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Inoculations with Professor Koch's "Tuberculin"

BY

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LATE PRESIDENT OF THE NEW YORK ACADEMY OF MEDICINE, CLINICAL PROFESSOR IN THE COLLEGE OF PHYSICIANS AND SURGEONS, ETC.

Reprinted from the MEDICAL RECORD, *February* 28 *and March* 7, 1891

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INOCULATIONS WITH PROFESSOR KOCH'S "TUBERCULIN."[1]

INOCULATIONS were commenced by me December 10th in the Mount Sinai Hospital, on the very day when Dr. Kinnicutt made his first injections in St. Luke's. On the following day I began in the German, two days after, at the suggestion of Dr. Reid, attending physician, in the Foundling Hospital. At a later period a case of epithelioma was observed, and inoculated for a while in the Skin and Cancer Hospital. The majority of the cases in the Mount Sinai Hospital belonged to the service of Dr. I. N. Heinemann, attending physician, a number were also furnished by the other physicians and surgeons of the institution, and some of the most interesting material by Dr. Goldenberg. To Dr. Heinemann belongs the credit of having spent a great deal of time and labor on the numerous cases gathered in that institution, while I attended the other places. He will appear before you with the reports of what he has observed and accomplished. The cases which form the basis of my report number about sixty, fifty of which were observed in the German Hospital and are carefully tabulated. They comprise nearly all the varieties of tuberculosis, that of meninges, lungs, glands, bones, peritoneum, joints, every one of which was carefully watched by a most competent house-staff and painstaking nurses both day and night, and temperatures taken, with rare exceptions in rectum or vagina, almost in

[1] Read before the Medical Society of the State of New York, February 4, 1891.

every case every two or three hours for weeks in succession. I may be permitted to add a single remark, viz., that from the beginning I have tried to be as unbiassed in my observations and experiments as would be permitted by the overpowering sense of the influence of a scientific discovery of extraordinary weight and importance.

The effects claimed by Robert Koch for his "Tuberculin" are as follows:

Its action on tubercular processes of whatever nature, is specific. It is either general or local. Reaction in internal organs cannot always be proven, because it is not amenable to direct observation, with the exception of increased cough and expectoration; here the general reaction predominates. There are local changes in the visible tubercular processes. An injection of 1 ctgr. always has that effect. Therefore, the lymph is an indispensable means of diagnosis. When the diagnosis of tuberculosis cannot be obtained by the finding of bacilli or elastic fibres in the sputa, tuberculosis can with safety still be diagnosticated by the presence of the reaction. In the same way doubtful cases of glandular, osseous, and cutaneous disease can be recognized.

The action of the lymph on the tissue surrounding the bacillus is marked. It produces changes resulting in necrosis of that tissue without destroying the bacilli. In the beginning small doses are sufficient, afterward larger ones are required. When a tuberculous patient requires as large doses as a healthy person, at the same time exhibiting as little reaction as the latter, it is to be presumed that all the tuberculous tissue amenable to reaction has been destroyed.

Phthisical patients in the first—incipient—stage were relieved of all morbid symptoms in from four to six weeks, so that they could be considered as cured.

Patients with cavities of moderate size were much improved and almost cured. Thus it is to be presumed that incipient phthisis can certainly be cured through this rem-

edy. Relapses are possible, for the time of observation has been too short. Still it is fair to presume that relapses will be removed as quickly as the first attack.

The general reaction means increase in temperature. It seldom appeared after an hour or two, generally after from four to nine hours, reached its maximum mostly about the ninth or twelfth hour, and diminished gradually. Sometimes after it had commenced to sink it had another rise, as you will remember to have seen in many of your cases of typhoid fever, where a double curve is not unusual. In a number of my children the temperature rise was not marked. Proportionately large doses were required. There is a parallel, perhaps, with what we notice in other circumstances. For instance, cardiac stimulants require larger doses, comparatively, in children, and in them also the effect of the typhoid infection is less marked. Both the typhoid virus and the Koch virus are ptomaïnes. Still this is but a suggestion.

The general reaction was noticed in many cases after doses of 1 or 2 milligr. That effect was not obtained when, after a brief time, ten or twenty times as much was injected.

The increase of temperature would often correspond with pulse and respiration; sometimes these two would not, or not much, be affected. The general condition of the patient would mostly be altered with the change of temperature, but not always in the same proportion. Sometimes there was comfort with high temperature, sometimes great discomfort, languor, muscular pain; once a localized pain in a distant organ (the left arm) when the right elbow was affected, rigor, perspiration, with a moderate temperature; in one case (with no rise of temperature) there ensued very great dyspnœa, angina pectoris, fear of annihilation, which required active medicinal interference.

Instead of rising after the inoculations, the temperature may fall, but the patient's comfort may increase. At the

same time, with a low temperature, and feeling comfortable, he may improve, or not improve, or get worse. The temperature may also fall, but the patient, while getting worse, may also feel worse.

In cases of non-tubercular lungs (suspicious or not) the temperature may rise, or no. In those of tubercular lungs I have seen inoculation raise the temperature, not influence the temperature, and reduce the temperature. The changes in the lungs were not uniform. The usual results of an inoculation were diffuse rhonchi, sometimes dyspnœa, and increased expectoration, which became more mucous, and was a few times tinged with blood. Thus it happened that in one case the number of râles and of indurated areas increased in number and extent; sometimes with dangerous, either temporary or persistent results. Sometimes this effect remained more or less stationary, sometimes it wore off in a day or two. In other cases there were no direct local changes, and still there was an improvement of both subjective and objective symptoms. The absence of bacilli in the sputum does not speak against the tubercular nature of the case as long as the time of observation is but a few weeks.

Respiration was often accelerated and superficial, but seldom more than in its due proportion to the increase of temperature. Anorexia and nausea were frequent, vomiting not uncommon. Jaundice I have not seen, with the exception of a very slight touch in a single case; a few times I met with small quantities of albumin in the urine, mainly during high temperatures.

In a small number of cases, mainly such as had a high temperature, the spleen would swell and sometimes be painful, on the second day or later. Another symptom of ptomaïne infection was the peculiar appearance of the tongue, accumulations of epithelium in the middle, elevation and redness of papillæ, intense raspberry or scarlet redness of the edges.

Local reaction was sometimes observed round the site of injection; in many cases there was no pain, in others

there was. In a minority there was some local redness, in a few some swelling, a day after the inoculation. The eruption was in one case of the size of a hand. A general eruption I have seen but once, when, three days after the first inoculation was made (this time of 1½ milligr.), almost the whole body of the child was covered with a papular rash; afterward 10 milligr. were injected without any such result. Another form of local reaction is that observed near the tubercular locality. It consists in local congestion, redness, swelling, sensibility of the affected parts, be it lupus, gland, sinus, or bone; or such changes in the pulmonary tissue as have been alluded to. It must be said, though, that this may also take place in tissues not affected by tuberculosis.

For the purpose of diagnosis lymph was injected into Louisa K— , aged twenty. She was admitted November 14th, with the diagnosis of peritonitis, probably carcinomatous. There being a strong doubt expressed because of the youth of the patient and for other reasons, lymph was injected on four successive days—2 milligr., 4 milligr., 5 milligr., 5 milligr. No reaction. The larger number of such administrations in tuberculosis proving successful in producing a reaction, the diagnosis of carcinoma was considered justified.

Maria T— , aged twenty, admitted January 17th. Had a cough since last summer with moderate expectoration. sometimes with a little blood, and some dyspnœa. Ten days ago a chill, pain in her throat; stopped work four days ago; has a "cold," coughs considerably, bled from the nose once. Had no fever when admitted. Over right upper lobe anteriorly, dulness and coarse respiration, some bronchophony. Posteriorly, prolonged respiration. Bacilli not found. On three successive days, 2, 4, and 6 milligr. were injected without any effect. Meanwhile she improved while in bed. The physical lung symptoms are probably due to the results of an interstitial pneumonia in early life.

Lena K——, aged nineteen, admitted December 31st, with symptoms of gastritis, and coarse respiration, with moderate dulness over right upper lobe both anteriorly and posteriorly. No response to 2 milligr. Probably the same conditions as in the previous case.

Kate S——, aged twenty-three, admitted November 22d, with fibrinous pneumonia and pleuritis of the left side. When, about the middle of December, resolution was not complete, dulness and some cough, also rhonchi, persisting, the suspicion of the presence of tuberculosis induced me to use the lymph. Very soon bacilli were found. From December 16th to 23d she received five injections of from 1 to 4 milligr. Reactions were quite marked, and she felt badly. Therefore the treatment was interrupted ten days, and resumed with occasional doses of 5 or 6 milligr. Since January 22d she is on daily doses of 3 milligr., during which she had less fever than before and feels better. Still the physical examination of her left lung and pleura is unsatisfactory; particularly as when there was a considerable reaction the whole chest was full of crepitant, subcrepitant, and sibilant râles. Indeed, she is one of the cases which appear to respond so thoroughly, locally, that the fear is justified that the congestion of the pulmonary tissue resulting from the injection may prove dangerous.

