Observations

ON

ASTHMA: RESULTS OF TREATMENT.

BY

D. M. LYON, M.D., D.Sc., F.R.C.P.Ed.,
PROFESSOR OF THERAPEUTICS AND CLINICAL MEDICINE, UNIVERSITY
OF EDINBURGH;

AND

R. M. MURRAY-LYON, M.D., M.R.C.P.Ed.,
EDINBURGH.

GENERAL impressions gained from clinical experience, though sufficient for the individual observer, should be confirmed by definite evidence whenever possible. A series of nearly 500 cases of asthma examined in the Royal Infirmary of Edinburgh seemed to offer an opportunity of obtaining information regarding the course of the disease and of the results which may be expected from treatment. A preliminary analysis of these case records has already been published.¹ The patients were all recommended to the hospital by their own doctors as cases of "asthma." The majority of them were examined as out-patients, while a proportion of the more severe cases were treated in the wards for a time. A diagnosis of "asthma" was based on the finding of the patient's own doctor, and on an examination of the individual and a careful history of his illness. Cases of dyspnoea dependent on obvious cardiac or renal disease have not been included. On the other hand, patients with marked bronchitis have only been accepted as asthmatic when a definite account of paroxysmal attacks of dyspnoea was forthcoming. Exception may be taken to the inclusion of cases which have developed asthmatic symptoms only after a long history of chronic bronchitis, but it has been found impossible to draw a hard-and-fast line. There is a tendency on the part of medical writers at the present time to regard "true" asthma solely as a manifestation of the allergic syndrome and to set aside, as not being asthma, cases in which the presence of allergy could not be proved. True asthma, then, would include those cases which show a positive inheritance of asthma, hay fever, or one of the other exudative diseases, and those in which sensitiveness to some protein can be demonstrated, while patients who only develop asthmatic symptoms after severe or repeated attacks of bronchitis are merely regarded as "asthmatic bronchitis." It has not been possible for us to make such a distinction on account of the large part which respiratory disorders play at the onset of true asthma even in early life; in addition, evidence of constitutional predisposition is often found in cases of late development. All our cases have therefore been taken together as examples of the asthmatic syndrome.

The Edinburgh inquiry has now been in progress for about nine years, a steady stream of patients coming for examination and advice at all seasons. As an estimate of the value of treatment can be made only after a sufficient interval, it has been decided to leave out of this survey all patients seen for the first time within the past twelve months. This leaves a total of 379 patients about whom we have endeavoured to obtain information. The short, simple questionnaire employed has been completed in some cases by the sufferers themselves, in others by their medical attendants. Many of the patients have recently reported in person, giving us an opportunity of obtaining more detailed information. For various reasons it has been impossible to trace 88 of the patients, chiefly because of change of residence, which appears to be more frequent than has been suspected. Replies concerning 291 patients have been received. These records reveal that 36 patients have died; 63 state that their asthma is still as bad as ever; the remaining 192 have derived benefit from treatment. These may be divided into four classes according to the degree of improvement. No fewer than 63 claim to have been "cured," by which is meant that they now enjoy complete freedom from attacks. Some of them have been in good health for years. Those "improved" but not cured number 129. Very great improvement is recorded by 60 patients, many of whom have now only

occasional attacks, and these usually mild in character. The third class—those much improved—contains 57 individuals, while only 12 record their improvement as slight. It will thus be seen that a large proportion of the asthmatics still living have received substantial benefit from treatment. The "improved" and "cured" together total 66 per cent. of the whole. Reports concerning those now dead show that some in this group had improved or were free of asthma for a time before death, and that they died from some other condition unconnected with asthma.

While these results are highly encouraging, it is clear that no definite improvement can be guaranteed to an individual sufferer. Many cases are readily amenable to treatment; others appear to be quite resistant, and superficially it is not obvious why this should be so. These differences in the results obtained stimulate inquiry into the factors which lead to them. The points of importance in this connexion appear to be: (a) the form of treatment employed; (b) the age at which symptoms originally appeared; (c) the duration of the asthma before satisfactory treatment is begun; (d) the patient's age when first seen; and the questions of (e) heredity; (f) sensitization; and (g) the relation to respiratory infections. Attempts to classify patients according to the severity of the disease have not been successful. The gravity of the condition is difficult to assess for statistical purposes. Patients vary so greatly in their estimates of what constitutes a severe or a mild attack, and the frequency of asthmatic paroxysms is often so variable throughout the seasons, that comparison of one case with another is almost impossible. The physical condition of the patient and the presence or absence of other disease also have considerable influence upon the ultimate result, but the information recorded on these questions is not sufficient to enable an analysis to be made.

