were more likely to have been ventilated previously (P=0.0001). There was no difference in the prescription and compliance with inhaled corticosteroids. There was also no difference in the numbers ingesting prednisone before admission. Cases also did not have higher bedroom concentrations of dust mite or cat allergen than asthma patients who were controls (74).

This study again confirms, but for the first time in a prospective manner, that a history of previous mechanical ventilation for asthma is a significant risk factor for NFA. The use of inhaled medications was not identified as a risk factor. The data also suggest that asthmatics with NFA are not exposed to higher concentrations of home allergens than are asthmatics hospitalized without NFA. Dr Turner noted that the sample size was small and a larger prospective study would be required to categorize better risk factors and potential interventions to prevent hospitalizations and episodes of NFA.

LESSONS FROM THE NEW ZEALAND CASE CONTROL STUDY OF NFA

Dr John Kolbe outlined the rationale for an NFA study from New Zealand; he agreed that, although NFA is an important entity in its own right, it may also be regarded as a proxy for asthma death. Data collected in the context of NFA have considerable advantages over those collected in relation to asthma death. Obviously in the latter situation, data have to be collected from friends and relatives, who are particularly likely to experience recall bias, or from case notes where incompleteness and inaccuracy of data are a concern. Obtaining data directly from both cases and controls is especially valuable in terms of details of events in the 24 h before the index attack, identification of psychosocial factors, assessment of the quality of medical care (both acute and long term) and assessment of practical self-management knowledge. Campbell et al (75) have shown considerable discrepancy between the information provided by persons sustaining an NFA attack and their close acquaintances even in terms of medication use, limitation of activities and simple conventional measures of asthma morbidity; there were also discrepancies between the prescribed medications as listed by the patient and those recorded in the hospital record at the time of an acute admission for asthma (unpublished data).

Direct interview also allows for the collection of complete detailed information using instruments specifically addressing clearly defined variables of interest. In asthma, psychosocial factors may operate via effects on symptom reporting, compliance, self-management behaviour, health-seeking behaviour and methods of use of the health system, response to educational and other interventions, and may affect quality of medical care.

Dr Kolbe and colleagues are attempting to investigate the complex relationships among psychological factors, socioeconomic factors, quality of medical care, disease severity and asthma death and near death in a case control study; cases are those admitted to an intensive care unit with NFA, and controls are patients admitted to general wards with acute asthma. Normative data for the instruments are also being obtained from a random sample of adult community-based asthmatics. Preliminary data from the initial 124 subjects, not analyzed in a case control format, show that those admitted to hospital in Auckland with acute asthma have the following:

- severe asthma on admission (pH 7.32±0.17, $PaCO_2$ 54.1±39.1 mmHg, n=75) but short hospital stay (3.75±2.75 days);
- acute precipitous asthma in only a few – only 7% stated that they had an attack lasting less than 6 h;
- indicators of good ongoing medical care – 96% had a regular family doctor, 80% had been prescribed inhaled corticosteroids, 87% owned a peak flow meter, 78% stated that the family doctor measured their peak flow or asked about their readings, 49% had their metered dose inhaler technique checked in the previous 12 months, 52% had a written 'action plan' and 98% of those who had tried (n=62) had experienced no difficulty obtaining an urgent appointment with their family doctor;
- high morbidity from asthma – 33% and 73% had a previous intensive care unit and hospital admission, respectively, for acute asthma, 40% had a hospital admission in the previous year, and 60% indicated that

they had moderate to severe interference with sleep and/or exercise intolerance;

- poor levels of practical asthma self-management as assessed by responses to scenarios describing the rapid and slow onset of severe life-threatening attacks of asthma (76);
- severe economic disadvantages – 48% had experienced financial difficulties in the previous year, 43% were in paid employment but 17% had looked for work for more than one month; for 30% the household's only income was a social security benefit (compared with 12% for New Zealand as a whole) and 14% indicated that concerns about costs had a detrimental effect on the management of the index attack (primary health care is subsidized, but not free, in New Zealand, and in the past few years charges for attending public hospitals have been introduced);
- high levels of clinically significant anxiety (52%) but lower levels of clinically significant depression (15%);
- high levels of general social support, but in 43% this is deficient in asthma-specific terms and in 22% there had been moderate to severe conflict between the patient and their primary social support person;
- a high number (3.1±2.4) of significant life events in the previous 12 months.