Max H——, aged four, admitted January 18, 1891; service of Dr. Kammerer. Scrofulous dermatitis of face. About the ascending ramus of maxilla, left side, the skin is red, indurated, and partly ulcerating and proliferating. Internal organs healthy. For the purpose of diagnosis some inoculations were made, twice of ½ milligr., once of 1, and once of 2 milligr. The latter dose raised the temperature to 102.6° F. within twelve hours, but there was no local reaction, and the inoculations were discontinued.

Conrad S——, aged forty-six, admitted November 11th. Tumor in larynx and ulcerations. Dulness over right lung, rhonchi, no bacilli found in repeated examina-

tions. Deglutition and articulation difficult. Had chancre twenty-eight years ago. Iodide of potassium and inunctions proving rather inefficient, he was given the benefit of the doubt, and three injections were made on January 16th, 17th, and 18th, of 2, 5, and 7 milligr. As no reaction became visible, the anti-syphilitic treatment was resumed.

Ernst S——, aged forty-two, admitted January 2, 1891, with temperature 101.1° F., has a small ulceration on the right side of epiglottis, with some surrounding infiltration. One cervical gland. The diagnosis of syphilis very probable, but as there was a dull area over the right apex, he was given the benefit of the doubt. Injections were made

January 2d. Two milligr. After six hours temperature fell to 99.5° F.

January 4th. Four milligr. No reaction, except, perhaps, the temperature of 101° F., which he had before, thus the anti-syphilitic treatment was commenced in earnest.

P——, grocery boy, aged fifteen, admitted January 12th, to Dr. Kremer's service. Dermatitis genu chronica. Scrofula in childhood. Popliteal gland removed six months ago. Since an indurated area in the popliteal region six inches in length. Internal organs negative. For the purposes of diagnosis four inoculations were made on January 13th, 16th, 17th, and 18th, of 1, 2, 4, and 6 milligr., without any reaction. The probability was that the dermatitis is not tuberculous, a piece of the skin was then removed for examination, and no bacilli found.

Caroline L——, domestic, aged thirty-six. Had the last of several pneumonias in February, 1889, frequent attacks of dyspnœa and catarrh since, and moderate cough. Some phthisis in the family. On December 21st, beside a number of gastric symptoms of which she complained, she had extensive dulness and diminished respiration on the right side, the seat of her last pleuro-pneumonia.

One milligramme of lymph was injected at noon, December 20th. Pulse rose from 90 to 100 at 2 P.M.; tem-

perature from 98.6° to 100° F., at 8 P.M. It remained at from 100° to 101.2° F., until next noon, when 2 milligr.. were injected. It did not influence the temperature, which remained about the same (100° to 101.2° F.) until noon December 22d. The first two nights, however, she coughed more than usual, had dyspnœa, palpitation, and perspiration, also dizziness and headache. She expressed the same complaints the following days, lymph or no lymph, while her average temperature was less. Only once, on December 23d, it rose to 100.4° F., also on December 24th, at 5 P.M. Then 3 milligr. were injected at 7 P.M. Ten hours afterward, at 5 A.M., December 25th, temperature 98.6° F., at 8 A.M., 101°, the highest temperature of the day except 101.4° F., at 8 P.M. Temperatures up to 101° F. were observed on December 26th; 100.8° F., also at 8 A.M., December 27th. After that time until January 5th, when she left the hospital, the temperature was normal, though she complained of alleged chills, headaches, back-aches, stomach-aches. After all we can say that as the lymph had a negative result, both generally and locally, the changes in the lungs were not likely to have assumed a tubercular character—provided that the majority of lymph results are of the diagnostic importance attributed to them by Robert Koch.

A. W——, aged fifty-six, musician, admitted December 20th. Complained these three months. Has anorexia, ascites, icteric complexion, is feeble. Urine scanty. No history of alcoholism. On examination: Temperature, 99.8° F.; pulse, 120, very feeble. Urine with trace of albumin. Heart negative. Over left lung, superiorly, dulness and coarse breathing. Ascites with but moderate sensitiveness. Iodide of potassium, 2 gm. daily. Paracentesis with permanent drainage; 2,000 gm. on December 25th, 3,000 on the 26th, and 500 on the 29th. On the last two days the fluid was less clear, and contained blood and pus-cells. He was gradually sinking; no good, no harm could be done. One milligr. of Koch's lymph was injected December 31st, at 7.50 P.M., while

his rectal temperature was 97.5° F. No reaction of any kind; he continued to sink until January 1st, when he died at noon. No autopsy permitted.

Betty S——, aged thirty, admitted November 22, 1890, six weeks after her sixth confinement, for general debility, dyspnœa, abdominal and dorsal pain, leucorrhœa, pelvic symptoms. Uterus large and catarrhal. Dulness over right lung, anteriorly, and coarse and prolonged expiration. For the purpose of diagnosis 1 milligr. of lymph was injected December 28th, with no increase of temperature, but marked perspiration. On the evening of January 14th, 2 milligr. were injected, temperature being as always, 98.6° F. Within seven hours, at 2 A.M., it rose to 100.6° F., and had commenced to fall at 5 A.M., when it was 99.6° F. Left the hospital.

Robert N——, aged forty-four, working man, admitted November 29, 1890. Complained of his stomach these fourteen years. For three weeks vomiting, mucous expectoration, and cough. Had chills and pleuritic pain, and lost flesh. Has some dulness over upper lobe, superiorly, and sibilant and mucous râles during inspiration and expiration. No pus, no bacilli. Had temperatures in the first ten days, on December 8th, 103° F., but only once, after that temperature, mostly normal, some few times 101.2° F. On the afternoon of December 16th temperature rose once to 102.8° F., and again on the 17th. For the purpose of diagnosis, 1 milligr. of lymph was injected on the evening of the 17th. For twenty-four hours subsequently the temperature changed between 101.2° and 102.5° F., then it rose to 103.2° and 104.2° F., about twenty-four hours after the inoculation. There were more rhonchi, this time over the whole chest; more dyspnœa. Death occurred on the 19th. No autopsy permitted; perhaps the question might have been settled whether through our congesting and softening the tissue which surrounded the nests of bacilli we hastened the man's death. For though no bacilli were found, I have no doubt it was a case of tuberculosis.

Rosa J——, aged thirteen, had undergone an operation for swollen cervical glands on the right side. Left in September apparently in good health. Admitted December 31st, because of general indisposition and fever. At the upper end of the cicatrix a glandular swelling. Over the right upper lobe diminished respiration behind, and some dulness both anteriorly and posteriorly. A few days in bed restored her temperature almost to the normal. After the evening of January 4th the temperature never rose. For the sake of diagnosis lymph was injected. One milligr. on the morning of the 3d; 2 milligr. on the evening of the 4th; 5 milligr. on the evening of the 6th; 10 milligr. on the evening of the 7th; with not a trace of response. Inoculation was stopped. We also learned from Dr. Kammerer, who performed the operation in July, that the glands he removed were not considered tuberculous. This case would then be conclusive of the motto: "No tuberculosis, no reaction."

A number of cases of external ("surgical") tuberculosis, with two of epithelioma which were introduced as probable cases of lupus, are as follows:

A boy, aged four, with tuberculosis of right knee, tubercular glands of neck, and infiltration of right apex; also an abscess of the right thigh in which bacilli were found. Inoculations were made, twelve in number, ranging from one-half to ten milligrammes. There was some slight response to the first, induced rather more by the first small injections than by the later ones, which were large. No correspondence between such response as was elicited by the lymph in the beginning and the pulse and respiration. This correspondence was more distinct on the last two days of the observation when no inoculations were made; but then the fever was considered the result rather of the suppurating thigh than of the lymph. The final dose of 10 milligr. was rather a large one, but no reaction distinctly attributable to it made its appearance. No change.

Harry C——, aged five years eight months, with tu-

bercular abscess (bacilli found) in right inguinal region, presumably from lesions of lumbar vertebræ. Examination of viscera negative. The first inoculation of half a milligramme resulted in a distinct reaction, which showed itself in a rise of temperature and of respiration, not of the pulse. Afterward the reactions were but trifling, or negative, even with a dose of 10 milligr. No improvement.

E——, aged four years eleven months, tubercular disease of left hip; discharging sinus. Examination of viscera negative. Fourteen inoculations between December 13th and January 3d, from one-half to ten milligrammes. The first small inoculations resulted in positive reactions, the temperature rising to nearly 104°F.; the last large ones in none, or none attributable to the remedy. No improvement.

W. C——, aged four years nine months; dorsal spondylitis; kyphosis. Lungs negative. No bacilli were found, and therefore no tuberculosis could be proven. There was, however, a pretty smart double reaction after the first injection of half a milligramme. Very little reaction took place after the subsequent doses, from one to ten milligrammes. Cervical glands became tumefied. Induration and moderate redness of the injection site appeared a day after inoculation in this and the preceding three cases. Reaction, such as it was, took place in from four to fourteen hours. The pulse was more influenced than respiration.