Relation of Treatment Employed to the Results Obtained.

Since asthma is such a variable disorder, and individual cases differ so greatly, it is impossible to lay down a uniform plan of treatment for all types. Patients must be treated individually. The clinical examination usually indicated what lines of therapy would be most successful, and an appropriate scheme was drawn up for the patient. Instructions regarding general hygienic measures, alterations of diet, avoidance of late meals, attention to the bowels, and so forth, were given at the time of the examination. The principal treatment was, in many instances, carried out under the supervision of the patient's own doctor. Those who suffer from such a chronic and distressing malady as this are apt to become dissatisfied with one line of treatment and try one remedy after another. Where information on this point has appeared of importance it has been included in our analysis. The figures for treatment have been compiled from the patients' answers to the questionnaire, checked and supplemented from our records.

The recognition of a specific causal agent and its removal or avoidance is clearly the most satisfactory line of treatment when it is applicable. Sometimes the matter is extremely simple and a relatively slight modification makes all the difference. Such minor adjustments are apparently not considered of importance by the patients, for they are seldom mentioned in the returns. Avoidance of an irritant plant or removal of a domestic pet can easily be arranged, but when the irritation arises from some common protein which cannot readily be eliminated, recourse may be had to specific desensitization. Such specific irritants have not been numerous in this series, but the results of their removal have been striking. In the majority of cases in which elimination has been practised the patients have been completely relieved of symptoms.

The importance of environment in aggravating or in relieving symptoms of asthma is well recognized by the general public, and many of our patients (86) have sought relief in a change. Rather more than half of this group found their condition to be just as bad in their new surroundings; two patients believed that they became definitely worse; but 45 per cent. of those who changed their residence claimed improvement thereby. A few asthmatics claimed that they had obtained complete relief

from symptoms as the result of changing their surroundings.

Examination of the nose and throat has been carried out in the majority of the patients (252). Most of the subjects were found to show some abnormality, though not necessarily severe enough to require treatment. While remarkable cures may occur after nasal operations, experience shows that such results are exceptional, and caution is necessary in recommending this class of treatment. It is safer never to suggest an operation as a cure for asthma, but only to recommend it when it appears desirable for other reasons—for example, to remove a definite obstruction or to lessen a tendency to recurrent catarrh. In spite of this conservative attitude, 115 patients have been operated on. The operations include 67 for tonsils and adenoids, 18 for polypi, 24 for turbinectomy, 14 for submucous resection, and, in addition, cauterization has been carried out when considered desirable. These procedures undoubtedly benefited the patients by removing irritation or sepsis and by giving a freer airway, and so have contributed to the general results of treatment. Our figures do not show this very clearly. Of patients upon whom operations were performed 18.3 per cent. are returned as cured, in contrast to 29.4 per cent. of cures among those who had no operation. When the "cured" and "improved" are taken together the position is reversed, the figures 65.9 per cent. and 63.2 per cent. showing a small advantage in favour of those who had undergone operation.

Since respiratory infections play so large a part in relation to asthma, either as causal agents or as secondary complications, their treatment, including avoidance of prophylaxis is of great importance. Where this factor seemed to be prominent, the patient was given a course of autogenous vaccine made from a laryngeal swab. The results of this treatment have been most gratifying. Patients have not only suffered less from colds, but after the course of vaccines have often had complete freedom from asthma for some time, or no further return of symptoms. It is significant that the proportion of cured and improved patients who received vaccine treatment is distinctly higher than that of the unfavourable groups. A few of the more resistant cases have undergone treatment by diathermy, ultra-violet radiation, or by x rays, with apparent benefit.

Probably all the patients at some time or other have received drug treatment, yet only half of the returns (153) include this item. The figures given in the table for each group form an interesting commentary on the value of drugs as curative agents, favourable cases showing less than the others. This may be merely that, having failed to benefit from other measures, the unresponsive patients have had greater opportunity for trying such remedies. Though it is interesting to find that the patients who were cured received less drug treatment and a higher proportion of vaccines, and that the position with regard to patients who were not cured is reversed, too much weight must not be given to these figures, since they also reflect to some extent the types of case dealt with.

Age at Onset.

The average age at onset of the asthmatic symptoms is much the same in all the groups, except the fatal cases, which have a much higher age-incidence (see table). It is found that in about a third of all the cases (35.4 per cent.) the onset occurs in the first decade. Taking the patients who began to suffer in the first five years of life it will be found that the number "cured" is somewhat low, while the proportion of "unchanged" is relatively high. These differences do not hold for the second quinquennium, nor up to middle life, but a large proportion of the cases commencing after the age of 40 are also unfavourable; 66 per cent. of those who became asthmatic late in life are in the two lower categories. From these observations it would seem that the prognosis is not so good in cases commencing in the first five years, or after middle life.

