Management of Asthma in Out-Patients

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Recent social and medical trends have increased interest in the assessment of medical performance, or medical audit[1]. In hospitals, this practice has been concentrated largely on mortality and management of in-patients[2-4]. Asthma, a chronic and variable disability with an easily measured parameter of severity, provides an ideal condition for audit in out-patients. This study was designed to audit performance in three different types of clinic in two adjacent, but socially different, health districts.

Subjects
Five hundred and twenty-nine patients, attending five clinics for at least three months since first referral, were monitored at the first opportunity in 1980. All had a clinical diagnosis of asthma. Non-smokers showed a reversibility of ventilator function of at least 20 per cent. Patients who had smoked within the last five years were required to show reversibility, with bronchodilator or spontaneously, of at least 25 per cent to a peak expiratory flow rate (PEFR) of at least 200 litres/min. Patients, who were encouraged to attend while taking their normal treatment, including bronchodilators, were not warned of the study.

Method

Record
A single line of data was recorded on a previously prepared sheet which had sufficient room for 30 patients. The following were noted: clinic, age, sex, smoking habit, atopic status, pulmonary function, therapeutic status, drugs prescribed and doses of selected drugs.

Clinics
The clinics were divided into three supervision and three social groups (Table 1).

Table 1. The five clinics and the numbers attending.

| Clinic          | No. of clinics per week | Time | Supervision | Social group | No. of patients |
|-----------------|-------------------------|------|-------------|--------------|----------------|
| General Clinic 1| 2                       | am   | C           | C            | 256            |
| Asthma Clinic   | 1                       | pm   | B           | C            | 68             |
| General Clinic 2| 2                       | am   | C           | B            | 133            |
| General Clinic 3| 1/2                     | pm   | A           | B            | 17             |
| Private         | 1                       | am   | A           | A            | 35             |

*Most patients

Supervision. Group A: Private consultations and a peripheral clinic in a small country town where all the patients were seen personally by the author. Group B: A special asthma clinic staffed by a research registrar and a GP clinical assistant. Patients were either specially selected from the general medical clinic as fully reversible, predominantly intrinsic adult asthmatics, or had been referred as children and were participating in a long-term study into the prognosis of childhood asthma. Group C: General medical clinics staffed by the author and non-specialist junior staff, mainly senior house officers.

Social Groups. Group A: Private patients. Group B: Patients attending in a prosperous rural district centred on a small country town. Group C: Patients attending in a district in which 90 per cent of the population are resident in a mixed industrial, commercial, and residential town.

The town in which the patients in group B attended had had the highest per capita income in the country. This was reflected in a substantial difference in the social status of those attending groups B and C, although there was, of course, considerable overlap. On the other hand, in group C the industrial areas are principally to the northeast of the residential areas of the district and so downwind. Thus the atmospheric and environmental conditions are not as different as might be expected.

Smoking Habit
Subjects were divided into smokers, current smokers (within the last 3 months), ex-smokers (3 months to 5 years), and ex-smokers (longer than 5 years). The total amount smoked was recorded in pack years.

Atopic Status
Prick tests had been performed on all subjects to at least the following allergens: house-dust mite, grass pollen, Aspergillus fumigatus, and cat (Bencard). Patients with absolutely no immediate response were regarded as non-atopic and those with a weal of 3 mm greater than the control were atopic.