I. T——, aged four years and a half. Cold abscess, probably from right sacro-iliac synchondrosis. Heart and lungs normal. Operations on September 26th and October 13th. Afterward the general condition good. No temperatures. Wound almost healed on December 1st, but his condition remaining stationary for some time, ten inoculations were made between December 13th and 30th, gradually rising from 1 to 5 milligr. On January 1st the examination of the boy showed condition generally good, the wound, however, but slightly improved.

The first injection of 1 milligr. showed the most marked results; reactions occurred in from ten to twenty-two hours, and grew less and less unless the doses were increased.[1]

Auguste M——, aged three. Tuberculosis of left tibio-tarsal articulation. Removal of sequestrum, etc., in September, after that temperature normal, moderate suppuration of fistula, swelling of inguinal glands.

December 11th, one milligr. at 4.45 P.M. After midnight temperature 102°, 102.5°, 102.8° F. As the temperature was still high on the twelfth, I injected only three-fourths milligr. Temperature rose in a few hours to 103.5° F., child somnolent, perspiring. Perspiration continued all night, though temperature was gradually falling.

On December 13th temperature only 100.8° F., less suppuration, no pain. Injected 1½ milligr.

December 14th. Child feels well, suppuration trifling. Temperature, 101.2° F.

December 15th. Injected 1 milligr. Sinus is closing.

December 16th. Injected 2 milligr. Perspiration; rhinitis.

December 18th. Injected 3 milligr. No symptoms.

December 20th. Injected 3 milligr. Temperature rose to 103.8° F., and remained above the normal all next day.

December 22d. Injected 4 milligr. Temperature, 101.4° F.

On December 24th, 26th, 28th, 30th, and January 2d, injections of 5 milligr. each, with but slight elevation of temperature and improvement in the local symptoms. Within a week after the doses were increased, with but slight increase of temperature, until on January 13th and 16th 10, and on the 17th 15 milligr. were injected without a rise of temperature. Four days afterward the child had a temperature of 101° F., a flushed face and a rapid pulse, without any assignable cause, unless it be a retarded

[1] A detailed account of these five cases will be published in the Archives of Pediatrics, March, 1891.

effect of the inoculation. On January 27th the fistula greatly improved, not so deep as before, and with less secretion, still not entirely closed. The child in a fair condition.

Elise W— , aged eleven. Cutaneous tuberculosis, admitted December 18th. Family is tuberculous. Child had eczema. Underwent an operation at elbow-joint five years ago. Has an ulceration of the size of a silver dollar on the right side of neck, also one two inches long on chest; lungs normal. Inoculations the only treatment.

December 18th. Injection of 1 milligr. Highest temperature, 101.2° F. Itching on ulcerations.

December 20th. Injection of 1 milligr. 101.2° F.

December 21st. Injection of 1 milligr. Temperature normal.

December 22d. Injection of 2 milligr. Highest temperature, 102.3° F. Epistaxis and headache.

December 25th. Injection of 3 milligr. Temperature, 102.8° F.

December 26th. Injection of 3 milligr. No reaction.

December 27th. Injection of 3 milligr. Highest temperature, 102.6° F. Epistaxis, headache, palpitation.

December 29th. Injection of 5 milligr. Temperature, 100.6° F. Mild collapse. Subcutaneous injection of camphor.

December 31st. Injection of 6 milligr. No reaction.

January 3d. Injection of 6 milligr. Highest temperature, 101.1° F.

January 4th. Injection of 6 milligr. Little reaction.

January 6th. Injection of 6 milligr. No reaction.

January 7th. Injection of 8 milligr. No fever. Epistaxis. Headache.

January 9th. Injection of 10 milligr. No reaction.

January 13th. Injection of 10 milligr. No reaction.

January 16th. Injection of 10 milligr. No reaction.

January 17th. Injection of 15 milligr. No fever. Epistaxis.

January 27th. Injection of 10 milligr. No reaction.

On this day the ulcerations were much improved, but not altogether well.

Annie T——, aged nineteen, housewife, admitted December 13th. Diagnosis: tuberculosis of right knee. Swelling began a year ago; also treatment, with variable results. Father died of consumption. All organs normal.

December 13th. Injection of one milligramme. Pain in the affected knee extending to hip; otherwise no change. On the 14th, swelling and fluctuation appear less.

December 14th. Injection of 4 milligr. Slight pain and redness and swelling at point of inoculation. After seventeen hours temperature, 101.2° F.

December 15th. Injection of 4 milligr. On the 16th highest temperature, 100.3° F. No other symptoms.

December 17th. Injection of 5 milligr. Next day temperature, 100° to 100.3° F. during twelve hours.

December 19th. Injection of 6 milligr. After twelve hours, temperature, 100.1° F.

December 20th. Injection of 8 milligr. After four hours, temperature, 101.4° F.

December 22d. Injection of 10 milligr.

December 30th. Injection of 10 milligr., with a temperature of 100.4° F. twenty-one hours after inoculation.

By some mistake the impression was gained that no reaction had taken place after the several doses, and inoculations were discontinued. They were renewed only after some weeks, when the true state of affairs was found out. At that time the apices also seem suspicious. No improvement.

Daniel D——, aged forty-two, admitted December 12th. Tuberculosis of right elbow-joint. Slight dulness over apices. Eight inoculations were made, of from one to five milligrammes in the course of a month, besides two surgical operations on December 16th and January 7th. The reactions after the injections were very

marked, particularly after the first three or four, but the general condition and the total trouble of the patient leave much to be desired.

A——, working-man, forty-three years of age; admitted December 31st. Underwent a resection because of tuberculosis of ankle-joint years ago, with complete recovery. Suppurating fistule in the cicatrix this last month, an inch and a half deep, terminating in carious bone. Over right upper lobe, anteriorly, slight dulness and slightly bronchial respiration.

January 6th. Injection of 1 milligr. Temperature normal; pain in joint; headache, dizziness; appetite impaired.

January 11th. Injection of 2 milligr. Temperature, 102.6° F. Severe headache; palpitation; oppression.

January 13th. Injection of 2 milligr. Temperature, 101.4° F., twenty-four hours after injection.

January 16th. Injection of 3 milligr. Temperature, 103° F. Palpitation, headache; feels "as if he were going to die."

Refused to be inoculated. An operation on diseased joint. General condition good.

Elise S——, aged sixty-two. Admitted December 19th. Knee swollen a year ago, is painful and stiff; some cough; some dulness over right upper lobe; universal rhonchi. Temperature, 101.4° F.; pulse, 110.

December 22d. Injection of 2 milligr. After twelve hours, temperature, 103.1° F.; begins to fall six hours after.

December 23d. Injection of 3 milligr. After sixteen hours, temperature, 102° F. Pain in knee.

December 25th. Injection of 3 milligr. No change.

December 28th. Injection of 3 milligr. Temperature, 101.3° F.

December 29th. Incisions into the joint on either side; removal of tubercular granulations. Drainage and iodoform; ether. Purulent secretion from vagina; pain in abdomen.

December 31st. Injection of 6 milligr. The usual increase of temperature.

January 4th. Injection of 6 milligr. After sixteen hours, temperature, 104.2° F.; pulse, 122. Pain; some cough.

January 10th. New operation. More removal of granulations. Fever, dry tongue, intermittent and frequent pulse. Fever and increasing debility; pulse weaker; some cough the following days. Dies January 17th.

Autopsy: Tuberculous knee-joint; large abscess of fifth left rib; general miliary tuberculosis of lungs, liver, and spleen.

Ida S——, aged sixteen, caries of vertebræ and ribs. Admitted October 2, 1890. Was well up to two weeks before her admission, with the exception of general discomfort, debility, and emaciation, which had lasted five or six months. Family history, heart, lungs, and kidneys negative. She was treated with incisions, scraping of the carious rib, injections of Thiersch's solution and iodoform in oil. Temperature ranged from 99° to 104° F.; pulse, 90 to 135. Her general condition improved gradually.

First inoculation of 1 milligr. on December 11th, while temperature was 102.2° F. Next morning temperature, 99.3° F., with pulse and respiration diminished accordingly, and less pus.

December 12th. Injection of 2 milligr. Temperature, 100.4° F., some perspiration; some cough. After sixteen hours, temperature, 99.3° F.; pus much less. After sixteen hours, temperature, 98.7° F.

December 13th. Injection of 3 milligr. Old sites of injections congested and painful. Feels well. Pale face. Next day more pus. Feels improved.

December 14th. Injection of 3 milligr.

December 15th and 16th. Injections of 4 milligr. Secretion less.

December 17th. Injection of 5 milligr.

December 18th. Injection of 7 milligr. Profuse perspiration; thirst; secretion trifling.