Following recognition of the 'epidemic' of asthma deaths in New Zealand in the late 1970s, a number of educational and management initiatives were introduced (77). Subsequently there was a progressive and sustained decline in asthma mortality during the 1980s and early 1990s and more recently a decline in various morbidity indices (77). Currently, despite achieving high levels of indicators that would be generally accepted as indicating good quality of ongoing asthma management (78,79), patients admitted to hospital with acute asthma had considerable chronic asthma morbidity. The data strongly suggested that psychological, social and economic factors may be playing major roles.

In New Zealand further reductions in asthma morbidity and mortality are unlikely to result from additional conventional educational and management interventions. Initiatives such as community-based asthma clinics staffed by ethnic health care workers have been prospectively evaluated (80). However, the health problems of these asthmatic patients will not be comprehensively addressed unless the social, economic and psychological factors that limit the affordability, availability and accessability of health care are also addressed. To not recognize or understand these influences, along with certain cultural issues, means that the health care services provided will not be effectively used.

PRAIRIE PROVINCES FATAL ASTHMA STUDY

Ms Suzanne Tough outlined the design and implementation of the epidemiological component of the Prairie Provinces Fatal Asthma study (PPAS). The presentation focused on the design, logistics and administration of the project and the challenges associated with establishing and running this multicentred trial. The study initially was pilot-tested for one year in Alberta to determine feasibility.

The objectives of the PPAS are to determine risk factors associated with mortality among asthmatics and to determine the risk of a fatal outcome among those experiencing acute asthmatic attacks. The case control study has two epidemiological control groups and a pathology control group. Cases are identified as those persons aged five to 50 years dying from asthma in Saskatchewan, Manitoba and Alberta. Suspected asthma fatalities are reported by medical investigators and rural examiners, pathologist and emergency department physicians in each province through a 24 h 1-800 number. In the event that a case is not reported, the Division of Vital Statistics in each province notifies the PPAS coordinator of an asthma case on receipt of the death certificate.

Within a month of the fatality the family is invited to participate by completing a questionnaire and allowing access to pathology specimens for study purposes. The grieving process leads to variability in questionnaire return, but the study coordinator keeps in contact with next-of-kin and may offer to do a personal or telephone interview. Controls identified during the same period include subjects who have attended an emergency department with acute asthma as well as unmatched community controls identified through random digit dialling.

Dr John Butt outlined preliminary pathology results from the Prairie provinces asthma mortality study group (81). In this study the lungs of 18 adults (six asthmatics dying from acute asthma, six asthmatics dying of other causes and six deaths not related to respiratory disease) were removed at autopsy and fixed by bronchial and vascular instillation of 2.5% phosphate-buffered glutaraldehyde at 20 cm H_2O pressure. Nine samples were taken at equally spaced intervals along the main anterior and posterior basal segmental bronchi of the left lower lobe. Paraffin sections were elastic trichrome stained. Projected areas of the bronchial lumen (Alp) and smooth muscle (Amp) were determined by point counting, and the length of the basement membrane by intersection counting. The expanded cross-sectional area (Aex) of the bronchial lumen in each section was calculated. Normalized to the Alp, Amp in the asthma death group showed a dramatic peak in the middle third of both segmental bronchi that was significantly different from nonasthmatic control bronchi. The peak was lacking in the nonfatal asthma control group and in nonasthmatics. When normalized to Aex, however, the peak in Amp was much less pronounced. The results suggest that while smooth muscular hyperplasia does exist in severe asthma, its magnitude and pattern of distribution is profoundly influenced by the way in which the data are viewed.

NFA AND ASTHMA EDUCATION

Dr Louis-Philippe Boulet reviewed the role of asthma education generally. Subjects with a previous NFA episode are considered at risk of severe asthma event, including asthma death, as described in studies looking at factors in-

volved in an increased risk of fatal or NFA. Many of these factors can be addressed by asthma education and counselling; they include sensitizing environmental exposure, poor compliance and lack of understanding of the treatment, poor asthma control including management of asthma flare-ups, underestimation of asthma severity, overreliance on bronchodilators, underuse of corticosteroids, blunted perception of asthma symptoms and psychosocial problems.

