few were so eager to oblige that they were inclined to blow hurriedly into the peak flow meter without inhaling fully unless closely watched. The mean exercise lability of the children who had had bronchiolitis in infancy was significantly higher than that of the control children and the mean PEFR at rest significantly lower. Whether these findings have implications for the development of chronic respiratory illness in adult life will be known only after many years of further observation.

Rooney and Williams[7] thought that they had shown an association between family atopy and the development of wheezing episodes after bronchiolitis, but their data were incomplete, and some of their younger children may have developed wheezing later in childhood after a latent period. In our study there was no apparent link between atopy and either bronchiolitis or subsequent wheezing. Clinical questioning, however, is an unreliable measure of atopy and we plan to investigate the two groups of children further by skin tests and IgE estimations.

Our results suggest that cigarette smoking by the parents during the infant's first year of life may be associated with an increased risk of RS virus bronchiolitis for their baby. To establish this a study of smoking and non-smoking parents would be necessary. Similar associations between parental smoking and lower respiratory tract infection in infancy have been found by other investigators.[10-12]

There are three possible ways in which respiratory disease in infancy may be linked with that in later life: there may be a causal link between the two, a genetic predisposition to both, or common environmental factors. Of the three, a causal link, although it cannot be excluded, is perhaps unlikely in view of the small degree of respiratory disability we found in the 8-year-old children who had had bronchiolitis in infancy and the long symptom-free period that many of them had experienced. We have so far been unable to show that atopy constitutes a genetic link. McNicol and Williams have already speculated that bronchial hyperreactivity may be inherited independently of atopy,[13] and the results of our exercise tests are not inconsistent with this suggestion.

Environmental factors such as overcrowded housing, family size, air pollution, and cigarette smoking are increasingly recognised as influencing the prevalence of respiratory illness in children as well as adults.[1 3 14 15] Parental smoking was more common and family size larger in our bronchiolitis group, and the persistence of these factors may explain, at least in part, why many children went on to have further episodes of wheezing with impaired ventilatory function. Matching groups of children by father's occupation conceals wide variations in the way children are cared for,[16] and a search for more subtle differences in the home environment between children with and without respiratory disease may disclose new opportunities for prevention.

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Antinuclear antibodies in patients receiving non-practolol beta-blockers

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Summary and conclusions

Antinuclear antibodies (ANA) were found in 54 (7·0%) out of 767 treated hypertensive patients compared with 59 (2·4%) out of 2470 healthy controls. Inclusion of a non-practolol beta-blocker in the treatment regimen did not significantly affect the incidence of ANA. ANA was found in significantly more patients being treated with methyldopa (13·0%) than patients receiving other hypotensive agents (3·8%). Non-practolol beta-blockers in combination with methyldopa did not increase the incidence of ANA further.

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Introduction

Recognition that patients taking the beta-adrenoceptor-blocking drug practolol may develop serious oculomucocutaneous reactions[1] has raised concern about the toxicity of related drugs. There is little evidence that non-practolol beta-blockers induce similar reactions, despite the awareness of practitioners and government agencies of side effects. Practolol toxicity was not recognised until cumulative experience with the drug totalled one million patient-years,[2] and some patients developed symptoms only after many months of treatment or even after the

drug had been discontinued.[3] Thus with new beta-adrenoceptor-blocking drugs and drugs with both alpha- and beta-receptor-blocking activity reaching the market, the profession must be alert for toxic reactions. Most patients with advanced reactions to practolol, especially those with ocular complications, develop antinuclear antibodies (ANA).[1 4] The detection of ANA as a screening test for practolol-like reactions is therefore an attractive possibility, particularly because of its technical simplicity.

A study is in progress at the School of Medicine, University of Auckland, to examine the influence of beta-blocking drugs on the incidence in patients of various different autoantibodies including ANA. This report provides preliminary evidence that non-practolol beta-blockers as a group do not appear to stimulate the development of ANA.

Patients and methods

All patients (mean age 50 years) presenting to Auckland Hospital hypertension clinic during a 15-month period were venesected and had their serum tested for ANA. A drug history including dosage and duration of treatment was carefully recorded for each patient. Control data on 1598 healthy men (mean age 41 years) were available from a recently completed study,[5] and blood was collected from 872 healthy women (mean age 39·5 years) by the Auckland Blood Transfusion Service.

