LOCAL ASTHMATIC PROBLEMS — A CLINICAL STUDY

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Asthma is a common ailment in all countries. Its clinical picture is so obvious that there is a word for asthma in the daily vocabulary of almost every living language, and the symptomatology has been described in ancient medical texts. In contrast to its striking clinical picture, its treatment has been protean, ranging from psychotherapy to elaborate desensitisation techniques and complicated food and living regimes. An asthmatic patient nowadays is apt to run the gauntlet of a multitude of bronchodilators, expectorants, antibiotics, psychiatric and psychosomatic advice, and recently also the exhibition of steroids.

It is a curious experience that where the methods of treatment are protean, the efficacy is generally dubious. Further, in a common disease with obvious episodic character, reports of benefit from a new regimen are apt to be made very frequently, and just as frequently discredited after a careful follow-up.

Bronchial asthma has always been regarded as a relatively benign condition, but it is becoming increasingly recognised that some cases do end fatally. Williams (1953) estimated from the Registrar General's Reports for England and Wales, 1950-51, that asthma accounted for 0.6% of all deaths in England and Wales for the years 1939 to 1949. There have been several reports in the literature of fatal cases of bronchial asthma (Earle 1953, Robertson and Sinclair 1954, Pearson and Cardell 1959).

There is general agreement that the greatest number of deaths occurred in the older age groups, and the onset of asthma in later life carries with it a graver prognosis and runs a shorter course. In the series of Pearson and Cardell, the mean period between the onset of asthma and death was 27.2 years for those who develop it before 20 years of age, and only 6.4 years for those developing it after the age of 40 years. The commonest cause of death in this series was status asthmaticus, 49 out of 68 deaths were in status asthmaticus. In reviewing 160 cases reported in the world literature, Earle found that 49 patients (30.6%) had died within five years of the onset of asthma. This was remarkably similar to the findings of Cardell and Pearson who found 21 (30.9%) out of their 68 fatal cases had died within the same period.

In an attempt to learn more of asthmatic patients as individuals rather than the desire to add to the already large volume of reports on the value of various treatments in asthma, a number of asthmatic patients attending the Chest Clinic was investigated and followed up over a period of 4 years in order to see how they fared throughout this period. These patients normally attend the Chest Clinic of the Department where they were seen as outpatient cases, and received drugs of various kinds for relief. Whenever the attacks became incapacitating, they were admitted for treatment. No attempt was made to introduce a constant regime except that any unwarranted trial or risky procedures were disallowed, and the results were put into a standardised form to permit easy comparison.

In all, 14 cases were observed. They were all treated from 1956 and 1957 till the conclusion of the period of observation in 1960, which meant that the shortest period of a case under observation would be 4 years. Investigations were limited to available facilities and hence elaborate psychotherapy was not undertaken, although attention was paid to the psychosomatic aspect of a case, and whenever possible change of employment and mode of living especially with regard to diets and environment were affected. All the patients were encouraged to carry on their activities, and subjective accounts were confined to enumerating the number of attacks per month and their duration.

TABLE I: AGE AND SEX DISTRIBUTION

AGE	SEX	
	M	F
* 5 — 10	—	1
10 — 15	—	—
15 — 20	—	1
20 — 30	—	2
30 — 40	1	—
40 — 50	6	—
50+	3	—

* Cases below the age of 5 years were all treated by Paediatricians.

TABLE II: DURATION OF ILLNESS

Duration since onset	SEX	
	M	F
< 1 year	—	2
< 5 years	2	1
> 5 years	8	1

TABLE III: SEVERITY AND FREQUENCY OF ATTACKS

SEX	Number of episodes per year			Maximum length of attack			Minimum length of attack		
	1	1-10	>10	< 1 day	1-2 days	>2 days	< ½ hr.	½-1 hr.	>1 hr.
M	—	6	4	—	2	8	1	4	5
F	—	1	3	—	1	3	—	1	3

TABLE IV: SYMPTOMS

	SPUTUM			FEVER			COUGH	
SEX	Insignificant	Present	Copious	Nil	Low < 100.5°F	High >100.5°F	—	+
M	8	1	1	8	2	—	1	9
F	3	1	—	2	2	—	1	3

TABLE V: BLOOD COUNT DURING ATTACKS

	Leucocyte Count		Eosinophil Count	
SEX	< 10.000	>10.000	< 200	>200
M	8	2	—	9
F	3	1	3	1

TABLE VI: TREATMENT AND RESPONSES

	Medication in items			Responses		
SEX	< 2	2-4	>4	Poor	Indifferent	Good
M	—	6	3	—	8	1
F	1	3	—	—	3	1

TABLE VII: TYPES OF TREATMENT

	Adrenaline		Oral Isoprenaline		Penicillin		Broadrange Antibiotic		Sedation		Short Term Steroid	
SEX	Poor	Good	Poor	Good	Poor	Good	Poor	Good	Poor	Good	Poor	Good
M	—	14	—	2	—	10	—	5	—	11	—	2
F	—	—	—	—	—	1	—	—	—	1	—	1

