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A Contribution to the Treatment of Pulmonary Tuberculosis with Professor Koch's Tuberculin.

SUPPLEMENTARY REPORT, SHOWING THE PRESENT CONDITION OF TWENTY-FIVE CASES TREATED TWO YEARS AGO, READ BEFORE THE AMERICAN CLIMATOLOGICAL SOCIETY, MAY 26, 1893.

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REPORTS of cases showing the results of any particular procedure in therapeutics, made immediately or within a short time after their application, are current in medical literature, and while they unquestionably throw light upon the utility or otherwise of the treatment employed, it is not to be doubted that many such reports would require modification, indeed, might show the reverse of the conclusions first arrived at, if a longer time had intervened by which the permanency of the results or the final issue of the case could have been established.

We are the more ready with our reports if our work has apparently been successful and if the medical or surgical procedure is new and is attracting attention at the time; but if hasty reports and conclusions have ever been offered, it certainly was the case with the effects of Professor Koch's tuberculin. Indeed, in many instances a few weeks of experimental employment of the remedy was deemed sufficient for enthusiastic recommendation or for absolute condemnation.



It is now two years since I wrote a report of my first twenty-five cases treated with Koch's tuberculin, which report was presented to the American Medical Association at Washington on May 7, 1891, and subsequently published in the THERAPEUTIC GAZETTE for June 15 of the same year. In making the report it was my earnest endeavor to be conservative, and I purposely published with it the detailed history and all important data in connection with the treatment of each case, so that the reader might be able to judge for himself the benefit each patient had derived.

The cases were divided into three classes :

Class A, five cases who had one or both upper lobes involved, but without destructive changes, the general health of the patient being still comparatively good.

Class B, seven cases with more extensive disease or moderate destructive processes, but still in a fair physical condition.

Class C, thirteen cases still further advanced in local disease, with considerable constitutional impairment, but still in a condition justifying some hope for improvement.

I concluded that report with the following remarks :

“*First.*—That, according to my experience with the patient under constant medical supervision, and under the precautions used, the remedy CAN be given with the avoidance of all unpleasant symptoms or danger.

“*Second.*—That while I believe that I have derived material benefit, the experience of many additional observers, under a *similar mode of management and administration to that adopted by myself*, is required to establish the exact

value and range of applicability of the remedy ; and,

“*Third.*—That the combined means by which my results were obtained appear to deserve the favorable consideration of the profession.”

It is now my purpose to show the outcome of these twenty-five cases two years later, as a supplement to my first report, with such explanatory remarks as may be essential for each individual case. To this end careful inquiry has been made as to the present condition of each patient.

Case I., Class C, was reported as slightly improved when the treatment was discontinued on March 11, 1891.

This patient showed further improvement after the discontinuance of the remedy, and remained in the institution for fifteen months thereafter. Under a course of Liebreich's cantharadin, the larynx made remarkable improvement, the ulceration of the epiglottis healed, and the infiltration disappeared almost entirely, and sufficiently so as to result in the complete restoration of the voice ; her nutrition also improved. In March, 1892, active changes again recurred in the lungs, which were accompanied by the usual symptoms of fever, increased cough and expectoration, and loss of flesh. The larynx remained unaffected. All these symptoms subsided under a second course of tuberculin, thirteen injections, from one-tenth to one milligramme, and the patient left the institution in May greatly improved.

At this writing a relapse of her lung-affection of recent date has come to my knowledge.

Case II., W. S., Class B, was reported as apparently cured. This patient has remained well to this date, and is entirely free from all symptoms. In April, 1892, he had an attack of la grippe, with an intense bronchitis of one week's duration, from which he made a prompt and perfect recovery.

An affection of the respiratory organs like la grippe may be looked upon as a crucial test of the permanency of recovery, and the frequency with which we note active symptoms to supervene in latent tuberculosis in connection with la grippe is well known to every practitioner.

The sputum during the existence of the acute bronchitis in connection with la grippe contained no bacilli.

Case III., Class A, reported as improved, has made an entire recovery, and has remained free from all symptoms to this date.

