3. There is a tendency for a larger proportion of girls than boys to be above the normal.
4. There is a larger percentage of dull children among manual workers' children and of advanced pupils among sedentary workers' children.
5. There is a steady decline in nutrition, as judged by height and weight, from clever children to very dull children.
6. The majority of very dull children come from houses with only one or two apartments.
7. The majority of dull children, and, especially of backward girls, come from houses with more than two persons per apartment.
8. As a rule, children of good mental capacity are cleanly, while children of poor mental capacity are dirty and ill cared for.
9. The height and weight of children employed out of school hours and their hours of sleep per night are less than in the case of school children of similar age not so employed.
10. Defects in vision, speech, and hearing and organic cardiac defects cause retardation.
11. Minor defects do not cause retardation.
12. Intelligence and mental capacity figures can be substituted one for the other in the case of regular attenders.

I must express sincere thanks to Dr. Adam, medical officer of health for the County of Stirling, for the facilities he has given me in this investigation, and to his assistants, my colleagues, Dr. Rutherford and Dr. Learmonth, for their help in carrying through the mental tests in many of the children.

FURTHER REPORT ON THE TUBERCULIN TREATMENT OF ASTHMA

BY

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The treatment of asthma by means of subcutaneous injections of old tuberculin has now been carried out in this country for more than five years, but, so far as I am aware, there has been no recent published record of the late results achieved by this method. Papers were published in 1928 by Ling,¹ in 1929 by Simpson and Stone,² and in 1930 by the present writer,³ all of whom recorded considerable improvement in the majority of the cases treated. In each of these series, however, the interval of time which had elapsed since the treatment was instituted was too short to permit any reliable conclusion to be drawn as to the permanence of the results. The primary object of this paper is to review the present position of the series published from the Royal Chest Hospital in 1930, which consisted of cases presenting themselves for treatment during the year 1928. The time interval is now therefore between three and a half and four and a half years, which should be sufficient to afford a fairly correct perspective, and should enable some definite conclusion to be drawn as to the ultimate value of the treatment. In addition, it is proposed to record the present state of the series of cases treated during 1929, 1930, and 1931, and to consider briefly the indications for the adoption of tuberculin in the treatment of asthma. In this period of four complete years the total number of cases accepted as suitable for treatment was 103, and this would seem to be sufficiently large to enable the objects stated above to be achieved.

Any attempt to consider the value of a particular method of treatment in asthma is rendered difficult at the outset by the nature of the disease, which is so variable and so apt to be influenced by extraneous factors that one

cannot be sure that improvement is necessarily the result of the particular line of treatment adopted. In addition, the term "asthma" is applied to a number of conditions characterized clinically by dyspnoea but aetiologically separable into distinct groups, not necessarily related to each other. In the previous report cases of spasmodic asthma were considered without reference to their aetiology; in the present paper the cases are separated into two groups—first, cases of true spasmodic asthma of the so-called "primary" type, presumably allergic in origin; and, secondly, cases in which the dyspnoea is spasmodic yet apparently secondary to some chronic infection of the respiratory tract. This has been done because it would have been expected that the former group would react more favourably to treatment than the latter, and a comparison of the results actually obtained is therefore of value in guiding the selection of cases.

TECHNIQUE

On the whole, the dosage described in the previous report has been found to yield the best results. Much larger doses were given in the year 1930 and much smaller doses during part of the year 1931, but in each case the results were found to compare unfavourably with those previously obtained; failure was particularly noticeable when the larger doses were given. The material used in all cases has been Koch's old tuberculin, which may be conveniently kept in decimal dilutions from 1 in 1,000 to 1 in 1,000,000. It is not necessary for the dilutions to be prepared immediately before use; they keep quite well under ordinary conditions for at least a month. The initial dose is gauged by the response of the patient to the Mantoux test. One-tenth of a cubic centimetre of the 1 in 1,000 dilution is injected intradermally and the result is read after two or three days, attention being paid only to the area of swelling, for erythema is apparently of no significance. If there is no swelling, then it is quite safe to begin the treatment with a subcutaneous injection of 1/10 c.cm. of the 1 in 1,000 dilution; if there be an area of swelling less than one centimetre in its long axis, the initial dose should be 1/10 c.cm. of 1 in 10,000; if the area be between one and two centimetres in its long axis the initial dose should be 1/10 c.cm. of 1 in 100,000; and in cases where the area of swelling exceeds two centimetres in diameter the initial dose should not be greater than 1/10 c.cm. of the 1 in 1,000,000 dilution.

