

ORIGINAL ARTICLE

Asthma phenotypes in Niue Islanders

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Objective: The aim of this study was to identify asthma phenotypes in patients of Niue Island ancestry that might be suitable for susceptibility gene mapping studies.

Methodology: Two hundred and sixteen Niue Islanders with physician-diagnosed asthma that was not secondary to other medical conditions were recruited through community organisations. Fifty-one of the subjects with asthma were resident on Niue Island and 165 in New Zealand. Each subject was interviewed and tested for atopy, serum [IgE] (5% quantile, median, 95% quantile) and lung function.

Results: There were two groups of subjects defined by an age of onset of asthma less than 12 years of age (childhood-onset, boys:girls 64:65) and greater than 12 years of age (adult-onset, men:women 11:76). A positive response (wheal > 3 mm) to at least one aeroallergen was seen in 181 patients, with 168/181 (92.8%) responding to house dust mite. Twenty-eight subjects with asthma were non-atopic (no detectable wheal) and the atopy status of seven subjects with asthma could not be determined (wheal < 3 mm). In childhood-onset asthma, serum IgE levels were higher ($P < 0.0001$) in subjects with atopic than in subjects with non-atopic asthma. In adult-onset asthma, serum IgE levels were higher ($P < 0.0001$) in subjects with atopic asthma than in either subjects with non-atopic asthma or matched non-atopic subjects without asthma. The asthma phenotypes in Niue Island and New Zealand residents were similar.

Conclusions: Both atopic and non-atopic asthma phenotypes exist in Niue Islanders resident in Niue and New Zealand. The potential for mapping asthma susceptibility genes in this isolated population is discussed.

Key words: asthma, atopy, Niue, Polynesia.

INTRODUCTION

Atopic asthma results from aeroallergen-induced chronic inflammation of airways, and is associated with deteriorating lung function over time.¹ The management of this disease involves daily use of medications that suppress airway inflammation over many years. This type of management is expensive,² and produces problems with treatment compliance. The best possible treatment for atopic asthma would involve a single intervention, such as a therapeutic immunization, that permanently suppressed the IgE-

mediated response to aeroallergens.³ Designing such an intervention will require a more comprehensive understanding than is currently available of the molecular mechanisms that produce these IgE responses in people with asthma. As these IgE responses are strongly influenced by genetic risk factors,^{4,5} identification of the polymorphic genes that control them should allow identification and study of the crucial molecular mechanisms that precipitate atopic asthma. Strategies for the development of curative interventions could then be explored.

The history of Polynesian migrations from South-East Asia suggests that the population of Niue Island could have the genetic characteristics of a founder population.^{6–8} Founder populations have high levels of linkage disequilibrium, low levels of genetic diversity and have proven useful for identifying susceptibility loci for multifactorial diseases,⁹ including an asthma susceptibility locus in Europeans.¹⁰ It is pos-

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sible that the Niuean population could be valuable for identifying susceptibility genes for atopic asthma that are relevant not only to Polynesians, but to all human populations.⁹

Although asthma is a significant problem in Pacific Island populations,^{11,12} there is no published information about the common phenotypes of this heterogeneous disease in these groups. The purpose of the present study was to identify asthma phenotypes in patients of Niue Island ancestry that might be suitable for susceptibility gene mapping studies.

METHODS

Subjects

Two hundred and fifty-five Niue Islanders with a history of at least one, physician-diagnosed, acute asthma attack occurring after their 6th birthday agreed to participate in the study. The age of 6 years was chosen to minimize the number of subjects with the 'transient early wheezing' phenotype, in whom asthma is not associated with atopy.¹³ Each volunteer was interviewed with the assistance of an interpreter to determine the age of onset of asthma, the symptoms and the factors precipitating acute asthma attacks, cigarette smoking history, the history of hay fever and atopic eczema, medication use and frequency of hospitalization. Twenty-one subjects (10 men, 11 women) stated that their asthmatic symptoms had started after they began cigarette smoking, and they were excluded from the study. Eighteen current smokers and 13 ex-smokers who stated that their asthma symptoms preceded cigarette smoking were included in the study. Eighteen other subjects were excluded from the analyses because of myocarditis ($n = 1$), bronchiectasis ($n = 1$), symptoms suggestive of hyperventilation attacks ($n = 2$), chronic cough producing discoloured sputum ($n = 1$), cough as the only symptom ($n = 2$) or inability to give a clear history of their symptoms ($n = 11$). The remaining 216 subjects with asthma were resident in the Auckland metropolitan area ($n = 165$) or on Niue Island ($n = 51$) at the time of interview.

