Seasonal and recurrent intensive care unit admissions for acute severe asthma in children

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Abstract **Life-threatening attacks of asthma requiring intensive care unit (ICU) management at Red Cross War Memorial Children's Hospital in Cape Town were noted to occur in some patients in the same or adjacent months of different years.**

A retrospective case-controlled study was performed of 21 such 'seasonal' patients who presented to the ICU over a 14-year period. The group made up 6,5% of all asthma patients admitted to the ICU and their 65 admissions made up 15,6% of all ICU asthma admissions during this period. The control group consisted of patients with recurrent admissions that occurred in 'random' months. The two groups were compared in respect of demographic and clinical data. Patients requiring seasonal admissions were shown to form a distinct sub-population of children with severe asthma, some with a family history of fatal asthma, who were less likely to 'outgrow' asthma in childhood, were more likely to require maintenance steroid therapy for asthma management, and significantly more often had positive radio-allergosorbent tests to *Aspergillus* and *Cladosporium* sp. and to grass pollen.

A retrospective analysis of dates of severe asthma attacks may identify individual seasonality, which is a risk factor for life-threatening and intractable asthma.

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An audit of intensive care unit (ICU) admissions at Red Cross War Memorial Children's Hospital in Cape Town drew attention to a group of patients who had required recurrent ICU treatment for acute severe asthma and whose admissions occurred on or near an anniversary of a previous admission. This admission pattern suggested exposure to seasonally occurring allergens, precipitating recurrent attacks of asthma in individual patients at set times during the year.

Previous studies have identified seasonal asthmatics by studying those who present at hospital during periods of peak asthma frequency.[1] Whereas triggers such as pollens[2,3] have been incriminated as the cause of seasonally increased frequency, the association has been found difficult to prove.[1]

In the present study individual patients with attacks recurring at the same time of year were studied with the aim of supporting or disproving the hypothesis that they formed a distinct sub-population, with life-threatening asthma and sensitivity to seasonally occurring allergens.

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Method

A retrospective longitudinal case-controlled study of asthmatic children (under 15 years old) requiring 'seasonal' ICU admission was performed. Patients diagnosed as having asthma and admitted to the ICU more than once during the period 1974 - 1987 were included in the study.

The diagnosis of asthma was made by the doctor attending the patient at the time of hospitalisation. This diagnosis was based on evidence of reversible lower airway obstruction, responding to bronchodilators. To fulfil the criteria for a seasonal ICU admission pattern a child had to be admitted to the ICU at least twice (or more) in the same or adjacent months in different years. These admissions did not have to occur in adjacent years. In some seasonally admitted patients, non-seasonal admission occurred before, between or after seasonal admissions; these admissions were not included in the analysis of seasonal admissions. Patients admitted to the ICU with acute severe asthma more than once, but in an apparently random, non-seasonal manner, were studied as controls.

For each patient, data on sex, socio-economic status, family history of allergy, pet ownership, passive smoking, age of symptom onset, date of first hospital visit, maintenance therapy (including steroid therapy) and date of first ICU admission were collected. Further data on skin sensitivity and radio-allergosorbent test (RAST) results were obtained from patient records. Family income, occupation of the breadwinner and sleeping density were assessed as socio-economic indicators.

Admission-related data were studied for each 'seasonal' admission in seasonally admitted patients and for every admission in control patients. Time and date of admission, duration of preceding symptoms, possible precipitating factors, medication changes, history of compliance, evidence of infection and radiological and laboratory data were recorded from patient notes. Infection was diagnosed from information in clinical notes. Lower respiratory tract infection was diagnosed in patients with a chest radiograph showing a perihilar infiltrate or parenchymal lung consolidation. Details of intensive care unit treatment, including drug therapy, assisted ventilation and procedures, were also recorded for each admission.

Data were collated and analysed using the Epi-Info Version 5 database and statistical programme. Odds ratios (ORs) and 95% confidence limits were calculated from two-by-two tables.

