The Friedmann treatment for tuberculosis : a report of the board appointed for its investigation / by John F. Anderson and Arthur M. Stimson.

TREASURY DEPARTMENT
UNITED STATES PUBLIC HEALTH SERVICE

HYGIENIC LABORATORY—BULLETIN No. 99

OCTOBER, 1914

THE FRIEDMANN TREATMENT FOR TUBERCULOSIS

A REPORT OF THE BOARD APPOINTED FOR ITS INVESTIGATION

BY

JOHN F. ANDERSON

AND

ARTHUR M. STIMSON

WASHINGTON
GOVERNMENT PRINTING OFFICE
1914

TREASURY DEPARTMENT
UNITED STATES PUBLIC HEALTH SERVICE

HYGIENIC LABORATORY—BULLETIN No. 99

OCTOBER, 1914

THE FRIEDMANN TREATMENT FOR TUBERCULOSIS

A REPORT OF THE BOARD APPOINTED FOR ITS INVESTIGATION

BY

JOHN F. ANDERSON

AND

ARTHUR M. STIMSON

WASHINGTON
GOVERNMENT PRINTING OFFICE
1914

ORGANIZATION OF HYGIENIC LABORATORY.

RUPERT BLUE, *Surgeon General.*

United States Public Health Service.

ADVISORY BOARD.

Maj. Eugene R. Whitmore, Medical Corps, United States Army; Medical Inspector E. R. Stitt, United States Navy; Dr. A. D. Melvin, Chief of United States Bureau of Animal Industry; and John F. Anderson, United States Public Health Service, *ex officio.*

Prof. William H. Welch, Johns Hopkins University, Baltimore, Md.; Prof. Simon Flexner, Rockefeller Institute for Medical Research, New York; Prof. Victor C. Vaughan, University of Michigan, Ann Arbor, Mich.; Prof. William T. Sedgwick, Massachusetts Institute of Technology, Boston, Mass.; Prof. Mazyck P. Ravenel, University of Missouri, Columbia, Mo.

LABORATORY CORPS.

Director.—Surg. John F. Anderson.
Assistant director.—Surg. Arthur M. Stimson.
Senior pharmacist.—C. O. Sterns, Ph. G.
Junior pharmacist.—Clyde Ritter, Ph. G.
Artist.—Leonard H. Wilder.

DIVISION OF PATHOLOGY AND BACTERIOLOGY.

In charge of division.—Surg. John F. Anderson.
Assistants.—Surgs. W. J. Pettus, Hugh S. Cumming, Leslie L. Lumsden, Lunsford D. Fricks, Carroll Fox, Joseph W. Schereschewsky, Taliaferro Clark, Arthur M. Stimson, and R. H. Creel; Passed Asst. Surgs. H. E. Hasseltine, James P. Leake, W. F. Draper, and Asst. Surg. C. L. Williams.

DIVISION OF ZOOLOGY.

Professor of zoology.—Ch. Wardell Stiles, Ph. D., LL. D., D. Sc.
Assistant.—Surg. Joseph Goldberger.
Technical assistant.—Walter D. Cannon, A. B., LL. B., MD.

DIVISION OF PHARMACOLOGY.

Professor of pharmacology.—Carl Voegtlin, Ph. D.
Technical assistants.—Atherton Seidell, Ph. D.; Murray Galt Motter, A. M., M. D.; Martin I. Wilbert, Ph. M.; George B. Roth, A. B., M. D.

DIVISION OF CHEMISTRY.

Professor of chemistry.—Earle B. Phelps, S. B.
Sanitary chemist.—Albert F. Stevenson, S. B.
Technical assistant.—Elias Elvove, M. S., Pharm. D.

CONTENTS.

ILLUSTRATIONS.

THE FRIEDMANN TREATMENT FOR TUBERCULOSIS.

By JOHN F. ANDERSON and ARTHUR M. STIMSON.

PART I.

INTRODUCTION.[1]

As a means of protecting the public health Congress imposed upon the Secretary of the Treasury the duty of controlling the importation and sale in interstate traffic of serums, viruses, and similar biologic products used in the prevention and cure of the diseases of man. The Secretary of the Treasury bases his activities in these matters on inspections and investigations made by the Public Health Service and recommendations submitted by the Surgeon General of that service.

The treatment for tuberculosis proposed by Dr. Friedrich Franz Friedmann, of Berlin, Germany, belongs to the class of biologic products mentioned in the law, which is subject to consideration by the Secretary of the Treasury and investigation by the Public Health Service.

Aside from these considerations, however, the importance of the announcement of a specific for the treatment of tuberculosis made it incumbent on the Public Health Service to undertake an investigation to ascertain the merits of such a preparation in the prevention or cure of the disease, and to determine its harmlessness when administered to individuals.