Pulmonary Function
The best of three measurements of PEFR was recorded. The maximum PEFR, ignoring obvious ‘rogue’ readings, was extracted from the notes. The majority of patients, whose maximum PEFR was substantially below...
the predicted level, had been admitted to hospital and subjected to bronchodilution with nebulised salbutamol in maximal doses, usually by intermittent positive pressure ventilation, and a trial of corticosteroids. The PEFR was age-corrected, using the median height from Cotes[5], as height was not available in all cases. Three indices of performance were considered. (a) Actual PEFR: the age corrected PEFR recorded at the clinic, expressed as a percentage. (b) Maximum PEFR: the maximum PEFR for the patient expressed as a percentage. The difference between this and 100 was regarded as a measure of the irreversible element of the patient’s airway obstruction. (c) Actual/Maximum PEFR: this ratio was expressed as a percentage, being the measure of the proportion of potential reversibility achieved, allowing for the irreversible element in the obstruction. Calculations of actual/maximum PEFR were possible for all patients, but as predicted figures were not available for those under 20 and over 75 years, the other two indices were not calculated in the youngest and oldest patients. This explains discrepancies in numbers available for various calculations and in the relationship between actual, maximum and actual/maximum peak flow rate in some tables.

**Therapeutic Status**

Maintenance treatment was assessed as satisfactory if it was so regarded by both patient and doctor and if it had not been altered within the previous 3 months. Change in the dose of maintenance corticosteroids or disodium cromoglycate (DSG) was regarded as an alteration in treatment, but the use of a short course of oral steroids to cover an exacerbation was not. Minor deviations in dose were accepted. Patients not on satisfactory maintenance treatment were divided into those who complied and those who did not comply with previous advice. A second record was made if and when satisfactory maintenance treatment was achieved by 31st December 1980.

**Drugs**

The actual treatment over the previous 24 hours was recorded for all patients. Prescribed regular and ‘as required’ drugs were entered for those on satisfactory maintenance treatment. The doses of oral and inhaled corticosteroids and DSG were noted.

**Statistical Methods**

Students’ ‘t’ test and the $\chi^2$ test were used where appropriate for analysis of continuous and non-continuous variables respectively. The distribution of actual/maximum PEFR was skewed by the well-controlled subjects, many of whom achieved over 90 per cent of possible. Differences in this measurement were tested by the non-parametric Mann Whitney test.

**Results**

**Social Group and Supervision (Table 2)**

The supervision groups differed in age because the private patients were older and the asthma clinic patients younger than the rest. Selection also accounts for the lower proportion of current smokers in supervision group B. There is a highly significant trend towards decreasing atopy with increasing social status, which is reflected in significant differences between the supervision groups. The proportion of non-smokers is influenced by the exclusion of current or recent ex-smokers with a maximum PEFR of less than 200. More were excluded from social and supervision groups C, which accounts for the apparently higher numbers of non-smokers in these groups. Supervision cannot account for differences be-

| Social group | No. | Age | Male % | Atopic % | Current smokers % | Non-smokers % | PEFR maximum % | PEFR actual/max. | PEFR actual |
|--------------|-----|-----|--------|----------|-------------------|--------------|----------------|------------------|------------|
| A            | 35  | 56  | 54     | 23       | 14                | 37           | 95.6           | 89.8            | 87.4       |
| B            | 150 | 53  | 47     | 52       | 15                | 43           | 78.6           | 82.3            | 66.0       |
| C            | 344 | 47  | 47     | 60       | 16                | 51           | 81.1           | 79.5            | 64.6       |

Probability $\chi^2 = 16.0$  
$P < 0.01$

| Supervision | No. | Age | Male % | Atopic % | Current smokers % | Non-smokers % | PEFR maximum % | PEFR actual/max. | PEFR actual |
|-------------|-----|-----|--------|----------|-------------------|--------------|----------------|------------------|------------|
| A           | 52  | 56  | 46     | 33       | 11                | 35           | 90.0           | 86.4            | 80.2       |
| B           | 88  | 40  | 45     | 53       | 8                 | 65           | 90.3           | 86.2            | 74.4       |
| C           | 389 | 51  | 48     | 59       | 17                | 46           | 78.8           | 79.1            | 63.5       |
| All         | 529 | 50  | 47     | 55       | 15                | 48           | 81.4           | 81.0            | 66.6       |

Probability $\chi^2 = 13.2$  
$P < 0.01$
between social groups B and C, as 87 per cent of social group B and 76 per cent of social group C were supervised in the same way by attending general clinics.