Results

There were 415 ICU admissions for acute severe asthma in the 14 years between 1974 and 1987. Two hundred and eighty-two were single admissions and 133 (32% of the 415 admissions for acute severe asthma) were recurrent admissions in a group of 40 patients (12,4% of all patients). Of the patients requiring recurrent admission, 21 (6,5% of all patients) had 65 'seasonal' admissions (15,6% of all admissions) and 19 (5,9% of all patients) had 47 random, non-seasonal admissions. Fifteen of the 21 patients with 'seasonal' admissions also had 21 admissions which occurred at random, non-seasonal times.

Patients with seasonal admissions came from families that were significantly better off, both in terms of income and occupational grade (Table I), than families of patients with non-seasonal admissions. Insufficient data were available for assessment of differences in sleeping density. Five children in the seasonal group had lost a mother to asthma, compared with none in the random group (Table I).

There was no difference between the groups in age at onset of symptoms or age at first hospital visit for asthma, but children in the non-seasonal group were admitted to the ICU for the first time when significantly younger (Table II). Significantly more children in the seasonal group had received maintenance steroid therapy at some time during the years they attended the Allergy Clinic at the Red Cross War Memorial Children's Hospital (Table I). There was no difference between the groups in the frequency of passive smoking or pet ownership. Significantly more patients in the seasonal group failed to outgrow their asthma and required therapy into adulthood (Table I). The seasonal group generally attended the Allergy Clinic for a longer period and were older when last seen at the hospital (Table II).

Patients with a seasonal admission pattern were admitted to the ICU throughout the year, while patients with a random recurrent admission pattern were admitted regularly throughout the year except for a trough in October (Fig. 1). Admission rates were significantly different between the groups in October. Admission-specific data indicated no difference between groups in compliance with therapy, duration of symptoms before admission or identifiable precipitating factors, other than respiratory infection. The seasonal group had a significantly lower rate of pulmonary infiltrates present on the chest radiograph at admission (Table I). There was no difference between the groups in leucocyte or eosinophil counts.

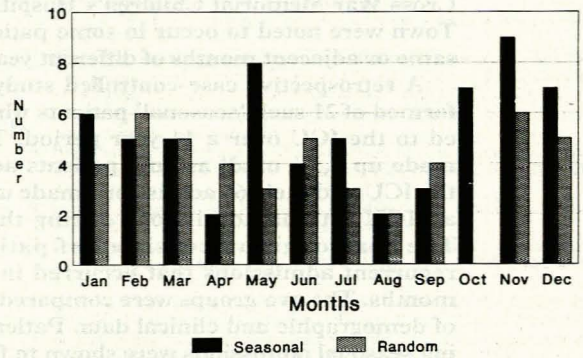

FIG. 1.
Recurrent monthly admissions to a respiratory ICU for management of acute severe asthma, 1976-1989.

TABLE I.
ORs for the positive association of a variable with a seasonal admission pattern

Variable	Rate of occurrence: Seasonal	Rate of occurrence: Non-seasonal	OR	Significance
Income under R500 per month	8/21	14/19	0,22 (0,04 < OR < 01)	$P < 0,025$
Occupation 'skilled' and higher	15/21	7/19	4,29 (0,95 < OR < 20,53)	$P < 0,06$
Maternal asthma death	5/21	0/19	Undefined lower limit 2,35	$P < 0,05$
Discharged well (outgrew asthma)	1/21	6/19	0,11 (0,00 < OR < 1,13)	$P < 0,04$
Died	2/21	0/19	-	-
Infiltrate on chest radiograph	16/57	27/41	0,28 (0,11 < OR <0,70)	$P < 0,004$
No clinical infections	37/65	12/43	3,41 (1,39 < OR < 8,53)	$P < 0,005$
Maintenance steroid therapy	18/21	10/19	5,4 (0,98 < OR < 33,17)	$P < 0,05$

TABLE II.
Age details and duration of illness for seasonal and non-seasonal groups

	Seasonal					Non-seasonal					
	Mean	25th %	Median	75th %	Range	Mean	25th %	Median	75th %	Range	Significance
Age (yrs) at:											
First ICU admission	6,6	3	6	11	0 - 13	3,8	1	2	4	1 - 14	$P < 0,03$
Any ICU admission	8,5	4	9	12	1 - 15	3,9	1	2	4	1 - 15	$P < 0,000000$
Last follow-up at RXH	13,6	12	15	16	5 - 20	8,3	5	7	12	2 - 16	$P < 0,0004$
Yrs of inclusion in study*	9,1	7	9	11	2 - 15	6,1	4	6	8	2 - 13	$P < 0,005$

*Date of last follow-up — date first seen at RXH.
RXH = Red Cross War Memorial Children's Hospital.