ANA was detected by indirect immunofluorescence, cryostat-cut sections from a composite block of tissues of human thyroid, ox adrenal, pig stomach, and pig salivary gland being used. Fluorescein-labelled antihuman immunoglobulin was applied to the slides after they had been incubated with serum and washed. After further washes the slides were examined for ANA under incident ultraviolet light with a Leitz Orthoplan microscope. When present, ANA almost invariably reacted with nuclei of all tissues on the slide. Titres of 1/8 or more were regarded as significant.

Results and comment

The incidence of ANA in patients grouped according to treatment is listed in table I. Results for men and women are given separately because of the greater incidence of ANA in women.[6] When all treated hypertensive patients were considered together they were found to have a significantly higher incidence of ANA than the healthy controls—7·0% compared with 2·4% ($P < 0.005$). Among the men, 5·6% of those who were treated for hypertension were ANA-positive, compared with 2·0% of the controls; 8·4% of the treated women had ANA compared with 3·1% of the controls. By classifying treated hypertensive patients on the basis of beta-blocker treatment we found that patients taking beta-blockers had a slightly decreased (though statistically insignificant) incidence of ANA compared with hypertensive patients receiving other treatments (table I). The numbers of patients in the groups were too small to compare them by age (in decades) or by duration of treatment.

Because of the association between methyldopa (Aldomet) administration and an increased incidence of ANA[7] the patient data were also grouped on the basis of methyldopa treatment (table II). Of the 269 patients taking methyldopa irrespective of other medication, 35 (13%) were found to have ANA. In contrast, significantly fewer patients (17 (3·8%) out of the 448) on hypotensive medication excluding methyldopa were ANA-positive ($P < 0.005$). Thus beta-blocking drugs did not increase the incidence of ANA in patients not exposed to methyldopa. In fact, the incidence was usually lower among those on beta-blockers. The pattern is less clear in patients taking methyldopa, as the addition of beta-blockers slightly increased the incidence of ANA in men and decreased it in women. There were too few patients for these data to be significant. When only men receiving any hypotensive treatment other than methyldopa were considered, 3 (1·4%) out of the 207 were ANA-positive. In the control group the incidence of ANA was 2%.

TABLE I—*Incidence of ANA in controls and hypertensive patients*

		No studied	No (%) with ANA	No (%) with all autoantibodies
Controls	Men	1598	32 (2·0)	335 (21·0)
	Women	872	27 (3·1)	174 (19·1)
	Total	2470	59 (2·4)	509 (20·6)
Untreated hypertensives	Men	73	1 (1·4)	11 (15·1)
	Women	46	3 (6·5)	14 (30·4)
	Total	119	4 (3·4)	25 (21·0)
Hypertensives receiving beta-blockers	Men	24	1 (4·2)	6 (25·0)
	Women	13	0 (0·0)	3 (23·0)
	Total	37	1 (2·1)	9 (24·3)
Hypertensives receiving beta-blockers and other drugs	Men	215	12 (5·6)	41 (19·1)
	Women	210	15 (7·1)	48 (22·8)
	Total	425	27 (6·4)	89 (21·0)
Hypertensives receiving other drugs	Men	134	8 (6·0)	32 (24·0)
	Women	171	18 (10·5)	36 (21·0)
	Total	305	26 (8·5)	68 (22·3)

ANA = Antinuclear antibody.

TABLE II—*Influence of methyldopa on incidence of ANA in hypertensive patients receiving hypotensive agents with and without beta-blockers*

		Patients receiving methyldopa		Patients not receiving methyldopa	
		No studied	No (%) with ANA	No studied	No (%) with ANA
Treated without beta-blockers	Men	83	8 (9·6)	66	1 (1·5)
	Women	63	10 (15·9)	98	8 (8·2)
Treated with beta-blockers	Men	64	9 (14·0)	141	2 (1·4)
	Women	59	8 (13·6)	143	6 (4·2)
Total	Men	147	17 (11·6)	207	3 (1·4)
	Women	122	18 (14·7)	241	14 (5·8)

ANA = Antinuclear antibody.

Discussion

Treatment with non-practolol beta-blockers is not associated with an increased incidence of ANA. In general, fewer patients receiving beta-blockers with other hypotensive agents were ANA-positive than patients on similar treatment regimens but without beta-blockers. When patients treated with methyldopa were excluded the incidence of ANA in men taking beta-blockers was slightly less than that in the control group (1·4% compared with 2·0%); in women it was higher than that in the controls (4·2% compared with 3·1%) but lower than that in hypertensive patients on treatment schedules excluding beta-blockers (4·2% and 8·2%, respectively).