Case IV., Class C., was reported as improved and the laryngeal disease cured. This patient made still further improvement, returned home, relapsed as to his lung-affection, and died in July, 1892. The result as to the larynx was permanent until death.

Case V., Class C, reported as not improved, died in 1891.

Case VI., Class C, reported as not improved, died in 1891.

Case VII., Class A., reported as cured, has continued free from all symptoms, and is entirely well at the present time.

Case VIII., Class B, reported as apparently recovered, returned home; relapsed in fall of 1891; returned, and was treated again with tuberculin in the winter of 1891-92. He was

again materially improved, but not to the degree as in the first course of treatment. He is free from fever, but coughs and expectorates. His general health is fair. He is still greatly improved as compared with his condition before his first treatment.

Case IX., Class A, was reported as apparently cured. He has remained entirely free from all symptoms to the present time, and is enjoying perfect health.

Case X., Class B, reported as greatly improved, returned home in May, 1891. His improvement has not only continued to the present time, but I have recently been informed of his entire recovery.

Case XI., Class B, reported as apparently recovered, has been free from all symptoms to the present time, and is entirely well.

Case XII., Class C, reported as improved, relapsed, and died in 1891.

Case XIII., Class C, reported as improved, relapsed in 1892, and died since.

Case XIV., Class C, reported as greatly improved. No recent report obtainable. He continued in his improvement to the date when last heard from,—October, 1892.

Case XV., Class C, reported as greatly improved, died in 1891.

Case XVI., Class A., reported as apparently recovered, has remained entirely free from all symptoms, and is perfectly well to the present time.

Case XVII., Class C., reported as improved, continued so when last heard from in November, 1892. No response to my recent inquiry.

Case XVIII., Class C, reported as greatly

improved, continued so when last heard from. No recent report obtainable.

Case XIX., Class C, reported as improved, relapsed, and died in 1891.

Case XX., Class B, reported greatly improved, according to recent information has entirely recovered without resorting to further treatment.

Case XXI., Class C., reported as improved, is about the same at the present time.

Case XXII., Class B, reported as improved, has entirely recovered.

Case XXIII., Class B, reported as apparently recovered, has continued in good health, free from all symptoms, to the present time.

Case XXIV., Class A, reported as greatly improved, has entirely recovered, and is free from all symptoms.

Case XXV., Class C, reported as improved, obtained still further improvement. He subsequently relapsed, but improved again, and is now free from all active symptoms.

We find, therefore, that I reported in 1891, in the early stage, five cases treated, three of which were believed to have apparently recovered, one to have been greatly improved, and one to have been improved; all of which have made an ultimate recovery, no relapse having occurred in two years.

In the more advanced stage—Class B—I reported seven cases treated, four of which were thought to have apparently recovered, two to be greatly improved, and one improved. Of these seven cases we find six to have made a final recovery and to be well two years later, while one relapsed and is again improved.

This gives us for the early stage one hundred

per cent. of recoveries, and for the middle stage eighty-six per cent. of recoveries and fourteen per cent. of improvements, without a death in two years.

In the far-advanced stage of Class C, I reported thirteen cases treated, four of which were greatly, six moderately, and one slightly improved; two had made no improvement. Of these cases, six are still alive, three of which have continued greatly improved and three others improved, while seven have died.

As to the share attributable to the treatment with tuberculin in obtaining these results, I am still and always shall be unable to mathematically demonstrate it. Every thoughtful reader who is free from prejudice must, however, admit that these results are such as have never been obtained by any mode or combination of treatment heretofore known.

In a paper upon the prognosis in pulmonary tuberculosis, published in the *Medical News*, September 13, 1890, I reported eighty-one early-stage cases corresponding to Class A, of which a subsequent inquiry, similar to the present one, showed twenty-four per cent. of recoveries and twenty-one per cent. of improvements. In a more advanced stage, of four hundred and thirty-four cases treated, nine per cent. recovered and eleven per cent. were improved. While a similarly large number of my cases treated with tuberculin might have shown the present results modified, yet it cannot be conceived that such a difference as this would be possible.

That it does not exist is, however, amply proven by my subsequent experience with a greatly increased number of cases treated since

paired during the course and advance of the disease.