TABLE III.
ORs for the positive association of a positive radio-allergosorbent test (≥ 2 +) with a seasonal admission pattern

Variable	Rate of occurrence: Seasonal	Rate of occurrence: Non-seasonal	OR	Significance
House dust mite	17/20	12/17	2,36 (0,38 < OR < 15,90)	$P < 0,43$
Bermuda grass	7/14	2/14	6,60 (0,96 < OR < 52,44)	$P < 0,056$
Aspergillus	5/13	0/10	Undefined L/L; U/L 0,83*	$P < 0,046$
Alternaria	7/12	3/11	3,73 (0,49 < OR < 32,40)	$P < 0,21$
Cladosporium	7/12	0/10	Undefined L/L; U/L 1,82	$P < 0,005$
Dog	8/15	2/12	5,71 (0,73 < OR < 55,40)	$P < 0,11$
Cat	6/14	2/12	3,75 (0,46 < OR < 37,02)	$P < 0,216$
Milk	6/15	3/12	2,00 (0,29 < OR < 14,69)	$P < 0,68$

* L/L = lower limit; U/L = upper limit.

RASTs indicated significantly more frequent sensitivity to grass allergens and the fungal allergens *Cladosporium* and *Aspergillus* in the seasonal group (Table III). The rate of RAST positivity for housedust mite, *Alternaria*, dog and cat dander and milk protein was higher in the seasonal group than in the control group, although this difference was not statistically significant.

Discussion

Children with asthma who required steroid therapy and have repeated admissions for management of acute severe asthma are well known to be at risk of increased morbidity and mortality[2] from their illness. From the present study, it appears that within this high-risk population there is an identifiable group at even higher risk. These children characteristically require repeated ICU admissions at about the same time of year, an admission pattern that may be obscured by additional admissions occurring randomly. They may have a family history of asthma-related mortality, and are themselves more likely to grow up to be adults with asthma.

RASTs and skin tests show this group of children to have an increased sensitivity to fungal and grass allergens, and an increased sensitivity to allergens in general. This finding may be explained by multiple allergy[3] or by a shared high response status[4] to multiple allergens. Their increased sensitivity to allergens in general might also explain their random non-seasonal admissions. Whereas acute lower respiratory tract infections commonly precipitate acute severe asthma in our community,[5] as seen in the control group, seasonally presenting children have significantly fewer such infections on seasonal admissions, an observation supporting the hypothesis that their admissions are precipitated by exposure to seasonally occurring allergens rather than by respiratory infections.

The severity of asthma in these patients (as assessed by their maintenance therapy requirements) and the increased frequency with which they required ICU admission is similar to recently reported experience of patients sensitive to fungal aero-allergens.[6] Our patients showed a similar increased sensitivity to fungal allergens. Spore counts are high in greater Cape Town throughout the year,[4] but their peak levels in October coincide with the spring season, which is often warm and humid.

The higher socio-economic status of the seasonal group may protect them from lower respiratory tract infections, which might be more frequent and thus precipitate more asthma attacks in less privileged children from overcrowded environments.

It is possible that patients in this study identified as having seasonal asthma are simply children with more severe asthma, who have more attacks of asthma and therefore a higher chance of recurrent attacks and ICU admissions in the same or adjacent months of the year. Nevertheless, our study shows that if seasonality as a characteristic of individual patients with asthma is assessed in terms of the individual patient's pattern of presentation rather than by a study of patients presenting during times of peak asthma frequency, a population at increased risk is identified.

In the sub-population identified by such an analysis the alarming association of maternal death from asthma with an increased risk of asthma persisting into adulthood, an enhanced risk of morbidity and mortality and a high-intensity response to environmental allergens suggests that these risks may be inherited from a parent with the same pattern of response. Children with a seasonal admission pattern in addition to known risk factors for severe disease should be managed with extreme care and possibly with additional medication such as oral steroids at times of known enhanced risk. Their families should be investigated for a genetically linked high responder status to fungal allergens and to grass pollen.

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