Both potential function and its achievement were better in social group A than in the other two groups. This better performance and the removal of selected patients from supervision group C to supervision group B must account for much of the difference in performance between supervision groups A and C. The particularly low actual/maximum PEFR seen in social group C is due to the exceptionally poor performance of the oldest patients in this group, who are not included in the other two measurements of respiratory function, which require a predicted norm.

Atopic Status

Actual PEFR was somewhat better in non-atopic subjects than atopics (Table 3). This is particularly true in social group B. There were only eight atopic subjects in social group A, but there was little difference in atopics between groups B and C, social group B doing marginally worse in all respects. On the contrary, in non-atopics there is a consistent social gradient in all three indices, particularly in the measure of achievement of potential reversibility. The mean difference in actual PEFR between groups A and C is more than 27 per cent. If ‘pure’ asthmatics only, with a maximum PEFR of greater than 80 per cent, are considered, there is still a difference between the achieved PEFR, which is entirely accounted for by non-atopic subjects. Actual PEFR was 13.6 per cent greater in social group A than group C ($P < 0.05$). As the non-atopic subjects do better with social advantage, the increased proportion of them in social group A raises still further the mean performance in this group.

Cigarette Smoking, Age and Control

These will be considered in detail elsewhere. There was a highly significant negative correlation between age and maximum PEFR ($r = -0.24$, $P < 0.01$). This relationship was not seen in social group A, but occurred entirely in atopic smokers in group B and in all sub-groups except non-smoking non-atopic subjects in group C. There was a similar trend for lower actual/maximum PEFR with age ($r = -0.35$, $P < 0.01$), for which social group C was principally responsible. Poorer achievement of potential in older patients was much more obvious in non-smokers than smokers, because all smokers over the age of 30 did badly.

Current cigarette smokers performed worse than any other group. The maximum PEFR was reduced in smokers and all ex-smokers compared with non-smokers, but the actual/maximum PEFR was similar in non-smokers and ex-smokers of more than five years’ standing. Recent ex-smokers showed a bi-modal distribution of actual/maximum PEFR. Although the mean was similar to that of non-smokers, recent ex-smokers tended to do either particularly badly or particularly well, being the group with the biggest proportion of subjects with an actual/maximum PEFR of greater than 80 per cent.

Light (<10 pack years) current smokers, together with light and medium ex-smokers, showed some increase in irreversible obstruction, but no difference in actual/maximum PEFR compared with non-smokers. Those who had smoked more than 30 pack years, whether currently smoking or not, performed badly in all respects.

Therapeutic Status

At the first attendance the maintenance treatment of 74 subjects was considered to be unsatisfactory. In five the dose of corticosteroids was dictated either by other manifestations of polyarteritis nodosa or pulmonary eosinophilia. Of the remaining 69 (Table 4), 56 were regarded as compliant and 13, all in supervision group C, were not. The 29 subjects satisfactorily treated by the end of the year included 5 who were previously non-compliant.

Of those who did not achieve satisfactory treatment by the end of 1980, 10 first attended after 1st October 1979, too late to allow for a whole year’s observation after they had become eligible for the study. Two with pulmonary heart disease died and one was lost to follow-up. All 13 were in supervision group C. Of the remaining 27 none were in the highly selected group B but they represented 6 per cent of both groups A and C.

