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

It has been further observed that a few preliminary muscular exercises would likewise abolish the phenomenon. The fact is known to every cardiologist that anginal pain sometimes disappears as the patient continues his effort. One such patient, who at necropsy was found to have extensive sclerosis of the coronary arteries, was accustomed to exercise vigorously "to work off the pain" when the attack began.⁴ Heberden described the most striking case of this type. Hence arises the assumption that some sort of antispastic substance is at work during the contraction of active skeletal muscle. Such substances obtained from skeletal muscle of a healthy young animal might counter-balance the spasm in angina pectoris. Their deficiency in the muscular system, on the other hand, would be an important factor in production of the anginal syndrome.

Reid (quoted from *Recent Advances in Cardiology*, by Terence East and Curtis Bain, p. 20) seems to approach this idea when he states that angina pectoris occurs when there is a failure of a depressor mechanism, which in moments of strain should lighten the load of the heart. He suggests that there are peripheral changes, which lower pressure by inhibiting the vaso-constrictor tone, so that in moments of stress in healthy individuals there is actual vaso-dilatation. In angina pectoris these mechanisms fail, and the strain on the aorta becomes too great. Such depressor mechanisms might be put into action by means of the above-mentioned antispastic substances. Since I intend to publish soon a detailed account of results obtained by me with muscle extracts in angina pectoris, I shall confine myself at the moment to the following illustrative case.

A man, aged 58, with no children and no history of venereal disease, had been suffering for six years from pain starting from the substernal region and spreading upwards towards both arms. This pain appeared on walking, and compelled the patient to stop for a couple of minutes, after which he could continue for another period. He could walk without pain for about 100 to 200 yards. Under the most favourable circumstances, including good weather, he could only walk half a mile.

On examination it was found that the heart was slightly enlarged to the left. The second aortic sound was accentuated, and the blood pressure was 170/100. The pulse was 84, and the radial artery was tortuous. On screening, the heart was shown to be enlarged, and the aorta considerably so. An electro-cardiogram (June, 1926) recorded obvious inversion of the T wave in leads 2 and 3, but the blood had a negative Wassermann reaction and the lungs were normal.

Treatment by daily injections of a muscle extract* was started on January 27th, 1930, and continued until February 17th. After the third injection improvement of sleep was noticed, and after the sixth injection the sensation of constriction around the chest became diminished. By the time that the twelfth injection had been given the patient was able to walk two and a half miles with no sensation of pain. The general condition is now much improved and he is definitely stronger, there being no discomfort on exertion, except immediately after meals. Treatment was stopped for ten days, but the improvement was maintained; it was restarted on February 27th, and is being continued twice a week. The walking ability is still two and a half miles at the patient's normal pace.

In view of the striking resemblance of angina pectoris to intermittent claudication (which is rightly termed by some angina cruris) I have felt justified in treating cases of intermittent claudication by the administration of muscle extract—a method not hitherto attempted, so far as I know. Whatever the pathological variety of this condition may be—(1) angiospastic or vasomotor (Oppenheim); (2) arterio-sclerotic (Charcot, Erb); or (3) thrombo-angiitis obliterans (Buerger)—it is the vaso-spastic factor in all three varieties which I thought might be influenced by the extract. This research is still in progress, but the encouraging results obtained so far seem to me to justify this publication.

The following are some of the cases under treatment.

CASE I.

An unmarried solicitor's clerk, aged 40, with no history of venereal disease or alcoholism, but smoking twenty cigarettes a day, complained of severe crampy pains in both legs on walking, chiefly in the thighs; these were first noticed in April, 1929. After walking a distance of forty yards the onset of the pain

compelled him to stop, but when he had rested for a minute or two the pain disappeared and he could continue walking. Restriction of smoking, rest, and medicinal treatment failed to alleviate the pain. As the result of reducing treatment he lost 2 st. in weight, but the condition was unchanged. He was admitted to Westminster Hospital under Sir James Purves-Stewart on January 28th, 1930.