December 19th and 20th. Injection of 8 milligr. each. Temperature normal.

December 22d. Injection of 10 milligr. After twelve hours, temperature, 104° F.; pulse, 98; headache, restless. Six hours later, temperature, 97° F.

December 25th. Injection of 10 milligr. After twelve hours, temperature, 100.4° F.

December 27th. Injection of 15 milligr. Highest temperature, 100.4° F.

December 31st. Injection of 20 milligr. After sixteen hours, temperature, 101.2° F.; pulse, 120. Face pale, eyes sunken, marked anæmia, but appetite good. Iron.

No inoculations on January 3d and 5th, with afternoon temperature of 101.4° F., and pulse, 120.

January 6th. Injection of 30 milligr. Twelve hours afterward, temperature. 101.4° F., and pulse, 110. Eighteen hours afterward temperature. 101.1° F., and pulse, 112. Twenty-four hours afterward, temperature, 101.4° F., and pulse, 112.

Inoculations were discontinued. General condition not changed. Fistula as deep as before, but secretion slightly less, purulent, contains bacilli. High degree of anæmia. Physical symptoms not altered.

Wilhelmine K——, aged nineteen, admitted December 11, 1890, for lupus vulgaris of upper lip, nose, and eyelid. Father died of pulmonary tuberculosis nineteen years ago. She had, when young, conjunctivitis, cervical adenitis, scarlatina, and measles; also eczema capitis. Lupus commenced eight years ago on the nose, and spread to upper lip and part of left cheek. Has been operated upon several times. The lower part of the nose is deformed by loss of substance, the nares impervious; the upper lip shows several hard cicatrices. Some noduli still present. Upper lobe of right lung somewhat dull. No bacilli found in sputum.

December 11th, 4.45 P.M. Injection of 1 milligr. Temperature rose to 100.2° F. within an hour; was subnormal, 97.2° F., within two hours; after five hours pain around site of injection; after seven hours, nose and lip congested and with the sensation of tension. Afterward some cough; little sleep. Redness and œdema of nose and cheek very marked within sixteen hours. Headache and dizziness. After eighteen hours, temperature 102° F., pulse 112° F., respiration 26. Nose and lip purplish; pain in chest; chilly, hot, perspiring. After twenty-four hours, temperature 101.2° F.

December 12th. Another inoculation of 2½ milligr. Pain; cough. Some distinct pustules in the area of lupus. Cough and rigor; temperature, 103.1° F.

December 13th. Itching of nose and lip. Temperature falls some; rises again to 103° F.; normal at 10 P.M. No injection. Still in the night two chills without a rise of temperature, and pain in left shoulder.

December 14th. 7.30 P.M. Injection of 4 milligr. Temperature rises after nine hours to 104.5° F. within fourteen hours; normal in twenty-six hours. Meanwhile four chills, headache, pain about chest. Nose and upper lip swelled and congested. Desquamation on nose.

December 16th. Injection of 5 milligr., with the same result as to temperature. Less local congestion, hardly a rigor, the newly-formed pustules and the noduli of lupus much smaller.

December 18th. Injection of 5 milligr.; highest temperature, 102.4° F. Coryza, scales fall off.

December 20th. Injection of 7 milligr.; highest temperature, 102.2° F.

December 22d. Injection of 8 milligr.; highest temperature, 101.7° F.

December 23d. Injection of 9 milligr. Highest temperature, 100.2° F.

December 24th. Injection of 10 milligr. Highest temperature, 99.2° F.

December 25th. Injection of 12 milligr. Highest temperature, 100.1° F. after the lapse of twenty-four hours.

December 26th. Injection of 15 milligr. Highest temperature, 99.9° F.

December 27th. Injection of 15 milligr. Highest temperature, 100° F. after twenty-four hours.

December 29th. Injection of 20 milligr. Highest temperature, 100.2° F. after twenty-four hours.

January 3d. Injection of 15 milligr. Highest temperature, 100° F.

January 5th. Injection of 15 milligr. Highest temperature, 99.4° F.

January 7th. Injection of 25 milligr. Highest temperature, 100.8° F. after twenty-two hours.

January 8th. Injection of 40 milligr. No rise of temperature. After thirty-three hours, 97.4° F. A few hours after the injection an attack of angina pectoris, pain, oppression, fear of impending death. Inhalations of amyl nitrite relieved her.

January 16th. Injection of 50 milligr. Highest temperature, 101.8° F.; pulse, 40.

January 18th. Injection of 60 milligr., without any reaction.

January 24th. Injection of 80 milligr. Some hours after, without a change of temperature, attack of angina pectoris, face pale, pulse so frequent as not to be countable. Pain and sense of constriction; distinct blowing murmur at apex. Morphine did not relieve her, amyl nitrite did.

January 29th. Injection of 30 milligr. No change of temperature, but palpitation and pain in chest. After seven weeks' treatment the lupus is very much improved, the deformed nose is of normal paleness, the lips still red in places, some lupus noduli on lip still perceptible, lip still hard, part of this hardness, however, due to old cicatrices resulting from operations. Though there be no cure, the improvement is such, when compared with the

results of any operative procedures known, as to be very encouraging.

Amos D——, aged sixty-six, admitted December 31, 1890. Diagnosis: Epithelioma of face, right side (was announced as lupus). Ulceration of face was observed fifteen years ago. Many attempts at a cure. Lately in Chicago arsenic paste, with the result of digging a square large hole into the malar bone which is superficially necrotic, and destroying the external angle of right eye. Normal organs. Insisted upon lymph treatment.

January 1st. Injection of 2 milligr. Eruption began to rise half an hour later. Temperature was 101.2° F. after three hours; fell; rose again, until after twelve hours it reached 101.8° F. It was not normal until thirty-six hours after inoculation. Wound not changed, but eyelids swollen and red.

January 3d. Injection of 2 milligr. Temperature, 100.3° F. four hours after inoculation, and slight rigor.

January 4th. Injection of 3 milligr.

January 5th. Injection of 5 milligr. No increase of temperature; some pain in eye and about the site of inoculation.

January 6th and 7th. Injection of 10 milligr. each.

January 8th. Injection of 15 milligr.

January 9th. Injection of 20 milligr., after which, on the next day, temperature, 101.5° F.

January 11th and 13th. Injection of 25 milligr.

January 16th, 20th, 22d, and 30th. On the 19th he had once a temperature of 100.8° F., but in no connection with an injection.

January 25th. Injection of 40 milligr. Through all these days no rise in temperature, and no local effect. The wound healed slowly under a boric and salicylic acid ointment.

Reactions set in at first as they do in the well, in from one-half to twenty-two hours. This effect was obtained with 2 milligr., while afterward 20 and 40 had no effect whatsoever. There was no apparent effect on, or im-

provement of, the local lesion attributable to the use of "tuberculin."

James C——, aged forty-one; admitted January 3d, for alleged lupus, which proved epithelioma of the eyelids and temporal regions of left side. It had lasted seven years and had undergone several operations in the last two years. Five milligrammes were injected January 4th at 4 P.M. at a temperature of 98.4° F. Nine hours later it was 97° F.; fifteen hours, 96° F.; seventeen hours, 98° F. During this time slight fulness in head, pulse smaller and somewhat quicker.

On January 5th injection of 10 milligr. Slight increase of temperature and swelling of spleen on the 6th.

On January 8th injection of 30 milligr. at 9 A.M. Temperature rose soon, and reached 103° F. within ten hours. Lymphatic glands enlarged on the side of his chest, which were quite painful.

January 11th. Injection of 40 milligr. Temperature rises only to 100.2° F. Feels perfectly well.

January 15th. Injection of 50 milligr., with no effect whatsoever.

January 18th. Injection of 33⅓ milligr. No effect.

January 21st. Injection of 66⅔ milligr. Temperature eight hours after, 101.4° F.; otherwise no effect either local or general.

January 25th. Injection of 87½ milligr. No effect at all; complains, however, on the 26th that his bones ache and his shoulders are lame. Better on the 27th.

January 28th. Injection of 72½ milligr. No effect, and the ulcerations in about the same condition as in the beginning; some new granulations on the edge of lower eyelid. No improvement.

A child nineteen and one half months of age was inoculated in the very last stage of tubercular meningitis on December 12th, with one half of a milligramme, on the 13th, with one milligramme of "tuberculin." There were no changes in her hopeless condition attributable to the injection.

E. R——, boy aged eleven, admitted October 23d, with tubercular peritonitis and ascites. Disease began six months previously, with frequent but moderate pain, but no fever or rigor. Convolutions of intestines are easily distinguished (adhesions). Constipation. Never a temperature beyond 99.5° F., never one below 98° F., until December 26th, when the first milligramme was injected at 6 P.M. Temperature at 9 P.M was 97.8° F.; pulse 80. At 12 M. on the 27th, 97° F.; pulse 88. At 3 A.M., 101°F.; pulse 100. At 6 A.M., 102° F.; pulse 120. At 9 A.M., 103.3° F.; pulse 114. At 12 M., 101.6° F.; pulse 116. At 3 P.M., 101.8° F.; pulse 112. At 6 P.M., 102.2° F.; pulse 116. At 9 P.M., 100° F.; pulse, 108.