In addition to the interview, each subject underwent spirometry, had a skin-prick test for atopy and gave blood for measurement of serum IgE concentration. Blood was also obtained from 224 non-asthmatic relatives of these asthmatic subjects and 70 of these relatives were tested for atopy. Recruiting was carried out through sports teams, community health and church organizations, radio and television appeals and through family contacts. The study was approved by the Auckland District Health Board ethics committee, and all subjects gave informed consent.

Atopy testing

Skin-prick testing for atopy was performed using house dust mite (*Dermatophagoides pteronyssinus*), cat pelt and seven-grass pollen mix (*Poa pratensis*, *Anthoxanthum odoratum*, *Lolium perenne*, *Festuca*

elatior, *Dactylis glomerata*, *Agrostis tenuis*, *Phleum pratense*) antigens according to the manufacturer's instructions (Bayer Corporation, Elkhart, CT, USA). A histamine-positive control and a glycerine/saline-negative control were also used. A wheal diameter greater than or equal to 3 mm was taken to indicate atopy, and detectable wheals less than 3 mm in diameter were taken to indicate unknown atopy status. Subjects with undetectable wheals to all three aeroallergens were classified as non-atopic.

Serum IgE concentrations

Serum was stored at -70°C and total serum IgE concentrations were measured by ELISA (ALerCHECK, Portland, ME, USA) according to the manufacturer's instructions. Sera with IgE concentrations exceeding the highest standard included in the kit were repeated with serum diluted 1:9.

Spirometry

Spirometry was performed using a portable Microloop II spirometer (Micro Medical Ltd, Kent, UK). Age-, sex- and height-adjusted measurements (per cent of predicted) of FEV₁, PEF and FVC were recorded for all subjects with asthma at the time of interview. The Caucasian reference range, which is known to be similar to the Polynesian range,¹⁴ was chosen for calculation of the percentage predicted values. No subject was having symptoms of an acute asthma attack at the time of spirometry and no subject had used an inhaled bronchodilator on the day of spirometry to treat an acute attack. However, all routine medications were being taken, and included inhaled salmeterol ($n = 5$), inhaled corticosteroids ($n = 112$), oral aminophylline ($n = 10$), sodium cromoglycate ($n = 1$) and reducing doses of prednisone ($n = 3$). No subjects were taking β -blocking medication.

Statistics

Numerical data are presented as (the 5% quantile, the median, the 95% quantile). Fisher's exact test was used to compare categorical variables between groups. The Wilcoxon rank sum test was used to compare continuous variables between groups, and differences in variance between groups were compared with a folded F statistic. Correlations were assessed by the Spearman rank order correlation coefficient. Multiple and logistic regression procedures were used for multivariate analyses. The P -values for type III analysis of effects are reported. All statistics were calculated using the SAS statistical package (SAS, Cary, NC, USA).

RESULTS

Two hundred and sixteen subjects with physician-diagnosed asthma reported having at least one acute

attack of symptoms consistent with asthma after their 6th birthday. The asthmatic subjects recruited in Auckland ($n = 165$) and on Niue Island ($n = 51$) were similar in age (5% quantile, median, 95% quantile: 6, 28, 68 years and 6, 28, 62 years, respectively), ratio of females to males (1.9:1.0 and 1.8:1.0, respectively) and age of onset of their asthma (1, 8, 48 years and 1, 6, 35 years, respectively).

Age of onset of asthma

Two hundred and ten of the 216 subjects with asthma (or their parents) were able to recall the age of their first asthma attack. All six subjects (two men, four women) who did not know the exact age of onset of their asthma had onset in childhood. Inspection of a histogram showing the frequency of subjects with asthma onset at each age identifies two groups of asthmatics, with an age of onset below and above the age of 12 years (Fig. 1). These groups have been defined as childhood-onset asthma and adult-onset asthma.