In the early stages of treatment the interval between the injections should be two or three days, although, in the case of hospital out-patients, this is not always possible, and a weekly injection must suffice. The interval between injections may be gradually increased, but weekly injections should be given for at least six months, after which, in the majority of cases, the treatment may be given fortnightly for a further period of six months. The injections may then be suspended for three months, but a further course of weekly and fortnightly injections should be given to bring the total period of treatment up to a minimum of two years. It would appear that one of the commonest causes of failure has been an inadequate course of treatment—frequently the fault of the patient, who concludes prematurely from the absence of attacks that the condition is "cured." In some cases (especially in elderly people with chronic respiratory infections) it may be desirable to administer a course of tuberculin every year from October to May. The rate of increase in the dosage must be decided for each individual, but on the whole it has been found best to increase the dose by 1/10 c.cm. at each injection, although in some instances this rate of increase may be too rapid. The maximum tolerable dose is found to vary greatly, for some patients

being only a fraction of a cubic centimetre of the 1 in 1,000,000 dilution; but in any event the maximum dose should not exceed 5/10 c.cm. of the 1 in 1,000 dilution. In many cases a stage is reached at which the patient has an attack of asthma a few hours after the injection. If this were unexpected it might be interpreted as a sign of failure of the treatment, whereas actually it is frequently a sign of overdosage; and indicates an immediate reduction in the dose. On the other hand, if no improvement at all has resulted after two months of adequate treatment, the method may be presumed to have failed and the course should be abandoned.

RESULTS

The thirty-six cases reported previously, in all of which treatment was commenced during 1928, have been followed up, and the present condition of thirty-one of them is considered here, the remaining five not having been traced. The position at the end of one year, reported in 1930, is reproduced in Table I for comparison with the present state of the same cases set out in Table II.

TABLE I.—Cases Commencing Treatment during 1928, Reported after One Year

Mantoux Test	Satisfactory	Improved	Failed
Positive	4	4	4
Negative	13	8	3

There is no evidence that the sensitiveness of the patient to tuberculin before the commencement of treatment exercises any influence upon the response to treatment; therefore the results of the preliminary tuberculin tests are not indicated in the tables which refer to the more recent cases. It would appear more useful to indicate the type of asthma, with regard to the presence or absence of any chronic infection of the respiratory tract, by rearranging the cases into primary or allergic and secondary or bronchitic groups, and the original series of cases is thus set out in Table IA:

TABLE IA.—Cases Presented in Table I Regrouped to Indicate the Type of Asthma

Type	Satisfactory	Improved	Failed
Primary	14	8	5
Secondary	3	4	2

The cases treated in the later years are all arranged according to this system. The scheme of results is that adopted in the previous paper. "Satisfactory" cases are those in which there has been no attack of asthma since shortly after the commencement of the course of treatment, although it is not possible to claim these cases as cures, for it will be seen that several previously classed in this group have since relapsed. The term "improved" indicates an occasional attack of asthma or a slight wheeziness, and this is obviously a more difficult group to assess, but cases are not included here unless the frequency of attacks is less than one-quarter of that prevailing before treatment was instituted.