The first temperature of 99° F. was reached at 3 A.M. on the 28th, at noon it was again 97° F., still with a pulse of 106. Second inoculation of 1 milligr. at 6 P.M.; only rise (101.2° F.) at 9 P.M. On the 29th at 6 P.M. 2 milligr., also on the 30th. No rise, several times 97° F. On January 2d, 3 milligr. at 6 P.M. At 9 and 12 P.M., and at 3 and 6 A.M. on January 4th the temperatures were 97.8° F., 97.4° F., 97–98° F. No rise.

January 4th, 6 P.M., injection of 3 milligr. Temperature at 9 P.M., 96.5° F.; at 12 M., 97° F. 3 A.M. of the 5th 99.4° F.; 6 A.M., 100.3° F.; the only rise. That night temperature for many hours was 97°, 96.2°, 96.9° F.

January 6th at 6 P.M., with a temperature of 97.3° F., 5 milligr. were inoculated. For twelve hours afterward temperature was between 97° F. and 96.2° F. No rise except once, to 100° F., at midnight of January 8th. This was the only time when the pulse was as low as 70.

On January 10th 10 milligr. were injected, temperature sank again to near 96° F., as heretofore, rose and fell, once at midnight of the 13th to 95.8° F., with a pulse of 62.

On January 16th with a temperature of 97.2° F., at 6 P.M., 10 milligr. were injected. The first effect was again

a fall to 97.8° F., and 97.2° F.; then, at 3 A.M., a rise to 102° F. and pulse, 116. At 6 A.M., 99.4° F.; pulse, 108. At 9. A.M., 101.2° F.; pulse, 120. At 12 M., 102° F.; pulse, 122. At 3 P.M., 99.6° F.; pulse, 108. At 6 P.M., 100.6° F.; pulse, 130. After that the temperature fell, with the exception of midnight the 19th, when it was once 101° F. It then fell a few hours, rose again in the morning hours of the 20th and remained twelve hours from 100.2° F., to 101.7° F.

On the 23d, about noon, I made an inoculation of 20 milligr. At 6 P.M temperature was 104.4° F., with a pulse of 112. All next day it remained above 100° F. He left the hospital on the 26th. During all these weeks he felt very comfortable except when under the influence of high temperatures, and his general condition improved. Still, it had improved before the lymph treatment was begun; his strength increasing and ascites diminishing.

M. C——, aged five years and six months. Tubercular peritonitis, ascites. Was said to have been sick a week with tumid abdomen and loss of appetite. For some days after admission the highest afternoon temperature was 100.5° F., morning temperature as low as 98 4° F. First inoculation of half a milligramme at 8.45 P.M. on January 3d. Within five hours the temperature was 103.2° F.; pulse, 148; respiration, 30. The temperature rose to 104.5° F., and the accompanying symptoms became so alarming that phenacetin and brandy were administered several times. Not before the 6th was the temperature again below 100° F. After the next inoculation reactions would always show themselves, but the effect grew less gradually, though the doses were increased from one half to 2 milligr. Very suddenly and unexpectedly, eighteen days after the treatment was begun, the temperature rose again to 104.6° F., with corresponding rise of both pulse and respiration. No particular change in the three weeks she was in the hospital.

The following are a number of cases of pulmonary tuberculosis in different stages:

Mrs. R——, twenty-five years of age. Admitted December 17th. Singing lessons from seventh to seventeenth year; hæmoptysis at seventeen; acute pulmonary complaint two years ago and a year ago. For eight years occasional dyspnœa, cough, and expectoration. Left upper lobe, extensive dulness and coarse respiration; right lower lobe, local dulness and rhonchi. Bacilli.

December 18th. Injection of 1 milligr. at 6 P.M.

December 19th. Slight rigor in afternoon, with temperature of 101.3° F., and perspiration; 9 P.M., 102° F. (highest temperature). Pain in site of inoculation. First normal temperature returned December 21st at 9 A.M. At 12 M., 1 milligr. After twenty-four hours, December 22d, 9 A.M., 100° F. Spleen enlarged. Highest temperature at 6 P.M.; at 9 P.M., below 100° F. Headache all day. December 23d some cough. At 12 M. temperature 100.2° F.; 6 P.M., 100.6° F.

Injection of 2 milligr. at 7 P.M. on December 24th; 2 milligr. the 26th; 3 milligr. the 29th; 4 milligr. the 31st; also the 2d, 4th, and 6th of January. The highest temperature on the 25th was 101.4° F.; the 27th, 102° F.; the 30th, 101.2° F.; January 1st, 100.7° F.; January 3d 103° F; the 5th, 102.4° F.; the 7th, 99.4° F. These temperatures were reached in from sixteen to twenty-two hours after inoculation. During all this period her general discomfort, local pain, cough, and perspiration became lessened.

Inoculations were made on the 8th, 6 milligr.; the 9th, 7 milligr.; the 11th, 8 milligr.; the 12th, 9 milligr.; the 14th, 10 milligr.; the 16th, 11 milligr.; the 17th, 13 milligr.; the 18th, 13 millgr.; the 21st, 23d, and 24th, each 15 milligr.; the 25th, 20 milligr.; and the 26th, 25 milligr. During all this time her general condition improved; her temperature was mostly between 98.5° and 99.5° F., and seldom rose to 100.2° F.

John H——, aged twenty-eight, admitted January 15th. Tuberculosis pulmonalis et laryngis. Family history of phthisis, of which a brother and a sister have died.

Hoarseness, dry throat, and occasional hæmoptysis more than two years ago. Permanently sick for a year, cough, some expectoration in the morning. Both increased three weeks ago. No pain, fever, or night-sweat. Short breath on exertion. Condition fair. Some retraction of left supra- and sub-clavicular region, dulness, crepitant râles down to third rib; posteriorly the same. About the middle of thorax some bronchial or prolonged expiration, a similar condition on the right side on percussion and auscultation.

Inoculations on January 15th, of 1 milligr.; January 16th of 2 milligr.; 17th of 3 milligr.; 18th of 4 milligr.; 20th of 6 milligr. had no visible effect whatsoever, the rectal temperature remaining at 99.6° F.

On the 21st, 10 milligr. were injected, with the result of raising the temperature to 103° F. within five hours and producing much cough. On the 25th, 5 milligr. were injected, the 25th, 10 milligr.; the 26th, 15 milligr. with no response on the part of temperature. It is probable that the dose of 10 milligr., if it had been the first, would have had the same result, and that this effect would have justly been claimed as pathognomonic for tuberculosis; though a later dose of 1½ centigr. did not in the least show the same effect. Six milligrammes, however, elicited no temperature response; while other cases respond to smaller doses so readily that, if larger doses were given to them, danger might be incurred. Thus for instance:

E. V—— , aged twenty-five, with undoubted pulmonary tuberculosis, dulness, bronchial respiration, purulent expectoration, bacilli, and night-sweats had 1 milligr. injected on January 25th, with no result; another on January 26th, with an increase in temperature, which reached its maximum, 101.8° F., after fifteen hours. In this case it is remarkable that the second effective dose was not larger than the first which refused its effect. Still, it is possible that the reaction following the first inoculation occurred only after more than a day

after—in accordance with some other observation of the same kind.

G. P——, aged thirty-two, admitted December 11th, with the diagnosis of incipient tuberculosis of the lungs. Had dulness and crepitant râles over clavicle and supra-scapular region of the right side. Respiration over fossa supraspinata diminished. Sputum not copious, but contains bacilli. Weight, 127 pounds.

Inoculation of 2 milligr. on December 12th; 3 milligr. the 13th; 4 milligr. the 14th; 4 milligr. the 15th. Temperature rose to 101.6° F. in twenty-two hours. Injection of 5 milligr. on the 17th with no visible effect. Patient weighs 137 pounds on the 19th. Injection of 6 milligr. on the 20th was followed by a temperature of 102.4° F. on the 21st; 6 milligr. on the 23d by 101° on the 24th; 7 milligr. on the 25th by 101.8° on the 26th; 7 milligr. on the 28th by 101.2° on the 29th; 9 milligr. on the 30th by 101° on the 31st.

On January 1st no inoculation, and no temperature above 100° F. (This but once.)

On the 2d of January a new start was taken with 2 milligr., and thirteen inoculations were made up to the 19th, when the treatment was discontinued. Meanwhile the doses had been gradually increased to 10 milligr. But twice was there a temperature as high as 100° F. during that time. The general condition improved from day to day, and about the end of the month the patient was discharged in good health, without cough, and without any râles and any dulness. Recovery (?).