In the group of subjects with childhood-onset asthma (current age; 5% quantile, median, 95% quantile: 6, 12, 48 years), there were a similar number of male ($n = 64$) and female subjects ($n = 65$), and no difference in the age of onset ($P = 0.09$) could be

detected between male (1, 1, 8 years) and female subjects (1, 3, 10 years). The age of the first asthma attack was also similar ($P = 0.63$) in the subgroups of people with childhood-onset asthma born in Niue (1, 3, 10 years) and New Zealand (1, 1, 9 years).

There were more women ($n = 76$) than men ($n = 11$) in the group with adult-onset asthma (current age; 5% quantile, median, 95% quantile: 28, 52, 70 years). The age of onset was similar ($P = 0.73$) in men (14, 34, 47 years) and women (15, 29, 57 years). The age of onset of asthma was also similar ($P = 0.18$) in subjects with adult-onset asthma resident on Niue Island (14, 28, 57 years) and in New Zealand (16, 31, 51 years).

Skin-prick testing for atopy

Twenty-eight subjects had negative skin-prick tests to all three aeroallergens and were classified as having non-atopic asthma (Table 1). The frequency of non-atopic asthma was higher ($P = 0.004$) among female (25/141) than male subjects (3/75). This effect was clearly present in the childhood-onset asthma subgroup ($P = 0.002$). The trend was also present in the adult-onset asthma subgroup but did not reach statistical significance ($P = 0.60$), probably because of the small number of men. There was no influence of smoking history ($P = 0.78$) or country of birth ($P = 0.68$) or residence ($P = 0.48$) on the frequency of non-atopic asthma.

Seven subjects had one or more detectable wheals that were all less than 3 mm in diameter. Serum IgE levels varied widely in this group of patients (5% quantile, median, 95% quantile: 2, 21, 860 IU/mL), and they were classified as having asthma with an unknown atopy status.

In the 181 subjects with atopic asthma (at least one wheal diameter ≥ 3 mm), house dust mite was the most frequently positive aeroallergen (92.8%), with high frequencies in both male (67/71) and female subjects (101/110), in both childhood-onset (100/105) and adult-onset (68/76) asthma, and in both subjects resident on Niue Island (37/39) and subjects resident in New Zealand (131/142).

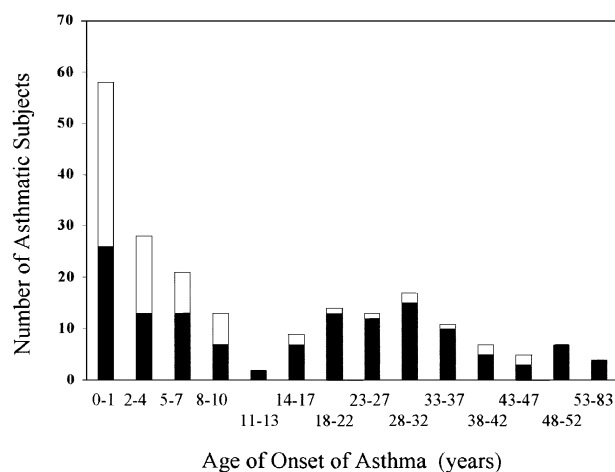


Figure 1 Histogram showing the distribution of the age of onset of asthma in 210 Niue Island males (□) and females (■).

Serum IgE concentrations

The range of serum IgE concentrations in Niuean asthmatic patients and the negative correlation

Table 1 Frequency of atopy to each aeroallergen in childhood- and adult-onset asthma in male and female subjects

Aeroallergen	Childhood-onset asthma		Adult-onset asthma	
	Boys	Girls	Men	Women
Total no. subjects with asthma	64	65	11	76
All tests negative (n (%))	3 (4.7)	16 (24.6)	0 (0)	9 (11.8)
At least one test 1–2 mm (n)	1	4	0	2
At least one test ≥ 3 mm (n)	60	45	11	65
House dust mite (n (%))	58 (96.7)	42 (93.3)	9 (81.8)	59 (90.8)
Grass pollen (n (%))	40 (66.7)	27 (60.0)	10 (90.9)	45 (69.2)
Cat (n (%))	28 (46.7)	17 (37.8)	5 (45.5)	30 (46.2)

