pain across the back. Lumbago was the obvious diagnosis; but after six weeks, though easier, the pain was still there, and no line of treatment gave any permanent relief. The weeks became months, and the first year passed into the second. The final months may have been interesting—clinically; they were painful to watch, and emphasized our hopelessness to help. A noteworthy feature was that never once did she realize that she would not recover; she was continually making preparations for going home.

An x-ray film taken within four months of the onset gave no evidence of any bone alteration; true, it was not a very good film. There was no fracture of any of her bones; but in this disease the long bones are not usually invaded. She had marked uterine fibroids, which accounted for the severe menorrhagia throughout life. But this cannot be taken as a predisposing cause. What was the cause of the initial lumbar pain? Was it a coincidence—a true attack of lumbago?

In comparing the notes of this case with those taken by MacIntyre in 1845-46 the similarity of the symptoms between the two is very marked. Sex is the chief difference. Myelomatosis is said to occur more frequently in men than in women.

Bence-Jones protein is found in other conditions, but only in a few; its appearance in any urine will naturally call attention to one of them. The fact that it precipitates at between 40° and 58° C., and disappears on boiling, may escape general observation unless a careful watch is kept for it. Many urines with this unusual peculiarity may have been examined and nothing particular noted. The source of this peculiar protein is still a matter of conjecture. Ottenberg, Gies, and Rosenbloom maintain that it is an osseo-albumoid.

THE TUBERCULIN TREATMENT OF ASTHMA.

BY

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THE multiplicity of methods advocated by various authorities for the treatment of asthma is an eloquent testimony to the complexity of the problem. A method which may give complete success in some cases may be quite valueless in many others not obviously different in any essential particular, and hence it is impossible to write of a "cure" which shall be applicable with certainty even to a majority of sufferers from this complaint.

We are therefore reduced to the employment of many different methods, empirically selected, and of which in most instances the mode of action is imperfectly, if at all, understood. Of these methods, one in particular, the subcutaneous injection of increasing doses of old tuberculin, has been under critical trial in the out-patient department of the Royal Chest Hospital for a period of two years, with results which appear to be worthy of record.

The method was introduced by Professor Storm van Leeuwen as a result of his observation that a considerable number of asthmatic patients were sensitive to tuberculin as shown by the cutaneous test. There was no suggestion that the asthmatic state was the result of sensitization to the protein of the tubercle bacillus, and the beneficial results of tuberculin therapy were ascribed to a non-specific desensitization. In a paper published over a year ago, T. M. Ling¹ reported good results following upon the use of this method in a series of twenty-four children. The initial dose was 0.1 c.cm. of a 1 in 1,000,000 dilution, but the maximum dose was not stated. The results showed two "cures" and fifteen cases improved, and Ling was of opinion that the method was of definite value in the treatment of asthma.

A series of nine cases was also reported by Simpson and Stone² a year ago. They found that in four of these cases the patients derived considerable benefit from this method of treatment, and they outlined a simple scheme of dosage.

It is noteworthy also that in none of their cases did they obtain a positive skin reaction, a finding which makes the rationale of the treatment a little difficult to understand.

The cases about to be described in the present series presented themselves for treatment at the Royal Chest Hospital during 1928. Thus all have been under observation for more than one year, and several for nearly double this period.

Difficulty was at first experienced in the selection of cases, for it is notorious that some forms of asthma will derive benefit from almost any form of treatment, whereas others appear to need one particular method to bring about a similar result. The obvious explanation of this discrepancy is that many widely different factors can produce asthmatic attacks in a suitably disposed individual, and that not all cases prove responsive to the same exciting stimulus.

In many cases there would appear to be some exciting factor in the home or place of occupation. It is necessary, therefore, in order to gauge the effect of one particular line of treatment, that the patient's routine life should not be disturbed. In other cases a predominant part is played by a septic focus, situated usually in the throat or nasopharynx. It is obviously an elementary principle that such foci should be eradicated in all cases if a permanently successful result is to be obtained, and this procedure was adopted as a routine. Only such cases as did not derive appreciable benefit from this treatment were considered suitable for tuberculin. In addition, routine protein sensitivity tests were performed, with, on the whole, disappointing results; a few positive reactions were obtained, chiefly to the epidermal group, and attempts were made when possible to relieve the condition by avoiding contact with the offending substance, with, as a rule, but scant success. In these cases, also, the failures were passed on and regarded as suitable for tuberculin. No attempt was made at specific desensitization.