Asthma education programs are effective in reducing asthma morbidity in asthmatic patients, including those recruited at the emergency room following acute asthma (82-85). There is, however, a need for studies looking at the influence of asthma education on specific interventions to prevent NFA, particularly in patients who previously experienced this severe form of asthma. Until such studies become available, it seems mandatory to provide to patients with previous life-threatening asthma the basic information and training that address the many deficiencies associated with NFA. Self-management skills should be improved, regular follow-up ensured and available resources offered. Particular attention should be paid to adolescents and people from low socioeconomic classes because they seem more prone to NFA (86-88).

For patients presenting with an acute asthma episode, education ideally begins in the emergency room, or in hospital if the patient is hospitalized; the interventions made by the different health professionals should be clearly articulated to provide uniform basic information as well as ongoing reinforcement of the educational process. The objectives of the educational intervention are threefold: cognitive (knowledge), psychomotor (skills) and psycho-affective (attitudes and behaviour). Teaching ideally should be tailored to each individual and emphasis placed on practical elements that will help to improve behaviour (83). It is important that asthma education programs be carried out in parallel with the use of appropriate anti-inflammatory therapy (89), as well as allergen avoidance and the use of specific therapy before unavoidable allergen exposure. The appropriate use of anti-inflammatory therapy is especially important (90) as is provision for ready direct access to health care in the event of an acute life-threatening attack of asthma (43).

Essentials of an education program: Basic elements have been suggested by different education programs, and although their usefulness in the prevention of NFA should be validated, they probably can improve asthma control and prevent severe asthma episodes in many of these subjects (9). The following summarizes the most frequently cited principles and content of asthma education programs.

- The goals of the treatment should be clearly understood.
- Avoidance or early treatment of the effects of triggers, mainly sensitizing agents such as allergens or industrial substances, or substances to which the patient is considered allergic or intolerant, such as foods and sulphites, as well as smoking cessation, are mandatory. These last measures are, however, among the most difficult to implement.
- The two main features of asthma – bronchoconstriction and inflammation – should be explained in simple terms and related to the treatment (bronchodilators and anti-inflammatory agents).
- The asthmatic patient should understand how to evaluate asthma severity and the criteria of control or lack of control. Peak flow meters are useful, particularly for those patients who have poor perception of symptom severity.
- The types, appropriate use and side effects of medications need to be explained. In patients who require regular use of bronchodilators, we should insist on regular anti-inflammatory therapy, particularly steroids, which seem to reduce markedly the risks of fatal asthma (90). Inhaled 'short-acting' beta$_2$-agonists (eg, salbutamol, terbutaline) are considered for use 'on demand' and can be used as another means to assess asthma control. 'Preventive' medications such as cromoglycate or nedocromil can also be used before potential allergen exposure.
- Adequate technique of inhaler use should be taught and potential difficulties detected.
- Most important, the patient should be instructed on how and when to change medication according to specific criteria (written action plan) with or without peak expiratory flow rate measurement. Delays in treatment modification or medical consultation contribute to the severity of attacks, and early intervention should be suggested (43).

Specific problems related to management of patients with NFA: Many problems related to asthma management have been described in the general population of patients with asthma but also specifically in fatal or NFA (90,91). In fact, the problems encountered in teaching all asthmatics are usually emphasized in a patient with previous NFA. They are physiological (symptom perception, marked airway hyperresponsiveness) (92), behavioural (compliance with treatment, management of flare-ups) and psychosocioeconomic (motivation, family and financial problems, disease acceptance and social pressures) (93). Poor perception or recognition of asthma symptoms can possibly be improved by symptom recording and peak expiratory flow rate measurements (94). Improvements in compliance with treatment and follow-up appointments can result from a better understanding of the principles outlined above and from specific techniques addressing this problem (95). Increased access to structured asthma education should be promoted, but since 'non-attendance' is frequent, this should be subject to specific interventions, to try to change patients' attitudes towards their disease (96). Finally, psychosocial problems are frequent and should be recognized and met with offers of counselling and, if required, referral to a resource person (97).