Table 3. Mean respiratory indices according to social group and atopic status in subjects available for all three calculations.

| Social group | No. | Maximum PEFR | Actual/Max. PEFR | Actual PEFR |
|--------------|-----|--------------|------------------|------------|
| A            | 8   | 88.9         | 88.9             | 79.5       |
| B            | 78  | 73.3         | 80.7             | 59.1†      |
| C            | 206 | 79.6         | 82.7†            | 65.1       |
| All          | 292 | 78.1†        | 82.3*            | 63.9*      |
| Probability  |     |              |                  | AvB 0.05   |

Probability: Atopic v. Non-Atopic

* $P < 0.05$
† $P < 0.01$
Table 4. Patients not on satisfactory maintenance treatment at their first visit.

| Supervision Group | No. | Total not satisfactory No. | % | Compliant Yes | No | Satisfactory by one year Yes | No | Not applicable |
|-------------------|-----|-----------------------------|---|---------------|---|-------------------------------|---|----------------|
| A                 | 52  | 4                           | 8 | 4             | 0 | 1                            | 3 | 0              |
| B                 | 88  | 3                           | 3 | 3             | 0 | 3                            | 0 | 0              |
| C                 | 389 | 62                          | 16| 49            | 13| 25                           | 24| 13             |
| Total             | 529 | 69                          | 13| 56            | 13| 29                           | 27| 13             |

Table 5. The features of patients not on satisfactory maintenance treatment after a full year’s attendance.

| Number | Mean age | Female | Social group A | Supervision A | Atopic | Non-smoker | Current smoker | Recent ex-smoker | PEFR | The remainder | Probability |
|--------|----------|--------|----------------|---------------|--------|------------|----------------|-----------------|------|---------------|-------------|
| 27     | 52.1     | 16 (59%) | 3 (11%)        | 3 (11%)       | 15 (56%) | 11 (41%)   | 11 (41%)       | 1 (4%)          | 27.4 | 502           | NS          |
| Mean age | 49.5     | 262 (52%) | 32 (6%)        | 49 (10%)      | 275 (55%) | 442 (48%)  | 70 (14%)       | 66 (13%)        | 81.7 | NS            | P<0.01      |
| Female | 262 (52%) | NS     | 32 (6%)        | 49 (10%)      | NS     | NS         | P<0.01         | NS              | 81.6 | P<0.05        |             |
| Social group A | NS     | NS     | 32 (6%)        | 49 (10%)      | NS     | NS         | P<0.01         | NS              | 67.4 | NS            |             |
| Supervision A | NS     | NS     | 32 (6%)        | 49 (10%)      | NS     | NS         | P<0.01         | NS              | 67.4 | NS            |             |
| Atopic | NS     | NS     | 32 (6%)        | 49 (10%)      | NS     | NS         | P<0.01         | NS              | 67.4 | NS            |             |
| Non-smoker | NS     | NS     | 32 (6%)        | 49 (10%)      | NS     | NS         | P<0.01         | NS              | 67.4 | NS            |             |
| Current smoker | NS     | NS     | 32 (6%)        | 49 (10%)      | NS     | NS         | P<0.01         | NS              | 67.4 | NS            |             |
| Recent ex-smoker | NS     | NS     | 32 (6%)        | 49 (10%)      | NS     | NS         | P<0.01         | NS              | 67.4 | NS            |             |
| PEFR | NS     | NS     | 32 (6%)        | 49 (10%)      | NS     | NS         | P<0.01         | NS              | 67.4 | NS            |             |
| On oral corticosteroids | NS     | NS     | 32 (6%)        | 49 (10%)      | NS     | NS         | P<0.01         | NS              | 67.4 | NS            |             |

The characteristics of these 27 subjects not on satisfactory maintenance treatment after at least one year’s observation are shown in Table 5. They are similar in age, sex, and atopic status to the others. There are in fact more subjects than expected in social group A, though this is not significant. There are more smokers than expected and the deficiency of non-smokers is nearly significant. All but five patients were actually taking oral corticosteroids, but an increased use of oral bronchodilators was not significant.

Drugs

A table showing the proportion of subjects prescribed the various drugs with the relevant respiratory indices and grouped by clinics has been deposited. At least 83 per cent of patients were prescribed inhaled bronchodilators in all clinics, but regular prescription was more frequent in the asthma clinic than elsewhere. Only 27 per cent of prescriptions were ‘as required’, while the proportion was approximately one-third in other NHS clinics and two-thirds for private patients. Oral β-stimulants (given to 14 per cent of all subjects), and xanthene derivatives (25 per cent) were consistently prescribed to those with a larger irreversible element of obstruction (P<0.01). Except at General Clinic 2, more than two-thirds of those on oral β-stimulants received a long-acting preparation (usually Ventolin Spandet) at night only.