TABLE II.—Present State of the Cases Commencing Treatment during 1928

Type	Satisfactory	Improved	Failed
Primary	6	10	8
Secondary	1	3	3
Last known state of cases not traced	4	1	—

Superficial comparison of the results contained in Tables I and II shows that the results after a further period of observation are not so encouraging as those previously recorded, but it must be noted that four of the cases previously classed as satisfactory could not be traced, and it need not be assumed that they have relapsed (although a contrary assumption is equally unjustifiable). A more detailed examination of the present state of these cases reveals the following facts:

(a) Of the seventeen patients originally classed as satisfactory no fewer than seven are known to have relapsed, two of them reverting to their original state and five to a much less extent—sufficiently controlled by further treatment to justify their being classified at present as improved. On the other hand, one patient originally classed as improved has not experienced any attacks for over two years, and is now grouped as satisfactory. Thus, leaving out of consideration the four cases which have not been traced, there are now only six of the cases originally classified in this group which have remained free from asthma for more than three years since the beginning of treatment.

(b) The patients who are considered to be improved number thirteen as against twelve in the original report. Analysis shows that of the original cases one is now transferred to the satisfactory group (as has already been noted), two have reverted to their original state and are now classed as failures, and one has not been traced. On the other hand, five patients previously classed as satisfactory are now included in this group, so that the numerical increase is seen to be due to the failure of cases previously regarded as successful to maintain their state of freedom, and not to any improvement of the original failures.

(c) The group of failures is now augmented by four cases, each of the other groups contributing two. Therefore the present position is that no improvement has been obtained after treatment in eleven out of thirty-six cases, or 30.6 per cent. Results have varied considerably in subsequent years, partly as the result of experimental alterations in dosage, and they are set out in Table III.

TABLE III.—Present State of the Cases which Commenced Treatment during the Years Indicated

Year	Type	Satisfactory	Improved	Failed
1929	Primary	3	3	2
	Secondary	1	1	1
1930	Primary	4	4	10
	Secondary	2	5	1
1931	Primary	12	7	4
	Secondary	1	5	1

As would be expected, the patients treated most recently have so far produced the best results, and in the course of time a certain number of these may be expected to relapse. The dosage injected has varied considerably, and may possibly account for the relatively poor results obtained in 1930, during which year much larger doses were given as a routine than those indicated in the foregoing section. It is interesting to compare the results obtained in the allergic types with those in which the bronchitic factor was pronounced. It would naturally be expected that little improvement would result in patients who were the subjects of advanced bronchitis and emphysema, yet even in some of these the distressing attacks of dyspnoea which are so frequent a concomitant of this condition were very materially relieved, although the cough and underlying chronic shortness of breath were not affected.

DISCUSSION

It is generally accepted that the action of tuberculin in asthma is non-specific to the extent at least that there is no suggestion that the asthmatic state is the result of a tuberculous infection. Van Leeuwen,⁴ whose great experience of this line of treatment must be admitted, originally selected this substance to produce a "reaction" because he noticed that the great majority of his asthmatic patients exhibited positive skin reactions to tuberculin, and he appears still to employ the skin sensitivity as a test for the suitability of the patient for treatment. On the other hand, Simpson and Stone² reported benefit from tuberculin in a series of nine cases, not one of which reacted positively to the cutaneous test. Again, the present writer³ found that the proportion of asthmatic cases sensitive to the intradermal test agreed closely with the result obtained in a series of normal healthy adults, and that the proportion of successes was actually greater in those patients who did not react to tuberculin. On consideration of the whole of the present series of 103 cases it is found that no fewer than fifty-seven exhibited no reaction to the Mantoux test, twenty-five gave a moderate reaction, and the result in the remaining twenty-one was strongly positive. In none of the cases in this series was there any evidence of active tuberculosis.