The role of asthma educators in NFA: The success of the education program also depends on the quality of the teaching. Many deficiencies have been observed in health educa-

tors (98,99). They should therefore be offered adequate training to update their knowledge, develop specific attitudes and appropriate teaching skills and be given basic pedagogical tools and methods (80,99-101). They should be able to offer the patient pertinent and specific data, adapted to his or her specific condition, severity level, degree of understanding, expectations about the disease, immediate needs, fears and prejudices. Ideally, close relatives should be involved. Patient understanding of basic notions and appropriateness of behaviour should be evaluated in follow-up visits. Training programs for health educators will help to improve uniformity and quality of educational interventions. Collaboration among general practitioners, specialists and other health professionals is essential to the development of an effective program. Early intervention, with improved access to health care, should be especially emphasized (102).

What remains to be done? In the past decade, asthma management has been reviewed and guidelines have emphasized asthma prevention, particularly from structured asthma education (103,104). However, most evaluations of asthma education have involved patients without previous NFA episodes (105). These interventions should be further studied in this 'at risk' group, to help us to identify which are the most important components and best methods to reduce asthma-related mortality and morbidity in those patients. Until then, we should aim at early recognition of this subgroup of patients, ensure optimal treatment, offer basic asthma education focused on specific deficiencies detected, and ensure close follow-up. Increased access to medical services, such as those provided by a self-admission service, has been suggested as a means of preventing severe asthma events, although this approach is not largely used and may perhaps be made up for by the increased availability of educators and physician consultation at earlier stages of worsening asthma (102). Further studies should look at means to improve preventive measures (smoking, allergies, etc), compliance and attendance for follow-up.

PATHOPHYSIOLOGICAL ASPECTS OF NFA

Dr Peter Macklem introduced and chaired the workshop proceedings, which dealt with the pathophysiological aspects of NFA.

There is consensus that a major pathophysiological abnormality in asthma is excessive airway narrowing. Normal subjects are protected from this by a plateau on the dose-response curve so that increasing doses of a smooth muscle agonist fail to produce increasing responses (106-108). Because a plateau is present, regardless of the means of measuring the response (forced expiratory volume in 1 s [FEV_1] [107], maximum and partial expiratory flow volume curves [108,109], airway resistance [110]), and regardless of the agonist or combinations of agonists used (107,108,111), it is usually taken to indicate supramaximal stimulation. Thus, the concept has arisen that susceptibility to fatal or NFA arises from loss of the mechanism(s) that normally limit the degree of airway narrowing and that may protect less severe asthmatics from near fatal episodes.

Assessment of hyperreactivity: Drs W Gibbons and A Sharma pointed out that the usual method of assessing bronchial hyperreactivity, the PC_{20} or PD_{20}, could not detect excessive airway narrowing because the independent variable was the response (a 20% fall in FEV_1) while the dependent variable was the dose that produced this response. For a test to detect excessive airway narrowing, the response would have to be the dependent variable. They proposed an alternative test, namely the fall in forced vital capacity (FVC) that occurred at the dose of agonist producing a 20% fall in FEV_1. The rationale for such a test is that the fall in FVC reflects an increase in residual volume due to airway closure. They showed in asthmatics that the FVC decreased in a dose-dependent manner and was not correlated with the fall in FEV_1/FVC, ie, some asthmatics had a decrease in the former with little change in the latter, and vice versa. There was no correlation between PC_{20} and the fall in FVC at the PC_{20}. Thus the two tests measure different parameters. To the extent that FVC decreases due to airway closure (which represents the limit to excessive airway narrowing) and that a rapidly decreasing FVC with increasing dose represents a rapidly increasing degree of airway closure, the test might prove useful in detecting asthmatics at risk for excessive airway narrowing and near fatal attacks.

In normal subjects given high dose (256 mg/mL) methacholine challenges, Gibbons and Sharma measured inspiratory pulmonary resistance (R_L) at different static transpulmonary pressures (P_L) as the response. They showed that the maximum increase in R_L at a P_L of 10 cmH_2O was almost negligible, whereas at a P_L of 3 cmH_2O the plateau was abolished, confirming the findings of Ding et al (110) in humans. The fact that asthmatics with near fatal attacks are hyperinflated indicates that the mechanism that protects normal subjects from any significant degree of airway narrowing at a P_L of 10 cmH_2O is abolished; asthmatics breathing near total lung capacity behave like normal subjects breathing at a P_L of 3 cmH_2O.