($r = -0.33$, $P < 0.0001$) to patient age is shown in Figure 2. In childhood-onset asthma, the median serum [IgE] and the variance in serum [IgE] were both significantly higher ($P < 0.0001$) in subjects with atopic (5% quantile, median, 95% quantile: 14, 119, 770 IU/mL; $n = 105$) compared with those with non-atopic asthma (2, 20, 85 IU/mL; $n = 19$). Similarly, in the women with adult-onset asthma, the median serum [IgE] and the variance in serum [IgE] were both significantly higher ($P < 0.0001$) in subjects with atopic asthma (10, 56, 415 IU/mL; $n = 65$) compared with subjects with non-atopic asthma (4, 15, 41 IU/mL; $n = 9$) and an age- and sex-matched group of subjects without any evidence of allergy or atopy (3, 15, 103 IU/mL; $n = 11$).

On multivariate analysis, a high serum IgE concentration was associated with young age ($P < 0.0001$), with male sex ($P = 0.04$) and with atopic relative to non-atopic asthma ($P = 0.0001$). There was no influence of the age of onset of asthma ($P = 0.94$), smoking history ($P = 0.86$), country of birth ($P = 0.53$), or country of residence ($P = 0.66$) on serum IgE concentration.

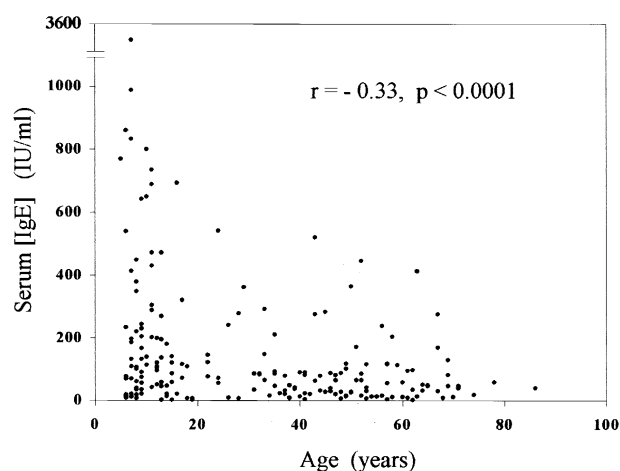


Figure 2 Scatter plot showing the negative correlation between serum IgE concentrations and age in Niue Island asthmatics.

Symptoms of asthma

The most commonly reported acute attack symptom was wheeze ($n = 201$, 93.1%), followed by difficulty breathing ($n = 157$, 72.7%), cough ($n = 131$, 60.6%), night cough ($n = 104$, 48.1%) and chest tightness ($n = 58$, 26.9%). The diagnosis of asthma was never solely dependent on the presence of episodic wheeze as a symptom. Although six subjects did report wheeze as their only symptom, four of these had the diagnosis of asthma confirmed by a physician at the time of emergency room treatment for an acute attack. One patient gave a clear history of attacks of wheeze precipitated by exercise and house dust. The final patient, whose asthma symptoms only occurred in association with respiratory infections, had detectable wheeze on physical examination (auscultation) at the time of being recruited into the study.

A comparison of the spectrum of acute attack symptoms in patients resident in New Zealand and Niue Island is shown in Table 2. Residents of Niue Island were more likely to report chest tightness ($P = 0.0001$) and cough ($P = 0.05$) and less likely to report wheeze ($P = 0.002$) as symptoms of their asthma, compared with residents of New Zealand. Subjects with asthma with onset in childhood were more likely to report wheeze ($P = 0.04$) and night cough ($P = 0.03$) and less likely to report difficulty breathing ($P = 0.009$) as symptoms of their asthma, compared with subjects with adult-onset asthma. There was no difference in symptoms between male and female subjects and between people with atopic and non-atopic asthma (data not shown).