J. W. B——, aged twenty-five, tuberculosis pulmonum. Father died of consumption; patient had symptoms these several years. Bronchial respiration over upper lobes both right and left posteriorly, also slightly over the left lower lobe; loud bronchial respiration over left upper lobe in front; moderate dulness over total right side. From December 20th to the end of January, when she left, twenty-two inoculations were made, ranging from 1 to 15 milligr., the latter dose being given

four times. The first rise of temperature occurred on December 26th, after a dose of 3 milligr. on the 25th; the first temperature of 102° F. was reached January 10th after a dose of 7 milligr. had been given twelve hours previously. The same was reached again on January 26th, sixteen hours after the fourth dose of 15 milligr. (the first on January 20th) had been administered; also on January 27th, sixteen hours after 15 milligr. on the 26th. It must be added, however, that after the temperature had come down to 98° F. in the early morning hours of the 28th, it rose to 102.9° F. in the afternoon. Thus it remains doubtful whether the higher temperatures of the afternoon (mostly sixteen hours after the inoculation) were due to the injection or to the pulmonary process. For when the patient left about the end of January, her claim of feeling improved was not justified by either increase of weight or any appreciable change in her lungs.

M. P——, aged twenty-one, admitted December 12th. Tuberculosis pulmonum et laryngis. Color of vocal cords grayish red; edges eroded, fossæ Morgagni ulcerated, posterior wall of larynx slightly thickened. Extensive rhonchi over chest, dulness below right clavicle. Bacilli numerous. Inoculations were made, December 13th, 1 milligr.; 14th, 2 milligr.; 16th and 18th, 5 milligr. each; 21st 6 milligr.; 23d, 25th and 28th, 5 milligr. each. Reactions were quite marked after the first inoculation, though they required nearly a day for their maximum. Cough, expectoration, and temperature increased, larynx became sensitive. At no time was the temperature anything like normal. Examination on December 26th revealed: No change in larynx, complete aphonia; over left upper lobe dulness, coarse respiration, moist and sibilant râles, over apex cavernous breathing; over almost the whole right lung bronchial respiration, and moist and sibilant râles. As his condition was so much impaired, I hesitated giving the same doses, being under the impression that possibly the injection might add to his high temperatures and the extension of the morbid process. There-

fore after waiting five days, during which the general condition and the temperature of the patient showed no difference from former observations, I injected 2 milligr. on January 2d. The last injection of this new series, which consisted of fourteen inoculations of from 2 to 5 milligr. was made on January 20th. No perceptible effect. Death on January 25th.

M. A——, aged nineteen, admitted January 7th. Pulmonary tuberculosis. Began with a pleurisy, October, 1889. Languor, cough, fever, night-sweats last spring, expectoration with bacilli, but seldom in bed. Right upper lobe has prolonged expiration and sibilant râles. Left, normal. Posteriorly, over right apex, wheezing and moist râles. Some dulness over right upper lobe, anteriorly.

Inoculations were begun January 9th, from the 9th to the 19th. They were repeated daily, commencing with 1 milligr., and gradually rising to 9 milligr. From January 21st to 29th eight inoculations were made, each of 10 milligr. During all this time no improvement took place; she coughed but little, with exceptions, perspired, felt often languid, expectorated some, slept well most of the time. During the first week (sixth day) the temperature reached 102° F.; but once, toward the end of the second week, it reached 102.5° F., touched 104.5° F. several times in the third, and more in the fourth week. Toward the end of the month the temperature fell below 103° F. Meanwhile, though the patient's râles would increase from time to time, the dulness did not extend; still, her general and local condition did not improve.

A. H——, aged twenty-one, admitted December 29th; tuberculosis pulmonum. Had pneumonia a year ago; coughed almost all the time since with the exception of some months passed in the mountains. Dulness over both apices (mainly left), both anteriorly and posteriorly. Rhonchi over both upper lobes, in some places during cough only.

Inoculations: December 31st, ½ milligr.; January 1st,

1 milligr.; January 3d to 7th, four inoculations of 2 milligr. each; January 9th to 25th, a daily dose of 3 milligr., with the exception of the 14th, 19th, and 22d; January 26th, 4 milligr.; 27th and 28th, 5 milligr. each; 29th, 6 milligr.; 30th, 7 milligr.; 31st, 8 milligr. After the smallest doses the temperature would rise, sleep was restless, there were headaches and mild chills, also much perspiration, also palpitation. The temperatures till January 22d varied from 101° to 103.5° F.; in very rare instances only would they fall below 100° F. In the last week of the month, however, most observations showed temperatures below 100° F., many below 99° F., very few as high as 101° F. About that time her general condition, which had not been good at all, improved very much indeed.

I——, a girl aged five, with undoubted pulmonary tuberculosis, slight dulness over left lung both anteriorly and posteriorly, and higher pitch in right side than left, but no râles, had her first inoculation of 1 milligr. on January 6th. The case is remarkable for its punctual reactions. Within four hours, once after two, the temperature would rise without affecting either pulse or respiration after the first two injections. Only with the third, and every subsequent injection, both pulse and respiration rose correspondingly. The reactions lasted about twenty-two hours, a little less than one-half of this time being spent on the rise. Respiration, with a single exception, returned more readily to the normal than the pulse, which remained accelerated for some time. Still, when a sufficient time was afforded, temperature, pulse, and respiration returned to the original condition previous to any inoculations. Not improved in three weeks.

S. S——, aged thirty-two, pulmonary tuberculosis, with infiltration of both upper lobes. The first injection of 1 milligr. appeared to have but little effect, the third of 3 milligr. given two days afterward increased his temperature within six hours. The maximum was 101.8° F., and was reached twenty-four hours after. Normal tempera-

ture on the following day (January 14th). On the 15th 3 milligr. with rise of temperature within twelve hours; maximum of 102.6° F. within eighteen hours; at the same time perspiration, cough, great discomfort. On the 18th 3 milligr. were again given without any such effect. Five milligr. on the 20th increased the temperature within six hours, to a maximum of 103.9° F. within nine hours. The same dose on the 23d had no similar effect. But when given on the 25th it had again the effect of raising the temperature within seven hours, with a maximum of 103.8° F. within nineteen hours. It appears, therefore, that the same dose may lose its effect, and recover it at a later time, the intervals between the several administrations being the same, viz., two days.

F. T——, aged thirty-six. Pulmonary tuberculosis. Had fifteen injections from December 28th to January 31st, in doses of from one to eight milligrammes, with but little reaction and little effect. The smaller doses appeared to prepare the patient for readily tolerating the larger ones.

J. F. L——, aged thirty-nine. Pulmonary tuberculosis. Had a pneumonia nearly two years ago, and never lost his dyspnœa. For five months past, cough, expectoration, emaciation, night-sweats, bacilli. Over upper halves of both upper lobes, dulness, and crepitant râles. Thirteen inoculations between December 17th and January 6th, amounting to from one to twenty milligrammes. The latter dose was repeated on the 16th and the 20th, a few days after he left the hospital. The brief observations permitted resulted in the following: The third inoculation (first of 3 milligr.) was the first that raised the temperature to 102.8° F. at 9 A.M. and 102.5° F. at 12 M., fourteen and seventeen hours after the inoculation. Nearly the same temperature was reached three and six hours after the next inoculation of 5 milligr. It was never reached again, either spontaneously or after increased doses. Indeed there appeared a gradual downward tendency from day to day. The general condition certainly improved, and he gained a few pounds.

A. B——, aged thirty-three ; admitted November 25th. Pulmonary tuberculosis. For a year and a half past, cough, four attacks of hæmoptysis, expectoration, night-sweats, emaciation, hoarseness. Bacilli. Family history negative. Supra- and infra-clavicular regions retracted. Dulness over both apices, also diminished respiration and some rhonchi. Over right lower lobe, posteriorly, dulness and bronchial respiration. During December, fifteen injections of from 1 to 10 milligr. ; in January, seventeen of from 2 to 50 milligr. After the first inoculation the patient coughed much, both cough and expectoration grew less after the second, and remained so. At no time was there a temperature which had to be attributed to the action of the lymph ; it seldom reached 101° F., then only in the afternoons (about a day after the injection) and for a short time. Within a week the patient felt better. Still, the examination of his chest made on December 26th revealed no changes except the disappearance of the rhonchi. During January, temperature almost normal ; but little cough and expectoration. Increase of weight in one month, nine pounds. General improvement.

A. H——, aged thirty-nine, admitted December 4th with dulness over both apices and crepitant râles, and bronchophony over right apex. Bacilli. From December 13th to the end of the month thirteen injections were made of from 1 to 10 milligr. During the course of January sixteen injections were made, from 2 with rapid increases to 60 milligr. The first injection of 1 milligr. raised the temperature of 98.5° F. to 105° F. within an hour and a half, with intense perspiration, followed by a rapid fall afterward to 99° F. Maximum temperature in the afternoon of the 12th, 101.7° F. ; of the 13th, 101.2° F. At that time 3 milligr. were injected, with no increase of temperature or any other signs of reaction. No such temperature was ever reached again, and the patient felt more comfortable from day to day. Still, the physical condition of December 26th revealed dulness

posteriorly over left upper lobe, with considerably increased voice. On the right side bronchophony posteriorly over upper lobe, dulness over the two upper lobes. Temperature remained normal throughout January, weight increased by twelve pounds, cough became less, also expectoration, crepitant râles disappeared, dulness remained. Great improvement in the general condition.