Effect of lung elastic recoil: Drs Irvin, Liu and Brugman pointed out that a mechanism that would allow for excessive airway narrowing in asthmatics is loss of lung elastic recoil pressure (Pel). They had noticed a number of steroid-dependent, asthmatic children who, following aggressive treatment and normalization of airflow, were still persistently hyperinflated. These patients were also perceived to be at high risk. Therefore, they performed a study to characterize these patients better and to address the postulate that patients with reduced elastic recoil are more prone to NFA episodes.

Pel was measured in the study group and compared with that in age-matched, severely asthmatic children without hyperinflation. Pel was assessed by static transpulmonary pressure-volume curves of the lungs. Pressure-volume curves were subjected to curve-fitting analysis with a single exponential function (112). Asthmatic children with hyperinflation were found to have significantly decreased Pel. Of note, many previously identified risk factors for NFA episodes were not significantly different between the two groups of severely asthmatic children. The most important finding of

this study was that the group with reduced Pel were characterized by episodes of exacerbations of asthma with a significant incidence of loss of consciousness, respiratory failure and requirement for mechanical ventilation.

Dr Irvin and colleagues concluded that a subset of severe asthmatic children with persistent hyperinflation are distinguished by pressure-volume curves exhibiting a marked loss in recoil and an increase in compliance. This group is also characterized by more difficult-to-control asthma and by a greater incidence of respiratory failure. Thus, airways hyperreactivity coupled with reduced lung elasticity may represent a situation of risk of near fatal attacks.

Airway smooth muscle contraction: Dr Macklem analyzed the load on airway smooth muscle when airways narrow during bronchoconstriction. There are three components to this load: the elastance of the airway wall; Pel; and airway parenchymal interdependence. All three of these decrease as lung volume decreases. He showed that at Pel of 20 and 10 cmH_2O (where Drs Gibbons and Sharma found little increase in R_L with high dose methacholine challenge) the load was large and little narrowing would be predicted, based on known maximum active force-length characteristics of smooth muscle. At Pel of 5 and 2 cmH_2O it was more than an order of magnitude less than at Pel of 20 cmH_2O. It is known that the plateau is abolished in normal subjects when Pel decreases from 5 to 2 cmH_2O (110), whereas in asthmatic subjects it is abolished at higher values of Pel. Peribronchial inflammation might account for this because, first, it would diminish peribronchial pressure, effectively lowering local elastic recoil pressure; second, the reduction in peribronchial pressure would allow the airway to recoil inward to a more compliant part of its area-transmural pressure relationship; and third, it would decrease airway-parenchymal interdependence.

He calculated the degree of peribronchial inflammation that would decrease the load by an amount equivalent to decreasing Pel from 5 to 2 cmH_2O. He found that an increase in airway wall thickness by a factor of 3 at a Pel of 5 cmH_2O would decrease peribronchial pressure from –5 to –2 cmH_2O and would mimic a decrease in lung volume from normal functional residual capacity to that at a Pel of 2 cmH_2O. With this degree of peribronchial inflammation, the change in peribronchial pressure per unit change in Pel would be less than normal. At a Pel of 20 cmH_2O, peribronchial pressure would be –11 cmH_2O, whereas at a Pel of 0 it would be positive.

Thus, peribronchial inflammation would not only decrease the load, it would diminish the stretch on airway smooth muscle provided by a deep inflation, reducing the slope of the relationship between peribronchial and pleural pressure from an assumed value of 1 to a value less than 1. This might account for Colebatch's (113) observations that R_L changed less with Pel in asthma than in either chronic obstructive pulmonary disease or normal subjects.

Effect of increased lung volume: Dr Sol Permutt emphasized the risks imposed by breathing at high lung volumes. Using a mechanical analogue of airway closure to produce hyperinflation in anesthetized dogs, he and his colleagues found that an average increase of 0.84 L for 30 mins decreased minute ventilation by 27% and increased arterial PCO_2 from an average of 40 mmHg to an average of 73 mmHg. This was accomplished without any airway narrowing. Continuous positive airway pressure (CPAP) restored minute ventilation and decreased arterial PCO_2. In humans breathing on a similar analogue of airway closure to impose hyperinflation he noted marked increases in esophageal pressure swings with inspiratory pressures falling to –20 to –30 cmH_2O and expiratory muscle recruitment. He reported that breathing at 2 L above functional residual capacity, while very distressing, could be tolerated for prolonged periods. However, greater degrees of hyperinflation were found to be intolerable. He suggested that CPAP might be a tool to determine how much respiratory distress is due to dynamic hyperinflation and how much is due to increase in the flow-resistive work of breathing.