On examination no abnormality was discovered in the digestive or cardio-respiratory systems. The blood pressure was 165/90. The knee-jerks were brisk, and the plantar reflexes flexor in type. The posterior tibial arteries were faintly felt on both sides, but neither dorsalis pedis artery was palpable. Movement of the right leg against resistance caused blanching of the big toe. The urine was normal and the Wassermann reaction negative. Radiographic examination of both legs revealed no arterial calcification.

Injection of muscle extract was started on January 30th, and while at the Westminster Hospital the patient had eleven injections. After the fifth he was able to walk a distance of 120 yards; with subsequent injections this was increased up to half a mile. He is now able to walk without pain; at the end of half a mile there is slight leg weariness, but no pain. His legs feel firmer, his general condition is improved, and he has resumed work. The pulse is now easily palpable in the dorsalis pedis arteries, and the blood pressure has fallen to 130/90. There is no blanching of the big toe on exercise against resistance. Treatment is still being continued three times a week.

CASE II.

A widower, aged 63, with no history of alcoholism or venereal disease, and a moderate pipe-smoker, complained of pain for about nine months and leg weariness on walking. The pain was localized to the calf muscles, and he was compelled to slow down or even to stop entirely. The distance which he could walk without pain ranged from 200 to 500 yards.

On examination the eyes and cranial nerves were found to be normal, the reflexes brisk, there was no clonus, and the plantar reflexes were flexor in type. Superficial and deep sensations were normal. The skin on the legs was bluish in colour, and the feet were rather cold. The pulse in the posterior tibial and dorsalis pedis arteries was palpable. X-ray examination revealed extensive calcification of the arteries down to the ankles. The heart was enlarged, half an inch outside the mid-clavicular line, and the second aortic sound was ringing. On screening the aortic arch was seen to present a bulging dense shadow, and the descending aorta was distinctly visible in the second oblique position. The radial artery was tortuous, and the blood pressure was 170/90. The liver was not palpable, the urine was normal, and the Wassermann reaction negative. The appetite was normal, and the bowels acted regularly.

After eight injections of muscle extract the patient noticed that the leg weariness and pain had decreased, and the legs felt stronger. After the twelfth injection the pain and tiredness had ceased. The treatment is still being continued at longer intervals.

CASE III.

A married manual worker, aged 52, with five children; there was no history of alcoholism or venereal disease; he was a moderate smoker—ten to twelve cigarettes a day; he complained of pain in the muscles of the calf, which "got hardened on walking." He had to stop for a time after proceeding for about 100 yards, and then could continue again for about the same distance. He had a sensation of cold in both legs. This condition had lasted for two years.

On examination the pupils and jerks were normal, and there was no evidence of any lesion in the nervous system; the toes, particularly on the right foot, had a bluish tint, and the pulse in the posterior tibial and dorsalis pedis arteries was not felt. Radiograms showed no calcification of the vessels, but the heart was slightly enlarged to the left; screening revealed enlargement of the aorta, both ascending and descending portions being seen to pulsate. The blood pressure was 150/80, and the Wassermann reaction was negative. The administration of iodides and bromides for more than a year had no effect.

Injection of muscle extract was started in February, but no change was registered until the eleventh injection, after which the patient began to walk better, feeling less pain and tiredness. After the sixteenth injection with an increased dose he could walk 300 yards. He was admitted to the London Jewish Hospital, and after ten more injections could walk 900 yards without inconvenience; at the end of this distance he feels pain in one leg only; he is still under treatment.

In conclusion, I wish to express my gratitude to Sir James Purves-Stewart for his interest and encouragement in this work, and for permission to carry out the treatment on his patient at the Westminster Hospital. I wish also to acknowledge my indebtedness to Dr. G. Konstam, assistant physician to the London Jewish Hospital, for permission to treat one of his patients.

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*The work is still in its experimental stage in so far as the dose, concentration, and method of preparation of the muscle extract are concerned, and the preparation has not appeared on the market yet; it is hoped that it will be obtainable in a short time.