TABLE VIII: SENSITIVITY OF BACTERIAL FLORA ON CULTURE

	Sensitive to Penicillin	Resistance to Penicillin
On prophylactic penicillin	6	5
Not on prophylactic penicillin	3	4

TABLE IX: SKIN SENSITIVITY TESTS

No. of Agents	16	15	14	13	12	11	10	9	8	7	6
No. of cases +ve	1	0	0	1	0	1	11	0	0	0	1

RESULTS

Quite obviously the number is not big enough to warrant any conclusions regarding sex ratio but it is interesting to note that M:F=10:4 for it is the same ratio for the admission into the General Hospital, Singapore (Gwee 1961). This ratio seems to apply to many diseases locally based on the annual returns as well. Thus from local figures it may be seen that the ratio for the following diseases were as follows:

Type	M:F Ratio
Neoplasm	1.7:1*
Tuberculosis	2.5:1 (Harvey et al. 1958)
Gastric Ulcer	8:1 (Yeoh. 1960)
Admission G.H.	2:1 (Gwee. 1961)
Death G.H.	2:1 (Gwee. 1961)

*Muir. personal communication. This figure includes sex-determined cancers and the ratio would have been higher if only General Hospital figures were considered.

From Table II, it could be appreciated that these were all chronic cases. Locally, an asthmatic seeking hospital treatment must come first to the Outpatient Department where treatment including adrenaline injection and exhibition of bronchodilators were given. As a rule, the Casualty Department in General Hospital gave 5 to 20 adrenaline injections a day. It was only when treatment failed at the Outpatient Department, or when the case was severe, that he was admitted and came under the care of the Chest Clinic. It would appear that the majority of cases gained entry to the Chest Clinic after more than 5 years of suffering. This could be subject to many interpretations. It may be that the Outpatient Department was very rigid in selecting cases for referral — this is probably not the real reason as the records show that the referral is in the region of an average of 10%, which is very high for dispensary practice. It may be that the asthmatic attacks are not severe in the beginning, and hence neglected by the patients for many years. This is probably also not the reason as none of the patients was able to say that his symptoms have aggravated very much recently. The time reason seems to be that the initial attacks were easily controlled by adrenaline in conventional doses, and hence the patients are kept attending the Outpatient Department from time to time till the day when the "magical" injection fails, and the patient gets admitted.

Table III shows that in spite of the severity of the attack, the morbidity is really confined to a loss of a few days each month, as the frequency is less than once a month in more than half of the cases, all of which have been rated as "chronic asthmatics".

In symptomatology, it would appear that most of the cases have cough with the attack, and in fact a careful history taking shows that in the overwhelming majority, cough preceded the attack by hours or days. No constitutional upset is seen on the whole, and the cough is generally dry and unproductive with occasional leucocytosis. Eosinophilia however, is a constant feature in 9 of 14 cases, and of these, only one had whipworm ova in the stool. This scarcity of worm infestation was probably a reflection of the intensity of treatment as these cases were chronic, and probably received a lot of medication including vermifuges.

Going into the history of their medicaments, it is an invariable story of polypharmacy characterised by the use of one new antiasthmatic agent after another. With the exception of one case

who quite extraordinarily did not receive more than ephedrine and adrenaline the rest had many varieties of medicine, and in general with only indifferent relief. In fact, the common story was one of initial relief for a few months followed by a gradual loss of effectiveness and finally another drug was employed. Only 3 cases were put on steroids for maintenance, and they all did well apart from the fact that in the course of the next few months steroids had to be supplemented by other drugs, like ephedrine and other patent preparations. It is probably worth noting that the only mortality occurring in this series was a case receiving steroids.

A scrutiny of the responses to the drugs used, showed that despite their frequent recourse to adrenaline in the Outpatient Department, and the fact that many came in because the Outpatient Department failed to break the attack, adrenaline continued to exert valuable effect in the ward when injected subcutaneously at the rate of 1 minim a minute up to a total of 20 minims. No case of adrenaline resistance was found although many of them had fresh attacks after the effect of adrenaline was over.

Oral isoprenaline was used only in two instances with good relief, but ulcer under the tongue was soon noticed. Penicillin was given in all cases as it appeared to decrease the liability of fresh attacks, and the use of broad-range antibiotics, like erythromycin and tetracycline, did not apparently give more speedy response although the result was comparable to Penicillin. The use of sedative and tranquillisers like phenobarbitone and chlorpromazine would appear to help in that patients became less anxious, and in all the twelve cases used, subjective satisfaction was expressed in that symptoms had become less, and restful sleep was more easily secured.

Culture of the sputum was done as a routine, and sensitivity tests were done. Only 4 showed pure growth of pneumococcus. The rest was a mixed bag of diphtheroids, streptococcus and occasional staphylococcus coagulase positive. Only 8 cultures were satisfactory enough for sensitivity test and of these 6 were penicillin sensitive and 2 resistant, although all cases benefitted from the use of penicillin in that the recovery was speedier. 4 of these cases were on oral penicillin between attacks, as a prophylactic for periods of six months to a year, and 2 of these 4 cases grew streptococcus viridans which were resistant to Penicillin. A number of cases receiving prophylactic oral penicillin 200,000 units a day, such as rheumatic fever and acute nephritis were investigated with others not on prophylactic. Their sputum results are shown in Table VIII.