Such application of the remedy had never been contemplated by Professor Koch, and all for which I blame him is that he permitted it in the hospitals of Berlin, and became aware of it through the literature of the profession elsewhere without entering his protest.

Remembering, however, that he is not a practising physician, that all treatment of cases was carried out by his colleagues, and that he himself possesses no recent clinical experience in the treatment of consumption or any other disease, it must at this time seem strange that no one for some time dared to depart from the original dosage based upon experience with half a dozen cases only, two of which were then said to have apparently recovered.

With the greatest admiration for Dr. Koch and his labors, this appeared to me ludicrous, nevertheless, and when I mentioned my convictions to one of the hospital chiefs in Berlin, he reproved me as though I had committed the "unpardonable sin." "Would you instruct the master?" said he, in utter astonishment.

All those who, after their first disappointment, did not throw the remedy overboard, have since, at least in part, adopted my method of administration, and I believe that I have been the first one on either side of the water to enter a protest against its use as originally employed. Since that time excellent results have been obtained from minute and slowly-increasing doses, some of which I cited in a paper published in the *Southern Medical Record* for September, 1891, and my results have continued

as favorable as ever under this method adopted by me within the first few weeks of its use.

The most recent report of Dr. Thorner, in Berlin, presented to the "Verein für Innere Medizin" on March 8, on his two years' use of Professor Koch's tuberculin, and which is highly favorable to the remedy, shows that he begins with $\frac{1}{20}$ milligramme, and increases about as I do. Under such doses he never saw any unfavorable effect. He emphasizes that the secret in its successful employment is the proper application of the remedy. My method of application is practically as follows:

Cases must be properly selected, and no patient is suitable for treatment with tuberculin who at the time presents symptoms of acute inflammatory changes in tubercular areas or evidences of softening, with septic fever.

Other modes of treatment, as indicated in my paper on the treatment of pulmonary tuberculosis (*Times and Register*, January 6, 1893), must be resorted to, by which these symptoms are first controlled. With these exceptions, patients in any stage where the disease is still confined to the lungs and throat are eligible to the treatment.

The treatment should be carried out in a special institution or hospital, where sufficient control and oversight alone are possible. It certainly must not be delegated to junior assistants or to physicians who do not possess large experience in physical diagnosis of chest- and throat-affections, or who are not otherwise well experienced in the treatment and management of cases of pulmonary and laryngeal tuberculosis. Close observation is indispensable.

A week's observation of local and general

symptoms, fully recorded at frequent intervals, must precede the use of the remedy, to assure the absence of contraindications.

A physical examination of the chest must precede and follow each dose given, the results of which, to the minutest changes observed, to be carefully recorded upon a diagram for comparison.

The difference between a local and general reaction must be clearly understood. The former consists in an increase of the local auscultatory phenomena, with or without slight increase in cough or a sensation of fulness in the tubercular area of the lung. In the larynx or other visible tubercular processes there are observable increased vascularity, sometimes slight swelling, and always increase of the secretions from that part.

Any effect beyond this is undesirable, and can be positively avoided if enough interest is taken in watching the case.

A general reaction, on the other hand, shows, in addition to the local effect, rise of temperature, increase in pulse-rate, sometimes nausea, even vomiting and diarrhœa. Those symptoms, if well marked, are signs of positive danger, and repetition of the same dose, or an increase of the dose, is almost sure to be followed by relapse.

No dose must be repeated until the effect from the previous dose has subsided, and then not until after twenty-four hours.

If the local reaction has been well marked or prolonged, a return to the dose which had previously been inoperative is required, and the increase must thereafter be the same as it would have been had a larger dose never been

given. The same is of course equally true if general symptoms have been produced.

The reaction occurs, as a rule, in from six to eight hours. I have, however, seen it as early as three hours and as late as thirty-one hours after a given dose; this must be borne in mind, and frequent examinations, especially in the beginning of the treatment, are necessary, so that the effect may be recognized. The duration of the reaction is, as a rule, about six hours, if only local; if general, it may last twelve hours and longer. I have found that the same patient reacts, as a rule, within about the same limit of time.