Environmental factors precipitating asthma attacks

The factors most commonly reported to induce asthma attacks were respiratory infection ($n = 177$), change in weather conditions ($n = 146$), exercise ($n = 117$), house dust ($n = 116$), food ($n = 55$), grass and/or pollen ($n = 39$), emotion ($n = 27$) and pets ($n = 23$). Only three subjects reported occupation-related asthma. Female subjects with asthma were more likely to report emotion as a precipitating factor

Table 2 Comparison of reported acute asthma symptoms in 216 Niue Island asthmatics by country of birth and country of residence

Country of birth:	Niue		New Zealand	
Country of residence:	Niue	New Zealand	Niue	New Zealand
Total no. subjects	43	95	8	70
Subjects reporting wheeze (n (%)) [†]	36 (83.7)	89 (93.7)	6 (75.0)	70 (100.0)
Subjects reporting difficulty breathing (n (%))	35 (81.4)	73 (76.8)	5 (62.5)	44 (62.9)
Subjects reporting tight chest (n (%)) [‡]	25 (58.1)	19 (20.0)	3 (37.5)	11 (15.7)
Subjects reporting cough (n (%)) [§]	30 (70.0)	50 (52.6)	7 (87.5)	44 (62.9)
Subjects reporting night cough (n (%))	16 (37.2)	44 (46.3)	4 (50.0)	40 (57.1)

[†]Symptoms reported more frequently by Niue Island residents ($P < 0.01$).

[‡]Symptoms reported less frequently by Niue Island residents ($P = 0.0001$).

[§]Symptoms reported less frequently by Niue Island residents ($P < 0.05$).

for asthma than male subjects with asthma ($P=0.04$). Subjects with asthma who were negative to all three skin-test allergens were less likely to report house dust ($P=0.02$), weather conditions ($P=0.03$) and grass/pollen ($P=0.08$) as precipitating attacks than subjects with asthma with one or more positive skin tests. Subjects with asthma who were resident on Niue Island were less likely to report exercise ($P=0.009$), change in weather conditions ($P=0.004$) and emotion ($P=0.0003$) as precipitating asthma than those resident in New Zealand. Exercise was reported to precipitate asthma less frequently in subjects with adult-onset than in subjects with childhood-onset asthma ($P=0.002$).

Pregnancy and asthma

Four subjects with established asthma before they became pregnant reported that their asthma was more severe after they became pregnant. Five women reported childhood-onset asthma that had disappeared, returned with pregnancy and then persisted for between 8 and 30 years. Sixteen women reported that their first ever asthma attack occurred when they were pregnant. One of these 16 women reported that she only had asthma when pregnant, and 15 of the 16 women reported that asthma persisted after pregnancy. Two of these 15 women stated that their asthma had disappeared at 6 and 15 years after pregnancy, and the other 13 women reported current asthma that had persisted for between 4 and 32 years.

Of the 15 women who developed long-lasting asthma during pregnancy, two had non-atopic asthma, 12 had atopic asthma with atopy to house dust mite and the atopy status of one patient was unknown. Serum IgE levels were similar in women with pregnancy-induced asthma and in women who did not report pregnancy-induced asthma.

Severity of asthma

All subjects had used a β_2 -adrenoreceptor agonist inhaler at some time. One hundred and eight subjects had been given at least one course of prednisone. Sixty-five subjects had attended a general practitioner or emergency room for treatment with a nebulizer, and a further 99 had been admitted to hospital. Prednisone treatment, emergency room treatment and hospitalization rates were similar in subjects with atopic and non-atopic asthma. Subjects with adult-onset asthma had higher rates of prednisone use ($P=0.03$) than subjects with childhood-onset asthma, but similar hospitalization rates ($P=0.68$).