The patients were therefore carefully selected, and consisted only of the more severe cases in which routine methods had failed, or were unlikely to afford relief. The total number accepted for tuberculin treatment during the year was thirty-six, and it is the object of this communication to describe the results of treatment in these cases. Of these thirty-six patients, twenty were males and sixteen females; the ages varied from 5 to 49 years, and twenty-one were under 14 years of age when treatment commenced.

A preliminary intradermal test was performed in every instance, after making every effort to exclude the presence of a tuberculous lesion anywhere in the body. The routine test consists in the intradermal injection of 0.1 c.cm. of a 1 in 1,000 dilution of old tuberculin, freshly prepared, in normal saline. The reaction is at its maximum in forty-eight hours, but readings had to be taken on the subsequent out-patient afternoon, so that the interval which actually elapsed in this particular series of cases before the results were read was three days. It was considered that the delay in reading the results made only a negligible difference to the recorded size of the reactions, and they were accordingly noted in the usual manner. The essential feature of a positive intradermal tuberculin test is an area of swelling, erythema being of little significance. The results were as follows:

Negative reactions	...	...	...	...	...	24
Positive reactions	...	...	...	...	...	8
Strongly positive reactions	...	...	...	...	...	4
Total	...	...	...	...	...	36

There was a considerable preponderance of negative reactions, a result not in accord with the original observations of van Leeuwen, but nevertheless corresponding closely with the result obtained by me in a separate series of 103 apparently non-tuberculous subjects, of whom 74 were found to yield negative and 29 positive reactions. The objects of this routine preliminary test were, first, to investigate the basis on which the test was originally founded, and, secondly, to furnish an indication as to the appropriate strength of the initial subcutaneous dose. As was to be expected, modifications in technique had to be

introduced from time to time, and the method about to be described is that which appeared to be suitable for the majority of patients, although it cannot be said that a routine standard method was employed in every case.

The material for injection consists of decimal dilutions of old tuberculin contained in rubber-capped bottles, the dilutions ranging from 1 in 1,000,000 to 1 in 100. The size of the initial dose depends upon the result of the intradermal test. With very marked reactions it is advisable to commence with 0.1 c.cm. of the 1 in 1,000,000 dilution; with weaker reactions, a similar quantity of either 1 in 100,000 or 1 in 10,000 dilution, according to the degree of swelling in response to the intradermal test; while with negative reactions it is quite safe to commence with 0.1 c.cm. of the 1 in 1,000 dilution. In all cases the injections are given weekly at first, and the doses are cautiously increased, care being taken to avoid even local reactions, as it is stated that an overdose may precipitate an attack of asthma. The usual method of increase when the weaker dilutions—from 1 in 10,000 to 1 in 1,000,000—are being employed, is to follow the initial 0.1 c.cm. with 0.2, 0.4, and 0.6 c.cm., proceeding thence to 0.1 c.cm. of the dilution immediately stronger. This course is followed until the 1 in 1,000 dilution is reached, and at this stage there are usually obvious signs of improvement in favourable cases. The interval between the injections is now increased to two weeks, and the dose is increased by 0.1 c.cm. at each attendance until a maximum of 0.5 c.cm. is attained. This dose may be repeated at monthly intervals as often as necessary. It will be seen that the exact length of the course must vary with the strength of the original injection, but it must also be understood that the exact details are susceptible of considerable modification to meet individual requirements.

When the selected initial dose is 0.1 c.cm. of 1 in 1,000 dilution—that is, in those patients who are not sensitive to tuberculin—the same dose is injected weekly for six weeks, and is then increased by increments of 0.1 c.cm. to 0.5 c.cm., this dose being repeated fortnightly as long as may be necessary.