Fifteen per cent of atopic subjects and only 3 per cent of non-atopics received inhaled DSG. There was little difference in atopic subjects between the clinics, but no non-atopics in the asthma or private clinics were given it. Patients on DSG were unique in that their actual/maximum PEFR was better than average, and therefore better than that of those patients who were not taking the treatment. Of the non-atopic subjects 57 per cent received inhaled corticosteroids. Within the social groups the proportion was virtually identical, in the range of 56-58 per cent. The frequency of prescription of inhaled corticosteroids was lower in atopic subjects (37 per cent).

DSG differed from inhaled corticosteroids in the relationship of dose to pulmonary function (Table 6). Subjects on two capsules of DSG or less were worse than those on a higher dose, despite their condition being potentially completely reversible. Those on inhaled steroids showed a consistent fall in both indices of function with increasing dose. These findings, together with the fact that DSG is unique in that those on the drug were better than those off it, suggest the possible under-use of this preparation with a threshold dose of three capsules per day.

Oral corticosteroids were used regularly in fewer patients in social group C, but the general clinic for this group showed the highest proportion of patients who had had a short course in the year before attendance. Thus

Table 6. Respiratory indices of patients receiving inhaled DSG and inhaled corticosteroids.

| Dose | PEFR Actual/max. (no.) | PEFR Maximum (no.) | Inhaled steroid PEFR Actual/max. (no.) | PEFR Maximum (no.) |
|------|------------------------|--------------------|---------------------------------------|--------------------|
| 1    | 79 (9)                 | 99 (6)             | 86 (30)                               | 95 (29)            |
| 3    | 86 (23)                | 88 (21)            | 84 (48)                               | 88 (44)            |
| 4    | 83 (22)                | 69 (14)            | 83 (103)                              | 84 (82)            |
| 5    | 73 (4)                 | 74 (3)             | 78 (26)                               | 81 (21)            |
| 6    | 69 (36)                | 69 (36)            | 69 (36)                               | 76 (32)            |
| r    | 0.50                   | 0.50               | -0.23                                 | -0.23              |
| t    | 3.60                   | 3.60               | 3.30                                  | 3.30               |
| P    | <0.01                  | <0.01              | <0.01                                 | <0.01              |
there was no overall tendency to under-use corticosteroids in patients who might be at a social disadvantage or receiving the least specialist supervision.

Discussion

All five clinics were supervised by the same consultant. Patients attending at General Clinic 3 as well as privately were seen by him on all occasions. A part-time research registrar and a clinical assistant attended the asthma clinic throughout the study; patients were seen by the author only occasionally. In the general clinics patients were usually seen alternately by the author and SHOs not particularly experienced in chest medicine. Except for short-term return visits of difficult patients, no attempt was made to ensure that the consultant would be available to see the patient on the next visit after he had seen a junior; by chance a patient could miss seeing the consultant on three or four successive visits. On the other hand, all notes were seen by the author when he was in the clinic, so difficult patients might have been seen by him several times in succession. This exercise was intended to provide a rapid and effective method of measuring the performance of different clinics. It took little additional time or work at the time the patients attended. A repeat skin test was occasionally needed when the previous results were not clear. The only information which required time for extraction was the highest recorded PEFR, but this valuable piece of information should probably be known by the doctor at each visit.

The proportion of atopic asthma was lower in the group with higher social class and better environment. This may be a genuine phenomenon, or may reflect a readiness acceptance by doctors of a diagnosis of adult asthma in non-atopic middle-class patients, and therefore a higher proportion of referrals to consultants. The better control of non-atopic asthma in social group A would support this view. However, it is difficult to accept this as the only explanation, and a study of the relative incidence of the two different types of asthma by social class would be of great interest.