Drs O'Donnell and Lougheed reported on the results of an experiment similar to that suggested by Permutt. Following methacholine challenges in asthmatics they assessed the sensation of effort caused by dynamic hyperinflation by applying CPAP, and compared it with the sensations engendered by airway narrowing, which they relieved by inspiratory pressure support. They found that CPAP relieved the sense of effort more than inspiratory pressure support.

Dr P Sliwinski also reported a study in which dynamic hyperinflation was imposed on normal subjects by expiring through a Starling Resistor, which limited expiratory flow to 0.3 L/s while rebreathing carbon dioxide. Tidal volume decreased in response to the combined effect of carbon dioxide and expiratory flow limitation while respiratory frequency was increased at any given level of end-tidal PCO_2 compared with the response in the absence of expiratory flow limitation. This increase in respiratory frequency aggravated the dynamic hyperinflation and drove the lung volume at which tidal breathing took place above the normally attainable total lung capacity. There was massive but ineffective recruitment of expiratory muscles, a substantial degree of loss of lung recoil and an inspiratory P_L swing that must have been close to the maximum that the inspiratory muscles could generate. He suggested that this was a reasonable model of ventilatory pump function in a severe asthmatic attack: that it produced loss of elastance and thus mimicked the loss of recoil frequently observed in asthma; that, if patients were forced to continue to breathe in this way, respiratory muscle fatigue and acute respiratory failure would surely ensue. This experiment in normal subjects may mimic the events of a near fatal attack of asthma.

Prediction of impending severe asthma: Vézina, Kenyon, Olivenstein and Macklem addressed the issue of predicting a severe attack of asthma. They pointed out that seismologists could predict the likelihood of an earthquake of a given energy over a defined time period in a given region by the equation $E = 1/f^x$ where f is the frequency of earthquakes of a given energy (E) over a given time period in the region in question and x is a constant. In a region where earthquakes are

common, x is high and can be used to predict the probability that an earthquake of a given size is likely to occur in the region in question over a given time period. The same approach can be used to predict frequency and severity of avalanches or of stock market fluctuations. Following Vézina's suggestion, Kenyon analyzed diurnal variations in peak expiratory flow over a six-week period in three asthmatics. The plot of log severity versus log frequency was linear with a slope of –0.83 and a correlation r of 0.8. If the slope of this relationship is high in a given asthmatic, the chances of a severe attack are greater than in an asthmatic in whom the slope is lower. This raises the possibility that the relationship between frequency and severity of asthmatic attacks follows similar relationships as frequency and power of earthquakes, avalanches and stock market fluctuations, and that this can be assessed by variations in simple measurements of lung function measured over a relatively short period of time. Thus, it may be possible to predict which asthmatics are at risk for fatal or NFA attacks, without being able to predict when they would occur.

There was general agreement that further research is necessary to predict which asthmatic is at risk to develop a near fatal attack.

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FUTURE PLANS

The workshop concluded by emphasizing the importance of developing appropriate studies to address current deficiencies in identifying subjects at risk of NFA. The group decided to establish a scientific working group to oversee three main areas of interest: the pathophysiology of NFA, with studies evaluating EL, the magnitude of dynamic hyperinflation, the degree of gas trapping and the power spectrum of variations in lung function; environmental issues in NFA, in particular the role of particulate matter and allergen; and intervention studies to reduce the risks of subjects having future NFA episodes emphasising factors that would optimize compliance.

WORKSHOP ATTENDEES (excluding speakers): Tony Bai, Alan Becker, Margot Becklake, Dennis Bowie, Andre Cartier, Moira Chan-Yeung, Debra Danoff, David Eidelman, Peter Goldberg, Anton Grunfeld, Jim Hogg, Martin Holroyde, Lisa Isaac, Diane Lougheed, Maria Ludwig, James Martin, Dennis O'Donnell, Ron Olivenstein, Ian Rodger, Art Slutsky, David Small, Norman Wolkove.

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