It sometimes happens that patients lose their symptoms readily under this treatment long before the highest stated dose is reached. In such cases it is not necessary to increase the dose to this extent, but the maximum dose should not be less than 0.1 c.cm. of the 1 in 1,000 dilution. On the other hand, some patients, while showing definite improvement, do not completely lose their symptoms when receiving 0.5 c.cm. of the 1 in 1,000 dilution. In these cases the dose may be cautiously increased with benefit. The maximum dose which has been given in this series is 0.4 c.cm. of the 1 in 100 dilution. This course should only be followed in cases where it is clearly indicated, as no benefit is gained, and the patients are actually not so well, when the optimum dose is exceeded. It is essential that the course of treatment should be prolonged, the minimum satisfactory period being six months.

The results of this form of treatment in the series of thirty-six cases can be classified as follows:—

(a) *Satisfactory Result.*—A period of between one and two years is much too short to enable the term "cure" to be applied. The cases included in this group have been strictly observed, and, after the first few injections, have been completely free from attacks and without any symptoms of respiratory embarrassment. The group, therefore, consists of those cases which have obtained the maximum possible benefit. Of the original thirty-six cases, no fewer than seventeen are classed in this group, all being still under observation, and this result agrees closely with van Leeuwen's observation that 50 per cent. of his cases were cured by this method.

(b) *Improvement.*—This group includes all cases in which there was a definite diminution in the number of asthmatic attacks, yet without complete relief of symptoms. In many of the cases the record was spoilt by only one or two attacks in the course of the year, and it must be remembered that all of the cases selected for treatment had previously suffered severely from the disease. Twelve cases are included in this group, making a total of twenty-nine patients who derived benefit from this course of treatment.

(c) *Failure.*—The criteria which determine inclusion here are obvious, and the remaining seven cases come under this heading. No patient was made worse by the treatment, their last state being as their first.

A glance at the accompanying table will make clear the relationship between tuberculin sensitiveness and the result obtained.

	Result.		
	Satisfactory.	Improved.	Failed.
Intradermal test:			
Positive	4	4	4
Negative... ..	13	8	3
Totals	17	12	7

It can be seen that, although the figures in each group are small, the proportion of successes is actually greater in the non-sensitive group, whereas in the cases which were sensitive to tuberculin the results are evenly spread throughout the three groups. From this it may be safely argued that sensitiveness to tuberculin plays no part in the production of the result, and that, in fact, the success of the treatment depends upon a non-specific desensitization.

In passing, it may be mentioned that the age of the patient made no difference to the result, although it was noted that in adults the relief of symptoms was sometimes delayed.

Conclusions.

Tuberculin treatment is of value in a considerable number of cases of asthma which prove resistant to other therapeutic methods. It can be used in spasmodic asthma in patients of any age, and in careful hands is without harmful effect upon the patient. To ensure success it is essential that the course should be prolonged, and, if necessary, it may be repeated. The results recorded compare very favourably with those of other and more complicated methods of treatment, and appear to justify its more general adoption, particularly in cases which do not yield readily to simple routine measures.

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MUSCLE EXTRACT IN THE TREATMENT OF ANGINA PECTORIS AND INTERMITTENT CLAUDICATION.

BY

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SUCCESSFUL results in the treatment by muscle extract of angina pectoris, particularly of the variety known as "angine d'effort" (Vaquez) or angina ambulatoria (Wenckebach) were reported some time ago by Professor J. S. Schwartzman of Odessa.¹ These results have since been confirmed in Russia and Germany. Among other observers, Fahrenkamp and Schneider of Stuttgart published gratifying results relating to the treatment of some hundred hospital heart cases with anginal syndrome. I have been trying this treatment for a few months now with very promising results, which I hope to be able to publish in full in due course. The underlying considerations on which the method of treatment of angina pectoris by means of muscle extract is based are as follows.

A peculiar phenomenon was described by Professor Schwartzman in 1927,² occurring invariably with a hypotonic heart muscle, as in infectious diseases, anaemia, cachexia, chronic pulmonary tuberculosis, starvation, heart failure, etc. If the patient is made to contract any muscle group, one notices muffling of heart sounds, shortening of the systole, diminution of intensity or even disappearance of systolic murmurs, if any; all this being the result of diminution of the amplitude of the cardiac contraction. The inhalation of amyl nitrite, injection of adrenaline, and the immersion of hands in hot water tended to abolish this phenomenon. This heart reflex was thought to bear a certain resemblance to what happens in an attack of angina pectoris, in which the coronary angiospasm might be accompanied by a muscular spasm.³