In some cases of tuberculosis small doses of the lymph appear to reduce the temperature without giving rise to any other symptoms except the sensation of comfort. Patients will apparently not react on the administration of 1 milligr., then the dose is increased from day to day, slowly; the later doses will not affect the system any more than the first; indeed, 10 milligr. the tenth day is attended with the same lack of consequences as 1 milligr. given the first day, in accordance with the fact that when a serious reaction is experienced after a single milligramme has been administered, very much larger doses are soon required to accomplish the same end.

A lady, aged thirty-five, Mrs. M——, mother of a number of children, one of whom died a few years ago of miliary tuberculosis, had tuberculosis of the lungs and abdominal lymph-bodies, probably also the peritoneum, these ten years. The abdominal symptoms were very much improved compared with what they were a few years ago. But for years she has expectorated, coughed, was emaciated, formed large cavities in both apices, both of which have diminished in size for a year past, has had numerous attacks of pleuritis and pneumonia, and brings up bacilli in almost every sputum. Besides the extensive cavities she has large areas of dulness and coarse respiration, besides all kinds of rhonchi. Lately she had a severe pneumonia of which she got fairly well. Still, she went on with her old symptoms, and high fever, which required repeated large doses of digitalia and antipyrin.

The first milligramme was injected January 25th while she had a temperature of 101.°8 F., which fell as low as 99° F. January 26th it rose in the morning to 100.4° F.

Injection of 2 milligr. at that time. Temperature sank to 98° F. Next morning again 100.4° F. and 3 milligr. Again 100.4° F. and 4 milligr. on the 28th; on the 29th the same and 5 milligr.; on the 30th the same and 6 milligr. in the afternoon. For the first time this week she had a temperature of 100 8° F. in the night through the course of a few hours. The following morning, January 31st, temperature below 100° F.; 8 milligr. at noon. First elevation twenty-four hours after, on February 1st, 100.5° F., rose to 100.8° F., was 100° F. again at 6 P.M., and fell below. Through all this week there was less cough, less expectoration, less perspiration, more appetite and comfort, in spite of the three daily doses of medicine being reduced to one, and that one reduced in size.[1]

A similar observation was made in E. L——, aged nineteen, admitted December 25th. He had been sick in bed seven weeks, his condition had been carefully watched, and temperatures recorded. They were seldom as low as 101.5° F., mostly from 102° F. to 104.5° F., and sometimes higher. Has been reduced to 102½ pounds. Dulness and fine rhonchi, crepitant and sibilant over the left upper lobe, also bronchophony. Over the right upper lobe posteriorly, over large area, dulness, rhonchi crepitant and sibilant, and bronchophony; anteriorly, dulness, bronchial and cavernous breathing, and rhonchi. Bacilli. Had twenty-nine inoculations from December 25th to February 27th, the latter day 5 milligr.; all the rest from 1 to 4 milligr., with a slow increase. On December 27th, the first temperature of 100° F. was reached, the lowest in seven weeks; 99.8° F. on the 28th; 99.4° F. on January 2d; 99° F. on the 3d, 9th and 10th;

[1] Four weeks have elapsed since. There has been some afternoon rise of temperature every day which could be controlled by a daily dose of digitalin and antipyrin. Meanwhile daily doses of tuberculin have been injected; they reach at present a decigramme without the slightest feverish reaction. The cough is reduced to one-fifth of what it was, expectoration is much less and easier, the râles are audible on one side only, large areas have their vesicular respiration restored to them, and the weight of the body has increased by more than six pounds.

98.4° F. on the 14th; 98.6° F. on the 22d. All this occurred while his local symptoms did *not improve*. On contrary his cavity in the right apex is increasing in size, expectoration still copious and bacillary, though more fluid. Lately he has again temperatures of 102° F., and even 103° F., which cannot be taken as the result of lymph-action, but are undoubtedly the outcome of the destructive process, which is not checked. This case shows that the patient may feel very much improved without an actual change in his pathological condition, even while getting worse.[1]

E. A. B——, aged thirty-three, admitted January 3d. Since January, 1890, loss of weight (now 152½ pounds) and strength. For some months past hoarseness. The posterior wall of larynx hyperæmic; left vocal cord unhealthy, will be described later on. No night-sweats. To those who saw him before admission, he looked feverish. Being a doctor, he never took his temperature. Right lung over clavicle: Dulness and during a cough crepitant râles; posteriorly crepitant râles over the whole upper lobe. Left lung: Dulness trifling over clavicle, slightly coarse respiration. Between January 3d and 13th, ten inoculations were made, from 1 to 10 milligr., increasing by 1 milligr. from day to day; on the 14th, 10 milligr.; 16th 17th, 18th, 15 milligr.; 20th, 20 milligr. The injections were made about 7 P.M., the only temperature above 100° F. would be found in the afternoons, the highest ever noticed being 100.8° F., and that only once; low temperatures were observed, down to 98.2° F. On several days the temperatures never reached 100° F. During all this period no bacilli were found, and therefore I stopped the inoculations on January 20th, when the last one of 20 milligr. was made. On that day the highest temperature was 100° F.; on the 21st, 100.1° F.; a single time, the 22d, 100° F.; a few evening hours, the 23d, over 100.8° F. very exceptionally. On that day

[1] In the course of the last few weeks, the general condition of the patient improved sufficiently to enable him to take long walks.

the sputum, which was always scanty, was again examined, and a large number of bacilli found, many of them broken up as described in *Deutsche Med. Wochenschrift*, No. 46. At 11.10 A.M. 25 milligr. were injected. At midnight the temperature was far below 100° F., and remained so (down to 98 6° F.) until 9 P.M. on the 24th—indeed the first day when there was no increase in the afternoon. On the 24th, at 8.30 P.M., 30 milligr. From 6 A.M. to 9 P.M. the 25th, temperature from 100° to 100.7° F., the first indications of a response such as every healthy person would show. The same occurred after 40 milligr., which were injected at 8.25 P.M., the 25th. Temperature rose, 9 A.M. on the 26th, to 100.3° F., reached 101.4° F. at noon, and was below 100° F. late in the evening. Two days later 60 milligr. were injected with no more marked result.

That case shows conclusively that the lymph did not cause any reaction pointing to the presence of tuberculosis when injected in doses varying from 1 to 60 milligr. The slight responses met with in these high doses may be found in the healthy. Besides, the case is noticeable as one of those in which bacilli may not be found for some time and still be present. The question whether the bacilli were freed by the action of the lymph must be answered in the negative ; for there were no marked rhonchi during the period of inoculations, and we have a right to conclude that the tissue surrounding the bacilli nests was not congested and softened by the action of the lymph.

This case is interesting from an additional point of view. On January 8th there was a flat, slightly granulating ulceration of the posterior half of the left vocal cord, paresis of the adductors, the whole mucous membrane quite pale. On the 22d two-thirds of the ulceration had closed, paralytic symptoms improved, the mucous membrane just as pale as before. There was no local reaction at any time after an administration of lymph, all of which shows that not only the general but also the local

reaction may fail, but still a local improvement may take place.

In the case of H. C——, aged nineteen, admitted December 15th, similar observations were made, though not so conclusive for the following reason. He had been sick with cough, purulent and bloody expectoration nine months, was emaciated, feeble, and feverish. There were dulness, crepitant and sibilant râles, coarse respiration, bronchial respiration over both upper lobes. Bacilli copious. The first inoculation of 1 milligr. was made on the 15th, the 9th of 9 milligr. on the 25th, with the result of reducing his temperature. He entered with temperature 103° F., which he did not reach again. Indeed, most of his temperatures were below 100° F., once 98.6° F., reached 101° F. but seldom, and were 101.7° F. but twice, and for a short time only. Two days after the first inoculation he slept well in the night, perspired less, cough but trifling, feels comfortable. But after the sixth injection, on the 20th (7 milligr.), cervical and axillary glands and a long string of lymph bodies were found swollen and painful on both sides of chest. On the 26th I stopped the inoculations because those lymphatic glands were increasing considerably, and in spite of the lowered temperatures the general condition of the patient was bad. On the first day when no injection was made, his temperature rose to 102.5° F., the next to 102.4° F., the third, 103.1° F.; the fourth, 104° F.; the fifth, 103.7° F., with general malaise, vomiting, and some albuminuria; the sixth, 103.6° F.; the seventh only 101.7° F.; the eighth, 102.1° F. But there were some temperatures below 100° F., and his general condition was better, the glands also smaller; thus I resolved to keep him as I thought under the constant influence of the powerful remedy by giving a daily dose of only 2 milligr.; this has been repeated sixteen times up to January 19th. When the first 2 milligr. were given there was no longer any albumin in the urine. The temperature decreased gradually, the periods of less than 100° F. became longer,

on the 8th it did not rise at all beyond 101° F., and did not reach this figure at all between the 9th and 14th. On the 19th, when no inoculation was made, 102.1° F. was again reached through five or six evening hours. His general condition is not improved; has left for the South.