A certain dose having been given without reaction following, this same dose is, nevertheless, to be repeated once before an increase is permissible.

If a too severe local or general reaction is observed, the patient must be put to bed and kept perfectly at rest until the reaction has entirely subsided.

Beginning with $\frac{1}{20}$ milligramme as a trial dose,—to which I have never seen a response,—the next dose is $\frac{1}{10}$ milligramme, and the increase is thereafter $\frac{1}{10}$ until 1 milligramme is reached; then I increase $\frac{1}{5}$ milligramme at a time until 2 milligrammes are reached. After that dose the increase is $\frac{1}{2}$ milligramme up to 10; from 10 to 20 milligrammes I increase $2\frac{1}{2}$ milligrammes, and thereafter 5 milligrammes, at a time.

Periods will be observed when for weeks together no local or general reaction is observed, while the subjective and objective improvement of the patient progresses favorably; and whenever a point has been reached where this

improvement is radical and active symptoms have entirely subsided, this is the time to stop the use of the remedy, allowing an intermission of from two weeks to a month. If no relapse has occurred in this time, if everything is highly satisfactory, and the recovery is apparent, we keep the patient under observation as long as possible, otherwise a repetition of the treatment is of course necessary.

In the second course we begin again with $\frac{1}{10}$ milligramme, but increase after each dose so long as no local reaction is produced.

My results have been obtained upon this plan; and while other plans may also be safe and accomplish good results, and while some one may devise even a better plan, until better results than mine are shown by others, no change from my method is, in my judgment, permissible.

I have thus treated over one hundred patients with between six and seven thousand injections, and, with the exception of my first week or two of experimental use, I have never produced any effect which has in any way been detrimental, nor has there been one single case in which the treatment has caused discomfort. I have not found any advantage from Hunter's modification, and am of the opinion that it is in no wise safe to increase it faster than the original tuberculin.

He who cannot have his patients under close and constant observation, or who gives the remedy with less care, simply takes chances, and if no disaster follows it is good luck, nothing more.

As shown in the earlier part of this paper, I have one hundred per cent. of recoveries in

the early stage ; in the second stage, recovery has resulted in eighty-six per cent. and radical improvement in fourteen per cent. ; in the last stage, marked improvement in forty-six per cent. ; and these results have lasted over two years. In the cases treated since, the results are equally good, and in the advanced cases promise to be slightly better still.

It is true I have had the advantage of an excellent climate. I have also made use of every other available means at my command whenever I believed that they could aid the patient's improvement. I have exercised the greatest vigilance in the use of the remedy, and have never allowed myself to take any chances, nor have I taken things for granted when I could satisfy myself by painstaking examination and inquiry, and the patients were all treated in my institution and under my constant care. The special treatment has not been delegated to assistants, but was carried out by myself, without sparing time and labor ; but, with all this, it is also true that I have been equally careful and interested with patients who were treated in the institution before the advent of tuberculin, and with those who, during the two years past, did not receive tuberculin for reasons stated before, and the results, as compared with those in connection with tuberculin, offer no chance for comparison.

In my previous writings on tuberculin I have been exceedingly careful not to commit myself too far. I am now ready to stand by the remedy, not in recommending it as a cure-all, or under all conditions and manifestations of the disease, but certainly as a remedy of the greatest value when used as indicated in this paper.

With me now it is no longer on trial as an experiment. On the contrary, I find its effects as reliable and as uniform as I could hope them to be under the great variety of individual conditions, such as constitution, stage of the disease, organs involved, and complications present.

If my precautions and methods in the use of tuberculin are really essential for good results, as I have found them to be, and which riper experience of two years or more of other observers seems to confirm, we must not blame the remedy if it failed to come up to our expectations under its erroneous use in unsuitable cases and in excessive and highly-dangerous doses. We should the less criticise it when the results were unsatisfactory in the hands of men with little experience in close physical diagnosis and in the management of the disease, some of whom dealt out their doses at their office hours without again seeing their patient until he came for his next dose, or until the physician was summoned to find how ill an overdose had made his patient.

Such experience was perhaps necessary to confine the use of the remedy to safe hands and to teach us the care and circumspection which are essential in its employment.