Duration of Asthma before Treatment.

The length of the illness before the patient came to the clinic has varied greatly. While most of the patients had suffered for a short time only, some had had the disease for

a longer period, and 10 had been asthmatic for over thirty years. Of all cases of less than five years' standing when first seen, no less than 32.6 per cent. were cured, while the percentage "unchanged" numbered only 14.0 per cent. These figures may be compared with the proportion that the "cured" and the "unchanged" bear to the whole

	Cured.	Improved.	Unchanged.	Dead.
Number of cases	63	129	63	35
Average age at onset (years) ...	21.5	17.5	20.4	31.4
Average duration (years) ...	7.3	10.6	10.6	10
Age at onset:	Per cent.	Per cent.	Per cent.	Per cent.
0-5 years	15.9	19.4	27.0	8.6
Over 40 years	12.7	7.5	20.7	40.0
Duration 0-5 years	44.4	25.6	19.4	37.1
Heredity positive	27.0	42.2	42.0	28.6
Protein sensitive	50.0	50.0	55.0	41.7
Respiratory infection	85.8	89.0	77.7	94.3
<i>Treatment.</i>				
Elimination	14.2	3.1	—	—
Benefit from change of house ...	41.7	47.2	10.5*	—
Drugs	23.8	48.8	79.4	69.5
Nasal operations	31.8	51.1	41.5	16.7
Vaccines	73.0	69.7	57.2	61.0

* Temporary.

The figures shown above are the percentages of all cases "cured," "improved," etc., which showed a positive heredity or were treated by drugs and so forth.

series, which is 21.6 per cent. in each case. Cases of longer than five years' duration naturally show a smaller proportion of "cures." The same point is illustrated also by the average duration of the illness in each group—the figure for the "cured" being 7.3 years, in contrast to 10.6 years for each of the "improved" and "unchanged," and 10 years for those who died. These figures indicate the importance of prompt and efficient treatment, and show that the earlier the case is attended to the better the result. The outlook is by no means hopeless, however, in cases of longer duration, for of the ten who had suffered for upwards of thirty years one was returned as cured and five as improved.

Age at Examination.

The ages of patients when first seen ranged from earliest years up to 70. The percentage in each decade for the different classes is shown in the accompanying chart. The

The age of patients when examined at the clinic. The percentage distribution by ten-year periods of the different groups is shown graphically.

numbers for the first ten years are probably unduly low, since many of the younger patients are dealt with elsewhere. In the succeeding age periods, the values for the groups other than the dead decline fairly uniformly. The "unchanged" group shows a slight excess between the ages of 20 and 30, and again after 50. The age when the

patient commenced treatment is in itself probably of little importance when allowance is made for the age at first onset of the disease and for the length of time it has been in existence.

Relation to Etiological Factors.

Heredity.—The occurrence of asthma in one or more of the near relatives of the patients has been taken for our purpose as evidence of a positive inheritance. Such an association has been found in 37.3 per cent. of all the cases in the present series. It should be noted that although a definite inheritance is more common in those patients who begin to have symptoms in the first ten years of life (about 1 in every 2 patients), there is a fairly uniform proportion of positives in each succeeding period (1 in 3 patients). From the table it will be seen that the figures for the cured and for the dead are distinctly lower than those for the other groups. If the occurrence of skin lesions among relatives is also included as evidence of an "exudative" heredity, the figures become even more definite. The percentage of positives for the whole series now becomes 41.0 and for the various groups: "cured" 31.7, "improved" 42.2, "unchanged" 48.4, dead 31.5. An attempt has been made to gauge the constitutional element by grouping the patients according to the number of the following factors which they show: asthma heredity, the occurrence of skin lesions among relatives, and the presence of hay fever, skin rashes, or protein sensitiveness in the patient. It is found that those subjects with the greater evidence of allergy begin to have symptoms earlier in life. From this it would appear that asthmatics having a positive heredity are somewhat less amenable to treatment, and that the less favourable results for the first five years of life might be explained by the greater proportion of hereditary cases commencing at this period.

Protein Sensitivity.—From a statistical point of view it is unfortunate that all the subjects have not been exposed to the same set of proteins. Owing to the large number of individual test substances available, it was not at first found possible to employ them all on each patient, and the choice was mainly guided by the history of the case. Later, the plan of testing every subject with a comprehensive series of "grouped" proteins has been adopted. The figures obtained, therefore, do not necessarily represent the true extent of sensitization, but merely the positive reactions found. The "positives" recorded include multiple sensitivity as well as single specific responses. The groups give a similar proportion of positive results, except that the figure for fatal cases is a little low. It should be observed, however, that in the case of the "cured" patients about half of the positives reacted to a single protein.