Although asthma has been defined as reversible airway obstruction[6], the possibility of incomplete reversibility has been studied[7-9]. In this study, both potential function relative to predicted function and the achievement of this potential were consistently worse with increasing age. Many of those patients who performed poorly showed a decreased response to corticosteroids as reported by Charmichael et al.[10]. A more rapid deterioration of function in smokers with age has also been reported in atopic subjects[11, 12], and in atopics exposed to relatively mild general atmospheric pollution[13].

The deterioration of potential achieved as age advanced was seen principally in those patients attending in the large town. As the maximum PEFR, irrespective of age, was itself lowest in this group, a further possible explanation of their poorer performance might be that poor achievement of potential was directly related to the presence of 'irreversible' obstruction. There was a highly significant, but low, negative correlation coefficient ($r = -0.17, P<0.01$) between actual/maximum and maximum PEFR. There are methodological and mathematical difficulties to be discussed elsewhere, but this does suggest a somewhat greater difficulty in controlling those patients whose conditions are less reversible. Nevertheless, much of the decreased achievement of potential with age is almost certainly due to other factors, including increased difficulty of co-operation with the drug regimen and with the use of metered dose inhalers in the elderly.

The follow-up clinics are consultative, and do not take over patient care from the general practitioner. Drugs are only supplied in an emergency. Despite this, the concordance between drugs advised and those actually taken appeared to be good. This may seem to be at variance with the findings of James et al.[14], but most of their patients did follow therapeutic policy, though there were discrepancies in nearly half the dosages. Our patients were allowed some experimenting with the dose of suppressive therapy, but where specific advice on dosage had been given to a poorly controlled patient and was not heeded, the patient was recorded as unco-operative. It is accepted that many patients did in fact take a lower dose of inhaled suppressive agents than they stated; nevertheless, the exercise suggested that there may be a critical frequency for inhaled DSG of not less than three 20 mg capsules a day. The better performance of those patients on DSG than on inhaled beclomethasone suggests that this drug is under-used compared to the inhaled steroids. Non-atopic asthmatics had a clear preference for inhaled corticosteroids rather than DSG. This is shown throughout the country but evidence[15, 16] that atopy makes any difference to the response to DSG or beclomethasone is not consistent[17-19]. DSG should probably be tried more frequently in non-atopic[20], as well as atopic, adult asthmatics, though too few of our non-atopics were actually on DSG to draw any firm conclusions.

Little difference between clinics was seen in the proportion of patients on any preparation, except that, in line with the prescription policy, the private and the asthma clinic patients were given fewer oral $\beta$-stimulants. The level of pulmonary function at which drugs were prescribed reflected the function of patients in the clinic as a whole, so that the less severely affected patients were treated in the clinics where performance was best. However, the separate analysis by clinic rather than supervision group showed that this difference was not greatly influenced by supervision. Private patients were more frequently given the discretion to use a bronchodilator as required, suggesting a greater confidence in the patients' judgement.

In practice, it was not difficult to assess whether or not a patient was on satisfactory maintenance treatment. The patient and doctor were both required to regard the treatment as satisfactory in the light of symptoms and PEFR. Our policy of reduction of oral corticosteroids requires increasing intervals of up to three months as the maintenance dose is approached. The majority of patients not yet on regular maintenance therapy were either clearly on a programme of dose reduction or were difficult patients in whom no maintenance levels had ever been established. Most of the former were among those in
whom a full year's observation had not been possible. Those who had been observed for a full year were equally distributed through the clinics (except the highly selected asthma clinic) and the social groups, confirming that it was not social disadvantage, nor poor supervision that determined the patients in whom management would ultimately be unsatisfactory. As all 10 patients who had not reached satisfactory maintenance treatment and had not had the benefit of a full year's observation were in supervision group C, it is possible that the establishment of satisfactory treatment takes longer in the general clinic.