It would appear that the use of the prophylactic penicillin for period up to a year did not materially affect the emergence of penicillin-resistant organism in the sputum. What is more interesting is the fact that the proportion of sensitive cases to resistant ones responding to the exhibition of penicillin was equal. In other words, penicillin remained valuable despite the cultural findings. This is in keeping with observations about the unreliability of cultural results, which for the moment should be regarded as of value but not decisive, and to base the use of any antibiotic solely on the cultural results of sputum would appear to be dangerous. This may however be due to the lack of homogenity of the specimen of sputum so that the culture might have come from an innocuous portion rather than a reflection of the bacteriological technique (May 1954).

Skin sensitivity tests were done on six of our patients using Bencard's test reagent of 16 kinds. This showed that no case was sensitive to one single allergen. In fact, repetition of these tests on the same cases showed that the sensitivity state is a global one involving many, and also subject to variation in that the sensitivity is less if the case has been free from attacks for some time and vice versa. There are many proponents of the theory that bronchial asthma is mainly allergic in basis. Thus a simple method of treatment would be the identification of the specific allergen, and followed up by either the elimination of the allergen from the environment of the patient, or the desensitisation of the patient himself. This would be possible where a single allergen is concerned such as a certain food or material handled. However, where multiple allergies occur, it would be impracticable to do this. As Boland (1952) sums it up: "The theory of desensitisation is a sound one but in the vast majority of cases not a practical one, possibly because the basis of asthma is the tendency to become sensitised and because the majority of patients have become or are capable of being sensitised to so many different unavoidable substances that desensitisation is difficult or impossible".

The value of steroids in the treatment of bronchial asthma has been the subject of many clinical studies. There were a number of early reports suggesting good response with cortisone in bronchial asthma (Savidge and Brockbank 1954, Davies and William 1955). The M.R.C. Trial (MRC 1956a) showed that there was initial improvement of symptoms in patients on cortisone but there was no significant advantage over patients on placebo at the end of the trial. Since

then, there have been other trials to evaluate the results of long term steroid therapy in chronic asthma (A.R. Somner et al 1960, Livingstone and Davies 1961, Pearson et al 1961). The general conclusion is that it is of definite value in improving the clinical state of these patients. However, prolonged steroid therapy leads to a number of fresh problems. There is the question of undesirable side-effects such as weight increase, moonface, osteoporosis with fractures, peptic ulceration, flare-up of tuberculous infection, which are liable to develop in long term steroid therapy. Perhaps more sinister is the problem of steroid dependence. It has been found difficult to withdraw or reduce the dosage of steroids in those patients who have responded well, reduction in dosage resulting in increased number of attacks, and deaths in status asthmaticus have been reported following withdrawal (Pearson et al 1961). It would seem that while long term steroid treatment may be of value in the management of chronic asthma, the dangers of side effects and development of steroid dependence would militate against its routine employment, and it can only be recommended where there is no alternative (Somner et al 1960). Though this may be the case in chronic asthma, there is no doubt that steroids have a definite place in the treatment of status asthmaticus (M.R.C. 1956b). It was shown to be effective in breaking an attack of status asthmaticus after the usual administration of adrenaline, aminophyline and isoprenaline inhalation had failed to do so. However, it was stressed in the report that the majority of patients responded to the usual antispasmodics, and only a small proportion of patients required the exhibition of steroids. There did not seem to be a reduction in the number of attacks of status asthmaticus subsequently, and in fact 9 out of 11 patients who received steroids had recurrences as against 7 out of 14 patients in the control group.

The use of steroids leads rapidly to steroid dependence. Steroids were used either in the form of intravenous hydrocortisone or oral prednisolone in cases where the attack persisted without relief. This happened in only 4 cases where the use of adrenaline gave temporary relief, and it was thought inadvisable to give again after a fairly large dose. The relief was dramatic as symptoms subsided within 4 hours. In 3 cases prednisolone by mouth was continued, and in all 3, after an initial phase of good control, the return of asthma gradually led to the restitution in 3-4 months of bronchodilators and cough mixture. Attempt to withdraw the steroids led to severe attacks and was abandoned. One of the cases died 7 months after being on maintenance, although he was under treatment for the last 5 years and survived previous attacks. At the seventh month, he developed a severe attack of asthma and was admitted into hospital. Adrenaline gave only temporary relief, and on the 2nd day, intravenous hydrocortisone was begun. However, he did not show the relief expected, but died suddenly on the 3rd day. Post-mortem showed generalised pulmonary oedema for which no apparent cause could be found. The circumstantial evidence is indicative that steroids might have contributed to the death.

CONCLUSION

1. There is no outstanding system of treatment in bronchial asthma at present.

2. Infective basis is common and responds well locally to penicillin in spite of cultural results to the contrary.

3. Steroids are valuable for acute attacks but in long term use, the other drugs in use originally have to be re-employed in addition.

4. Adrenaline resistance occurred but would appear not to be necessarily permanent.

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