Spirometry

The per cent predicted (pp) values for FEV₁ (5% quantile, median, 95% quantile: 55, 96, 124%; $P=0.001$), FVC (60, 95, 119%; $P<0.0001$) and peak flow rates (39, 79, 119%; $P<0.0001$) were all lower than expected. The ppFEV₁ was lower ($P<0.0001$) in subjects with

adult-onset asthma (49, 85, 116%) than in subjects with childhood-onset asthma (70, 102, 126%). The duration of asthma correlated negatively to ppFEV₁ ($r=-0.39$, $P<0.0001$) and ppFVC ($r=-0.24$, $P=0.0008$), but not to peak flow rate ($r=0.02$, $P=0.73$). Subjects with asthma who had required hospitalization for asthma had a lower ppFEV₁ ($P=0.0002$), FVC ($P=0.003$) and peak flow rate ($P=0.02$) than subjects who had never required hospitalization. Subjects who had required prednisone for management of their asthma had a lower ppFEV₁ ($P<0.0001$), ppFVC ($P=0.02$) and peak flow rate ($P=0.05$) than subjects who had never required prednisone. On multivariate analysis, there were independent effects of asthma duration ($P<0.0001$) and prednisone use ($P=0.0002$) on ppFEV₁. In addition, the interaction term between age of onset (adult, childhood) and duration of asthma was significant ($P=0.001$) indicating that the rate of decrease in ppFEV₁ in adult-onset asthma ($-0.96+0.24\%$ predicted per year) was greater than in childhood-onset asthma ($-0.55+0.12\%$ predicted per year) (Fig. 3). There were only minor changes in the significance of this relationship when patients taking salmeterol ($n=5$) or aminophylline ($n=10$) were removed from the analysis, or when current inhaled steroid use was included as a variable in the multivariate analysis. There was no influence of serum [IgE] ($P=0.54$), gender ($P=0.44$), smoking history ($P=0.33$), country of birth ($P=0.69$) or residence ($P=0.85$), or atopy status ($P=0.36$) on ppFEV₁.

DISCUSSION

The purpose of the present study was to determine if there are groups of Niuean patients with atopic asthma who might be suitable for recruiting into studies designed to map asthma susceptibility genes. The approach was to identify subjects with clinically significant (physician-treated) asthma, exclude all

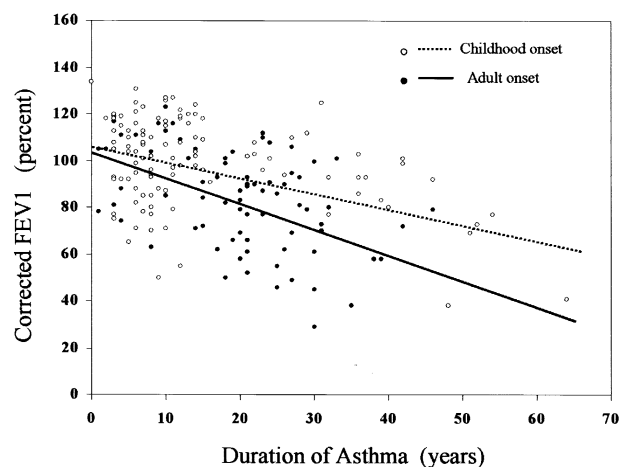


Figure 3 Scatter plot comparing the influence of asthma duration on FEV₁ in asthmatics with onset before (childhood-onset) and after (adult-onset) the age of 12 years.

subjects whose symptoms might be secondary to other respiratory conditions including transient early wheezing¹³ and cigarette smoking, and to determine whether the remaining subjects exhibited the features of atopic asthma seen in other populations. These features are a typical spectrum of symptoms and environmental exacerbating factors,¹³ a deterioration of FEV₁ with duration of asthma,¹ elevated serum IgE concentrations,^{13,15} and evidence of atopy,^{13,15} particularly to house dust mite aeroallergens.

These features of atopic asthma were clearly present in a group of 181 asthmatics. Although this number might not be enough for a successful asthma susceptibility gene-mapping project, it represents less than 1% of the Niue Island population. Because the prevalence of atopic asthma has never been measured either in Niue Island or New Zealand, it is not possible to determine precisely how many more subjects will be available for recruiting. However, the overall prevalence of the asthma phenotype in Pacific Islanders is usually reported as being higher than 10%.¹² As a recent study in a founder population in Finland identified an asthma susceptibility locus with a study size of 220 asthmatics,¹⁰ it is possible that a sufficient number of Niuean patients could be obtained with continued recruiting.