This simple study has proved extremely valuable, providing evidence of non-atopic asthma being possibly more common in higher than in lower social groups. As the difference in the control of asthma between the social groups occurs in non-atopic rather than atopic subjects, the better control of socially advantaged subjects was probably due more to the type of asthma than to the degree of supervision they received or their co-operation. A small proportion of patients scattered throughout all sub-categories of asthma proved impossible to control satisfactorily, and even the closest supervision did not seem to reduce the proportion. Useful information was obtained with regard to the prescription of drugs. Properly supervised junior staff, not particularly experienced in chest medicine and employed in general clinics, obtained results comparable with those of consultant-only or special clinics.

However, one question remains unanswered because there is no standard of performance; that is whether the achievement of 80 per cent of potential and two-thirds of predicted function are reasonable results of the treatment of asthma. Perhaps future studies will provide the standard.

Summary and Conclusions

Five hundred and twenty-nine patients attended five different clinics supervised in three different ways in two adjacent, but socially different, health districts. Performance was apparently better in the clinics supervised by the consultant personally or by specialised junior staff. Non-atopic asthma appeared to be more frequent in clinics attended by patients with a social advantage, where it also appeared to be more easily controlled. This difference in control was less apparent in atopic asthma. These differences and deliberate selection probably account for the differences in performance between the clinics. Prescription policy appeared to be uniform throughout the clinics, though there was a tendency for drugs to be given at a lower level of pulmonary function in those clinics where performance was generally worse. Five per cent of all patients failed to achieve satisfactory treatment after a whole year's observation. This was not influenced by supervision or social group. Analysis of the pulmonary function of patients for whom drugs had been prescribed suggested that there was possible under-use of disodium cromoglycate as opposed to inhaled corticosteroids.

The exercise proved a rapid and useful assessment of the performance of the clinics supervising asthma.

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References

1. Editorial (1979) British Journal of Hospital Medicine, 22, 421.
2. McColl, I. (1979) ibid., 22, 485.
3. Shaw, C. D. (1980) British Medical Journal, 1, 1256.
4. Shaw, C. D. (1980) ibid., 1, 1314.
5. Cotes, J. E. (1978) Lung Function. 4th edn. Oxford: Blackwell.
6. Ciba Foundation (1959) Thoras, 14, 286.
7. Beale, H. D., Fowler, W. S. and Comroe, J. H. (1952) Journal of Allergy and Clinical Immunology, 23, 1.
8. Cade, J. E. and Pain, M. C. F. (1973) Australian and New Zealand Journal of Medicine, 3, 345.
9. Sobol, B. J. and Emirgil, C. (1981) Journal of Chronic Disease, 282, 1419.
10. Charmichael, J., Paterson, I. C. et al. (1981) British Medical Journal, 282, 1419.
11. Burrow, B., Knudson, R. J. et al. (1977) American Review of Respiratory Disease, 115, 195.
12. Connellan, S. J. and Joyce, H. (1982) Thorax, 37, 232.
13. Van Der Lende, R., Kok, T. J., Peset Reig, R. et al. (1981) European Bulletin of Physiopathology of Respiration, 17, 775.
14. James, P., Henry, J. and Cochrane, G. M. (1982) Thorax, 37, 778.
15. Chan-yeung, M., Morton, J. and Grzybowski, S. (1971) Canadian Medical Association Journal, 105, 827.
16. Silverman, M. and Turnier-Warwick, M. (1972) Clinical Allergy, 2, 137.
17. Campbell, A. H. and Tandon, K. (1969) Medical Journal of Australia, 2, 535.
18. Brompton Hospital/MRC Collaborative Trial (1972) British Medical Journal, 4, 383.
19. Northern General Hospital, Brompton Hospital, and MRC Collaborative Trial (1976) ibid., 1, 361.
20. Munro-Ford, R. (1971) Annals of Allergy, 29, 3.