E. S——, aged thirty-two, admitted December 16th, with the diagnosis of tuberculosis pulmonum. Bacilli have never been found, there being very little sputum. But has coughed these two years, had night sweats, and some fever these four weeks. No history of tuberculosis in the family. On the right side dulness and fine crepitant râles over the clavicle, also below. Posteriorly the same. Over the lower right lobe diminished respiratory murmur and some dulness. On the left side, above and below the clavicle and in the supraspinal region, some crepitant fine râles during cough. This patient proved peculiarly immune against the effect of the lymph. He entered with a temperature of 101° F., and over, but never reached it again, seldom 100° F., was more frequently 98° F. than 99° F., and reached 97.2° F., lymph or no lymph. On December 1st, 1 milligr., and further on 2, 3, 5, 6, 10 (on the 30th), again on January 3d, 20 on the 8th, 25 on the 10th, 30 on the 14th, 40 on the 16th, 20 on the 23d and 25th; 50 on the 26th, 60 on the 27th, 70 on the 29th, 80 on the 30th. The doses were more than large enough to affect a healthy person. If it were not for the negative result of the search for bacilli, there would be no doubt in regard to the diagnosis. I do not feel, however, that I have a right to deny the presence of tuberculosis in the presence of all symptoms except bacilli. I have spoken of a case in which a two weeks' search for bacilli was in vain, and still they were present. Here, then, is an individual who in that condition is not affected by 360 milligr. administered within a week. Are we to call this absence of an effect the result of an idiosyncrasy? Though that term does not mean much and be only an expression of convenience, it shows that there

is an occasional person that is not affected by a reasonably large dose of the lymph.

The condition of the patient is very much improved. Dulness has disappeared and there are no rhonchi. Evidently the pulmonary tissue has expanded, and the secretion stopped entirely. Improved, perhaps well.

Conclusions.—After an inoculation of tuberculous patients with tuberculin the temperature of the body would rise in from two to twenty-eight hours. Or it would not be influenced at all, in a few cases. Or it would fall first and then rise some. Sometimes it would rise, then fall and again rise. Still the rise is the usual occurrence. The descent from the maximum would in most cases take a longer time than the ascent. Unexpected rises of temperature were occasionally met with in inoculation of persons not tubercular. Perhaps there are other conditions besides tuberculosis in which tuberculin has the same effect. It is therefore not absolutely reliable in ferreting concealed tuberculosis. As a means of diagnosis it is not positively infallible. The doses required to obtain a reaction would vary considerably. Some patients would respond readily to a milligramme, some demanded ten times that amount. Children required relatively large doses, except the cases of tubercular peritonitis. One of them, at one time, after having shown high temperatures following previous inoculations, had a rectal temperature of 95.8° F., with a pulse of 62. The nature of the cases—whether bone, gland, skin, or lung—did not influence the effect of the doses. Lupus and pulmonary tuberculosis would be influenced by very small, or sometimes by large doses only. Therefore it is not safe to begin anywhere with 10 milligr., as has been advised, particularly as possibly the reaction may be retarded, and a second inoculation may have a cumulative effect. The therapeutic effect did not appear to depend on the energy of the reaction; on the contrary, some of the most favorable cases were those in which no, or very little increase of temperature was observed;

while others, which exhibited high fever, and other symptoms of reaction, were endangered by dyspnœa, rhonchi, and the progress of local disturbance in the lungs. It seems advisable to begin with small doses in every case, and rather avoid than covet striking effects. At all events it is impossible to predict or calculate the effect of the remedy. Every case appears to require its own tentative treatment.

Other results of the inoculations were changes in pulse and respiration. In some these would correspond with the rise of temperature ; in a few they would not be influenced. Sometimes the pulse, other times respiration would be more readily affected. The comfort or discomfort of the patient would not always be in accordance with the variations of temperature, pulse, or respiration. The site of the induration would sometimes smart, and flush after a while ; indurations there were but few, abscesses none, local erythema extending beyond the site of injection a few, general eruption but one. No erysipelas. We have observed pain in the diseased part, in other limbs, swelling of glands sometimes in distant parts, perspiration, headache, rigors, languor, insomnia, palpitations, angina pectoris, nausea, increase of appetite, very slight jaundice, albuminuria in a few cases, increase of cough, diminution of cough, dyspnœa, rhonchi on expected and unexpected places, new regions of dulness, more expectoration—mostly in the beginning of treatment, change of its purulent into mucous character, increase or mostly decrease of secretion from accessible tuberculous parts, swelling of spleen and a peculiar form of glossitis in a few cases.

The results of, or events after, a protracted course of inoculations, may briefly be summed up as follows :

Tuberculosis of right knee. No change.

Dorsal spondylitis. No change.

Tubercular abscess in right inguinal region. No improvement.

Tubercular disease of right hip. No improvement.

Tuberculosis of right knee. No improvement.

Tuberculosis of right elbow. No improvement.

Tubercular ankle-joint, fistula. No improvement (in sixteen days).

Tubercular knee-joint. Death from miliary acute tuberculosis.

Caries of vertebræ and ribs. No improvement.

Cold abscess from right sacro-iliac synchondrosis. Slight improvement.

Tuberculosis of left tibio-tarsal articulation. Improvement.

Cutaneous tuberculosis. Great improvement.

Lupus vulgaris of nose and lip. Great improvement.

Epithelioma of right temple and face. No improvement.

Epithelioma of left temple and eyelid. No improvement.

Tubercular meningitis, almost moribund. No change.

Tubercular peritonitis. Two cases. Not influenced.

Pulmonary tuberculosis. Five cases. Improved. One of them relapsed and got worse.

Pulmonary tuberculosis. Four cases. Much improved.

Pulmonary tuberculosis. Two cases. Disappearance of local symptoms. Recovery. (Bacilli found in one.)

Pulmonary tuberculosis. Four cases. Not improved. Laryngeal tuberculosis in one of these much improved.

Pulmonary tuberculosis. One case. Died. Laryngeal ulcerations much improved.

I repeat: Of eleven cases of tuberculosis of bones and joints, eight were not improved, one died, two were improved.

Two cases of epithelioma not improved.

Two cases of cutaneous tuberculosis (one lupus) greatly improved.

Tubercular meningitis and peritonitis not influenced.

Of sixteen cases of pulmonary tuberculosis one died, four were not improved, five were improved, four were

much improved, two recovered, even with disappearance of local pulmonary changes.

The two cases complicated with laryngeal tuberculosis did not thrive. One was not improved, one died. But in either the laryngeal ulcerations improved.[1]

I do not wish to compare these results with any other statistics, but offer them simply as contributions to the general stock of observation. The number of favorable cases of joint and bone tuberculosis strikes me as small, of pulmonary tuberculosis as large. When I ask myself what became of sixteen average cases of pulmonary tuberculosis admitted to our hospitals, before the inoculation epoch, the answer is very discouraging. It is true that most of the patients whose cases have been detailed above were placed in better conditions than ever before, and thus were given a more favorable chance for improvement. But so were all those who were admitted with tuberculosis any season, and any year; with hardly any resting place awaiting them but the dead-house.

Altogether, tuberculin has proven a remedy of great power for good, and for possible evil. It required credulous people believing in miracles to expect the impossible, and it took all the accumulated ignorance of centuries to believe in the possibility of reversing the rules of nature, which is as impartial in restoring as it is pitiless in destroying, subject to irrevocable laws. When great genii like Pasteur and Koch enrich the world with new discoveries in the fields of pathology and therapeutics, even then we must not look for infallibility. Tuberculin has been heralded as witchcraft by sensationalists. What it has done, and can do, is more than any other remedy —except climatic treatment in pulmonary tuberculosis and surgical interference in select cases of local tuberculosis—has succeeded in accomplishing. From what little I have observed it would appear that the next future of

[1] A number of cases treated have not been accounted for, for the reason that the time of observation was too brief to yield any reliable result.

successful treatment of pulmonary tuberculosis consists in the combination of climatic cures with the careful and persistent use of tuberculin. That is what we have to be thankful for even at this early date. At all events it is more becoming to honor our great men by appreciative criticism than to apotheose them first and exile them afterward. The former is the way of professional intellect and decorum, the latter that of a whimsical and flighty personal "government." [1]

[1] To the house staffs of the German, Foundling, and Skin and Cancer Hospitals, I herewith express my appreciative thanks for their many and persistent labors connected with the accumulation of facts referring to the inoculations. They were indeed labors of love, with all of them.