Our results are subject to some qualifications. The mean age of the treated patients (50 years) was higher than that of the controls (41 years for men and 39·5 years for women). The incidence of ANA rises with age, so the optimal comparison between groups is one between results in age groups matched decade by decade, rather than between total results. This study did not include enough patients in each group to make this a valid exercise, but later, more detailed figures accorded with the trend seen here. The duration of exposure to various drugs is also relevant in the induction of ANA. Breckenridge *et al*[7] showed that the incidence of ANA rose with the duration of treatment with methyldopa. A detailed comparison including the length of treatment was not made tor our patients. Some of the newer beta-blockers had been available for only a few months, and, if they were capable of inducing ANA, it might still have been too early to have detected a rising incidence.

The beta-blockers were considered as a group in this paper, but data for individual drugs have been analysed. Only a propranolol-treated group (144 men and 130 women) was large enough for separate statistical evaluation, and in it the incidence of ANA was similar to that in the group as a whole. More data on the other drugs are required to relate the group conclusions to each individual drug. One of the drugs was associated with a

higher incidence of ANA than the other beta-blockers in both male and female groups, but there were too few patients for this to be significant, and more patients are being sought. Most of the ANA-positive patients were also on treatment with methyldopa.

If the non-practolol beta-blockers are shown eventually to precipitate practolol-like reactions—even if all are associated with ANA—the assay will have little value as a screen for at-risk patients because of the many hypertensive patients who are ANA-positive. Most of these patients are taking methyldopa, which confirms the original observation of Breckenridge *et al*[7] that this drug induces ANA in over 10% of patients. Apart from the occasional case of methyldopa-induced lupus, however, there seems to be no clinical risk with this drug in patients who develop ANA.

The effects of beta-blockers and other hypotensive agents on other autoantibodies will be the subject of a later report.

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Immune status of children of immigrants to poliomyelitis

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Summary and conclusions

Four ethnic groups of children from the Glasgow area—155 Asians, 85 Africans, 85 Chinese, and 93 Scots—were examined for neutralising antibodies to poliovirus types 1, 2, and 3. Only seven of the 418 children had no detectable antibody, and of these, four were aged less than 7 months; none had received polio vaccine. The best-protected children were the Chinese (93% with antibody to all three poliovirus types), followed by the African (81%), Scottish (78%), and Asian children (77%).

We conclude that children of immigrants are no more vulnerable to poliovirus infection than their Scottish counterparts.

Introduction

Since the last outbreak of poliomyelitis in Scotland in 1962, at least eight poliovirus antibody surveys of different sections of the Scottish population have been carried out.[1-4] Of these, four have disclosed potentially serious gaps in immunity. Because of the increasing number of immigrants in the United Kingdom we decided to extend our polio antibody surveillance to include these ethnic groups, which in Scotland are centred mainly in the Glasgow area. A study of the prevalence of various pathogenic organisms (parasites, bacteria, and hepatitis B) among the children of immigrants in Glasgow had already been conducted,[5] so we took the opportunity to investigate the polio-immune status of these children, from whom serum specimens and detailed sociological information had already been obtained. Four ethnic groups were investigated—namely, Asians (from the Indian subcontinent), Africans (from various parts of Africa), Chinese (from Hong Kong), and Scots (included as a control group).

Subjects and methods

Of the sera taken from 500 children in the original study,[5] only samples collected during 1974-5 from 418 were available for virological examination; these comprised samples from 155 Asian, 85 African, 85 Chinese, and 93 Scottish children aged 4 months to 16 years. Details of sex, age distribution, social class, and country of birth are given in table I. Thirty-one per cent of the children of immigrants were born abroad, the proportion being highest among the Chinese (51%).

The modified micrometabolic inhibition test[6] was used to assess the specificity of neutralising antibodies to the three types of poliovirus. Titrations were started at a final serum dilution of 1/8. All tests were carried out in parallel with British Standard Poliovirus Antisera types 1, 2, and 3. Antibody titres below 8 were regarded as negative.

Results

Seven of the 418 children—namely, three Asians, two Africans, one Chinese and one Scot—had no detectable antibody to any poliovirus type (table II). None had received polio vaccine. Four were aged 4-7 months and were therefore too young for the polio vaccination programme, two were aged 1 year, and the Scot was 6 years old. After the completion of the study five of these seven children received a full course of polio vaccination, but the other two could not be traced.

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