Respiratory Catarrhs and Infections.—These appear to be of great importance in the development of the asthmatic condition at all ages. It is sometimes said that in early life the exudative diathesis manifests itself by respiratory symptoms indistinguishable from bronchitis. After middle life a history of prolonged or severe bronchitis is more commonly found as a forerunner of the asthma. The patients, when examined, were merely asked whether such conditions were present at the time of, or immediately before, the first attack of asthma, and no account has been taken of previous health in regard to respiratory disorders. The proportion of individuals who give this history is high, and is much the same in each group. There is really no significant difference between the groups in this respect, and this factor does not appear to influence the result of treatment.

The Fatal Cases.

This group stands out from the others in various respects. Inheritance and protein sensitization are rather lower in this class, while respiratory infections are much the same as in the others. The average age of onset in the group is considerably higher—namely, 34.4 years, as contrasted with 21.5, 17.5, and 20.4 for the others. While 7 cases began before the age of 20, a large percentage of this group developed symptoms after middle life. A number of deaths is to be expected in such a group, but the proportion actually recorded is very much greater than would occur in a similar age sample of the community during the same length of time. Of the 36 deaths, 28 occurred in subjects

over the age of 40, 3 were under 20 years of age, and 5 between 20 and 40. Acute illnesses accounted for at least 8 of the deaths; these were influenza (patients aged 7, 14, 48, 55); pneumonia (aged 17); cholecystitis (54); meningitis (40); gastric haemorrhage (39). There were two suicides (50 and 61). Two fatalities were due to phthisis (26 and 32), both patients having previously had undoubted asthmatic symptoms. Syphilis accounted for 4 deaths (36, 60, 60, and 70) and cerebral haemorrhage for one (51). Five were attributed to heart failure (36, 43, 58, 63, and 70). In the case of the remaining 14 the exact cause of death has not been ascertained. These include some of the most severe cases, in which the patients are known to have been almost constantly dyspnoeic and in a condition of status asthmaticus with advanced emphysema and cardiac embarrassment. Additional information shows that before death 2 of the patients had been "cured" of their asthma, 7 were considerably improved, 2 slightly benefited, and 15 were unchanged. These figures have not been incorporated in the other sections.

Summary.

The results of treatment in 291 cases of asthma are reported. Of these, 66 per cent. have been benefited and 12.4 per cent. have died. No single scheme of treatment can be laid down for all cases; each patient must be treated individually. The most successful forms of therapy appear to be elimination when applicable, and vaccine treatment where respiratory infections complicate the asthma. Cases which react to a single protein are usually favourable, but the occurrence of multiple sensitivity is of little importance in relation to treatment. Among many factors less easy to assess, change of residence and general hygienic measures have contributed to the patients' improvement. The results of operations on the nose or throat are disappointing, and such treatment should only be recommended to relieve definite local symptoms. Cases arising in the first five years of life are less successful than those beginning later. This may depend on the unfavourable factor of a positive heredity. Asthmatic symptoms commencing after middle life are also apt to be less amenable to treatment. The duration of the disease before effective treatment is undertaken is of the greatest importance; the longer the delay the less satisfactory the result, although certain cases of long standing have benefited considerably under adequate treatment.

REFERENCE.

Lancet, March 9th, 1929, p. 517.

A GOITRE SURVEY IN ALBINO RATS.

BY

ROBERT McCARRISON, C.I.E., K.H.P.,
M.D., F.R.C.P.,

COLONEL, INDIAN MEDICAL SERVICE; DIRECTOR, NUTRITIONAL RESEARCH,
I.R.F.A., PASTEUR INSTITUTE, COONOR, S. INDIA.

DURING the past three years the practice has been followed of recording, at post-mortem examination, the state of the thyroid gland in all animals used in the laboratories of the Pasteur Institute, Coonoor, for experimental work on diseases of faulty nutrition. Post-mortem records of 2,561 albino rats have accumulated during this period. It is with these that the present survey deals.

Of the 2,561 animals 393 were "controls" fed throughout life on complete diets, and 2,168 were rats fed from an early age (approximately 40 days) until the time of their death on various deficient diets. Goitre did not occur in the former group; 148 cases of the disease occurred in the latter. The goitres were classified as follows: (a) Small enlargements amounting to less than twice the size of the normal organ, 84; these were called "slight goitres." (b) Moderate enlargements amounting to more than twice but less than four times the size of the normal organ, 41; these were called "small goitres." (c) Marked enlargements amounting to four or more times the size of the normal organ, 23; these were called "large goitres."