The results of treatment in the two groups show clearly that the original sensitiveness of the patient does not affect the response to treatment, for improvement has been found to result in forty-six out of the fifty-seven non-reactors and in thirty-one of the forty-six cases found to be tuberculin-sensitive. This result throws doubt on van Leeuwen's original premisses and leaves the rationale of the treatment obscure, but it would appear definitely to be non-specific in its action. With regard to the indications for the use of tuberculin in asthma it is impossible to lay down hard-and-fast rules. It has been found best to consider each case on its merits and carefully to assess the importance of the various factors which may contribute to the production of attacks in an individual predisposed to the condition. In all cases any local abnormality in the upper respiratory tract should be corrected as far as practicable, gastro-intestinal dysfunction should be relieved, and an attempt be made to assess the psychological state of the patient. In addition, by means of routine skin tests the presence of any sensitizing allergen in the habitual surroundings of the individual should be looked for. As well as the standard protein tests, examination of the sensitivity to dust collected from the patient's room may be carried out, and dust from the place of occupation is frequently worthy of investigation. If it be found that there is well-marked sensitiveness to a single avoidable protein, then tuberculin treatment may not be necessary; in all other cases, if the asthmatic state remains after the more elementary lines of treatment have been carried out, a course of tuberculin is a reasonable line of therapy to adopt.

It is frequently stated that the psychological effect of injections alone is sufficient to produce improvement in cases of asthma, and the proportion of asthmatics who exhibit some psychological abnormality is generally acknowledged to be high. In this series there were six patients in whom there was a marked neurotic element, and each of these is included among the complete failures; the more gross examples of this type therefore do not appear to be suitable for tuberculin treatment. In the secondary group of cases, in which there is an infection, often of long standing, in the respiratory tract, it may be preferable to adopt treatment by means of an autogenous vaccine. At times tuberculin may succeed when a vaccine has failed, and vice versa, but the results in the present

series are sufficiently satisfactory to encourage perseverance with tuberculin, which at times has been known to afford marked relief, even in severe cases. It is interesting to note that tuberculin does not appear to have any effect on the other allergic conditions so frequently present with asthma. Thus, although the chest condition may respond favourably, there is rarely coincident improvement in the commonly accompanying skin conditions. In no case of hay fever was any benefit noted, although many of the patients who responded well to treatment were also subject to this complaint.

Failure of treatment is easily recognized, and may be admitted if there is no improvement after two months. At the same time there does not appear to be any risk to the patient provided that a reasonable scheme of dosage is employed. It must be remembered that increase in the frequency and severity of attacks at any stage in the course may merely indicate that the dose is too high, and with suitable reduction unexpected success may be attained. The commonest apparent causes of failure in the present series have been overdosage, premature termination of the course, and marked psychological abnormality of the patient. Two of these causes can be to a large extent controlled, so that it would appear possible that with further experience improvement in results may be anticipated.

SUMMARY

The series of thirty-six cases of asthma treated by tuberculin described in 1930 has been followed up, and the present state of the patients is recorded. There has been a tendency to relapse, so that the present results are less encouraging than those previously reported. The cases treated subsequently, up to and including 1931, are added, bringing the total treated to 103. Dosage and indications are discussed, and it is concluded that the method yields results which, although less promising than they appeared to be at first, are still sufficiently good to warrant a trial of tuberculin in all apparently suitable cases.

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TEMPORARY VISUAL DISTURBANCE AS AN INITIAL SYMPTOM OF DIABETES MELLITUS

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Disturbances of vision in diabetes mellitus are traditionally associated with organic changes in the eyeball, giving rise to such gross and progressive lesions as those of cataract and retinitis. For a considerable time, however, it has been recognized¹ that symptoms of a temporary nature occur in this disease, which are referable to functional ocular disturbances manifesting themselves as changes in refraction. Duke-Elder² reported three cases, collected forty-five cases from the literature, and discussed the mechanism by which the symptoms arose. He was able to correlate the changes in refraction in his own and some of the collected cases with changes in the blood sugar, showing that a rise produced myopia and a fall hypermetropia. He came to the conclusion that alteration in the blood sugar level, by changing the concentration of crystalloids in the ocular fluids, induced temporary osmotic changes in the lens, with corresponding