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The Epidemiology of Asthma and Bronchial Hyperresponsiveness in Auckland Children

Philip Keith Pattemore

A thesis submitted in partial fulfilment of the requirements for the degree of Doctor of Medicine

University of Auckland

1991
Dedicated to my father, Errol Keith Pattemore, and my mother, Elizabeth Pattemore, who have always encouraged me to pursue excellence and aim for the highest.
ABSTRACT

In New Zealand (NZ) asthma mortality rates are higher than in any other developed country studied, and hospital admission rates for asthma are among the highest. Within NZ, both mortality and hospital admission rates for asthma are higher among Polynesians than among Europeans. To investigate the possibility that these differences were due to differences in asthma prevalence, a study was initiated to measure the prevalence and severity of asthma among both Europeans and Polynesians in Auckland, using methods identical to those used in an overseas study.

From all primary schools in the Auckland Urban Area, classes were sampled by two-stage, random, stratified sampling. In the winter of 1985, the children in the sampled classes were studied employing a questionnaire and a rapid, portable method of bronchial challenge testing with histamine which had been used to study schoolchildren aged 8 to 10 years in two areas in New South Wales (NSW), Australia. Participation was 83%, the participants comprising 1084 European, 509 Maori, and 460 Pacific Island children, who were closely matched in gender and age to the NSW children. Prevalence of various items was compared including asthma symptoms, diagnosed asthma, and bronchial hyperresponsiveness (BHR), defined as a 20% fall in the one-second forced expiratory volume (FEV1), on or before the administration of a cumulative dose of 7.8 µmol histamine.
The prevalence rates of respiratory symptoms, BHR, severe BHR and BHR combined with symptoms were similar among the 1084 Auckland European children and 769 inland NSW children, but lower among 718 coastal NSW children than the other two sites. In Auckland, the prevalence of respiratory symptoms was higher in Maoris than among Europeans or Pacific Islanders, whereas prevalence of diagnosed asthma was similar in all three groups. Europeans had the highest rate of BHR and severe BHR followed by Maoris then Pacific Islanders. Maori and Pacific Island children reporting symptoms were less likely to receive prophylactic medication than European children.

The study design also enabled assessment of the epidemiological correlates of BHR, which had been little studied in random populations before 1985. Among the Auckland children, bronchial responsiveness was found to be unimodally distributed, with no clear separation between children with a diagnosis or symptoms of asthma and those without. The presence or absence of BHR did not accurately identify children with a diagnosis or symptoms of asthma. A 14-variable multiple logistic regression model was developed which explained 27% of the variability in BHR rates. The main variables independently increasing BHR risk were: low baseline FEV1, a history of wheeze, diagnosed asthma, atopic conditions, or bronchodilator treatment, and European (as opposed to Polynesian) ethnicity. Climatic conditions at the time of the test were less strongly associated.

In summary, neither the international nor the inter-ethnic differences in asthma mortality and asthma admission rates were adequately explained by differences in the prevalence of asthma symptoms, diagnosed asthma or BHR; however, differences in asthma severity and in the management of asthma may be contributory. In this large population-based study of children, BHR was associated independently with a number of different variables but did not precisely identify children reporting asthma symptoms or a diagnosis of asthma. Thus a single bronchial challenge test is not an ideal tool on its own for diagnosing asthma or measuring asthma prevalence.
PREFACE & ACKNOWLEDGMENTS
The study which forms the basis for this thesis was instigated in 1984 by Drs. Innes Asher, and Edwin Mitchell, Department of Paediatrics, University of Auckland, Drs. Harry Rea and Adrian Harrison, Department of Respiratory Medicine, Green Lane Hospital, Auckland, and Mr. Alistair Stewart, statistician, Department of Community Health, University of Auckland. The study was funded by the Medical Research Council of New Zealand and the Asthma Foundation of New Zealand. I was appointed as MRC Research Fellow to the project in 1985 and have been continuously involved since then in analysing and writing up the data. I was supported with a part-salary in 1987 and 1988 to continue the analysis of the study by the Mackie Estates Trust of the Auckland Asthma Society and the Auckland Medical Research Foundation.

Three of the chapters of this thesis are based on the following published papers:

**Chapter IV**

**Chapter V**

**Chapter VII**
I am grateful to each of the co-authors for their assistance in writing the papers, and to Mr. Alistair Stewart for advice regarding the statistical analyses. Professor Anne Woolcock of Sydney has kindly permitted me to use her figures for comparison in chapter four of the thesis. The field work for the study would not have been possible without the endeavours of Mrs Joanna Innes-Walker, research nurse, who ably organised the school visits and performed necessary liaison work, Mrs. Jan Mulder, senior technician, who was responsible for the bronchial challenge testing and equipment and wrote comprehensive technical notes, and Mrs. Lindy Gregory, Mrs. Frances Jackson, and Mrs. Kathy Stirling, technicians who with Jan Mulder, performed over 2,200 bronchial challenge tests in two and a half months. All five assisted in the collection and coding of the data sheets. I would also like to thank various people outside the study team who provided advice and comments. Dr. Clive Osmond, statistician, MRC Environmental Epidemiology Unit, Southampton kindly provided statistical advice on the analyses in Chapter VIII and Drs. Lynn Josephs and Keith Godfrey, both research fellows in the Faculty of Medicine, University of Southampton, made valuable comments about Chapters I, VII and VIII.

I wish to express particular thanks to Mr. John Collins, Senior Lecturer in Surgery, University of Auckland, who first encouraged me to write up the work as a thesis and to Dr. Innes Asher, Senior Lecturer in Paediatrics, who, as my supervisor, has provided unstinting support for my work as a researcher, besides giving helpful advice on each of the chapters. Finally, I wish to pay tribute to my wife Wendy, who has made many sacrifices to enable me to write the thesis, has read and commented on the presentation, and who has given constant support, and encouragement.
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## List of Abbreviations

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<tr>
<td>BHR</td>
<td>Bronchial hyperresponsiveness, measured by a challenge test</td>
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<tr>
<td>DFP</td>
<td>Discriminant function predictor (for derivation see Section VIII.2.4.4, page 296).</td>
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<tr>
<td>FEV1</td>
<td>Forced expiratory volume in one second</td>
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<tr>
<td>ΔFEV1</td>
<td>Percentage change in FEV1 by a given dose of histamine</td>
</tr>
<tr>
<td>ΔFEV1_{3.9}</td>
<td>Percentage change in FEV1 by 3.9 μmol of histamine</td>
</tr>
<tr>
<td>FVC</td>
<td>Forced vital capacity</td>
</tr>
<tr>
<td>NPV</td>
<td>Negative predictive value</td>
</tr>
<tr>
<td>NSW</td>
<td>New South Wales</td>
</tr>
<tr>
<td>NZ</td>
<td>New Zealand</td>
</tr>
<tr>
<td>NZ1</td>
<td>Hospital board area of New Zealand with higher than average admission rate for asthma</td>
</tr>
<tr>
<td>NZ2</td>
<td>Hospital board area of New Zealand with average admission rate for asthma</td>
</tr>
<tr>
<td>NZ3</td>
<td>Hospital board area of New Zealand with lower than average admission rate for asthma</td>
</tr>
<tr>
<td>PD20</td>
<td>Interpolated provocative dose of histamine resulting in a 20% fall in FEV1 from the post-saline value</td>
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<tr>
<td>PPV</td>
<td>Positive predictive value</td>
</tr>
<tr>
<td>URTI</td>
<td>Upper respiratory tract infection</td>
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