It should be emphasized that this was not a random survey of asthma phenotypes in Niue Islanders, and the features of the asthma that have been described in this selected group of patients might not apply to the whole asthmatic population. However, there are a number of features of asthma in these patients that are noteworthy from the point of view of recruiting homogeneous groups of subjects for studies of asthma susceptibility genes. First, the recruiting strategy identified two distinct groups of subjects with asthma that are distinguishable by onset of asthma either in childhood or adulthood. A higher proportion of the group with adult-onset asthma reported difficulty breathing as a symptom of asthma, a higher proportion had used prednisone for treatment of an acute attack and there was a more rapid rate of deterioration in FEV₁ in the adult-onset group that was independent of cigarette smoking. Although hospitalization rates were similar in the two groups, most people hospitalized with childhood asthma had been admitted only as infants at the time of their first attack (data not shown). These observations raise the possibility that the subjects in the present study with adult-onset asthma have a more serious form of disease than the subjects with childhood-onset asthma, and should be recruited into separate studies.

There was a high proportion of women in the adult-onset asthma group in this study. It cannot be determined whether this is a result of a sex-related difference in asthma susceptibility or to a reluctance of Niue Island men to volunteer for research studies. However, this is not a problem from the perspective of performing genetic studies, as a more homogeneous single-sex phenotype should increase the chance of finding susceptibility genes.

In addition to the subjects with atopic asthma, 28 subjects were identified with asthma that was not associated with atopy. Non-atopic asthma, which was

previously known as intrinsic asthma,¹⁶ was more common in the present sample of female Niue Islanders, as has been reported previously in other ethnic groups.¹⁶ However, non-atopic asthma in the present patient group was not associated with more severe disease or with a higher prevalence in the adult-onset group as has been reported by other authors.¹⁶⁻¹⁸ This may be because of differences in study design. This group of subjects might be useful for identifying asthma susceptibility genes that do not influence asthma susceptibility through an effect on atopy. However, it is unlikely that a large enough number of these patients would be available exclusively within the Niuean community, and studies including subjects with non-atopic asthma from other Polynesian groups might be necessary.

The finding of a group of women who developed their first asthma attack during pregnancy is also of interest. Although asthma severity has been reported to be exacerbated by pregnancy in some women,^{19,20} the authors of the present report have not been able to find any other published reports of asthma developing for the first time in pregnancy. This finding could be an artefact of retrospective data collection, and would need to be confirmed in a prospective study.²⁰

The prevalence of asthma might be higher in Polynesian people resident in New Zealand compared with those resident in their native islands.¹¹ However, there is no published data addressing the issue of whether the phenotype of asthma is different in these two locations. The phenotypes of clinically significant asthma that were detected in Niueans living in Auckland were almost identical to the phenotypes in Niueans living on Niue Island. This does not exclude the possibility that the relative frequencies of these phenotypes could be different in Niue and New Zealand or that other undetected asthma phenotypes could exist in either location. However, there is no reason to treat the recruited Niue and New Zealand resident patients as separate phenotypes in genetic studies.

There are three opportunities for identifying genes that increase susceptibility to asthma and asthma-related phenotypes. First, children with atopic asthma have a wide range of serum IgE concentrations (see Fig. 2), and this parameter is believed to be significantly influenced by genetic risk factors.²¹ A case control study comparing marker allele frequencies in children with high and low levels of serum IgE could identify significant associations. Second, a case control study of women with adult-onset atopic asthma should be feasible using groups of non-atopic, non-asthmatic controls and atopic, non-asthmatic controls. This would require the recruitment of new groups of control subjects. Third, both parents of the subjects with childhood-onset asthma in the present study are generally available for study, and would be suitable for a linkage study of candidate genes using the linkage disequilibrium test approach. As it is difficult to obtain control DNA for case control studies in children, a study of this nature would focus on candidate genes identified in case control studies by other investigators.

In summary, subjects with either non-atopic or atopic asthma, who should be suitable for studies designed to map susceptibility genes have been identified in the Niue Island population. If population genetic studies show that Niue Islanders have the characteristics of an expanding, founder population, they could make a valuable contribution to understanding the mechanisms of asthma in all ethnic groups.

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