For a time the question of sending an officer of the Public Health Service to Berlin, Germany, to make an investigation of Dr. Friedmann's claims was given serious consideration; but this plan was abandoned when it was found that Dr. Friedmann contemplated an early visit to this country.

Upon his arrival in New York, representatives of the Public Health Service conferred with him and certain tentative arrangements were agreed upon for an investigation of his treatment and the results of its use upon patients.

[1] Manuscript submitted for publication July 30, 1914.

Accordingly, the following letter was written Dr. Friedmann:

TREASURY DEPARTMENT,
OFFICE OF THE SECRETARY,
Washington, March 3, 1913.

DR. FRIEDRICH FRANZ FRIEDMANN,
Waldorf-Astoria, New York.

SIR: As you are already aware, the attention of this Government has been called to your announcement of a preparation for the cure of tuberculosis. Through official channels the United States Public Health Service has been kept informed of events in connection therewith, and a copy of your letter of January 12, 1913, addressed to the American consul general at Berlin, was received by the Surgeon General February 3, which letter reads as follows:

"It has come to my notice that your Government has asked you to make a report upon my tuberculosis remedy. I would like to say that I extend to your Government through you an invitation to investigate my remedy and the results attained. I will place at the disposal of your Government's investigators all the facts at my command and afford them every aid to prepare a comprehensive and impartial report."

On account of the great importance of your announcement, and in view of your invitation, it was determined to send an officer of the Hygienic Laboratory to Berlin to take advantage of your offer to make such investigations as would enable him to make a comprehensive and impartial report. In the meantime it was learned that you expected to come to New York, and arrangements were accordingly made to have Surg. M. H. Foster, on duty at New York, meet the *Kronprinzessin Cecilie* on arrival for the purpose of informing you that the Public Health Service was prepared to accept your invitation to make an investigation, and that an officer would call on you at such time and place as might be convenient to arrange the necessary details.

On receipt of a telegraphic report from Dr. Foster, Surg. John F. Anderson, director of the hygienic laboratory, was sent to New York to confer with you. On his return Dr. Anderson reported that you would furnish him a culture of your organism in a few days, but that you stated that it would be of no use to him or to any one else for a proper study unless the person receiving it had been instructed by you during a period of from six to eight weeks as to its proper manner of preparation and use. He further reported that you would permit an investigation, but that the person who undertook to do so would have to have the necessary training under you, as above mentioned.

On account of the importance to humanity of an announcement such as yours, which gives promise that a means has been discovered to combat tuberculosis, and because of the great public interest that has been aroused by dispatches in the press, I desire to arrange at once for a comprehensive investigation of your preparation, and will have the studies conducted under the auspices of the United States Public Health Service. Under the act of Congress approved July 1, 1902, this department is charged with the supervision of the preparation and sale of viruses, serums, and toxins in interstate traffic. This act reads in part as follows:

"No person shall sell, barter, or exchange, or offer for sale, barter, or exchange in the District of Columbia, or send, carry, or bring for sale, barter, or exchange from any State, Territory, or the District of Columbia into any State, Territory, or the District of Columbia, or from any foreign country into the United States, * * * any virus, therapeutic serum, toxin, antitoxin, or analogous product applicable to the prevention and cure of diseases of man, unless (*a*) such virus, serum, toxin, antitoxin, or product has been propagated

and prepared at an establishment holding an unsuspended and unrevoked license, issued by the Secretary of the Treasury as hereinafter authorized * * *."

The provisions of the above-mentioned law make it incumbent on the department to make an effort to inquire into biologic products propagated for the cure of diseases of man.

I have to inform you, therefore, that the Treasury Department, through the Public Health Service, will enter into any reasonable arrangement for an investigation of your preparation, that after the necessary arrangements have been made cultures of your organism will be accepted for purposes of study, and one or more officers will be designated to associate themselves with you for the purpose of learning the method of preparation and use of your remedy and its effects on cases of tuberculosis. After necessary studies have been conducted to determine the harmlessness of inoculating human beings with your culture, arrangements can be made for admittance to hospital of such cases of tuberculosis as apply and may be selected, the treatment to be administered by you under the observation of the officers to be selected and such other experts as may be associated with them.

Respectfully,

FRANKLIN MACVEAGH, *Secretary.*

To this the following reply was received:

[Telegram.]

NEW YORK, *March 6, 1913.*

SECRETARY OF THE TREASURY, *Washington:*

Acknowledging letter of Secretary MacVeagh, I welcome an official test. My cultures at your disposal. Please wire if your medical representatives can be here March 9 for demonstration on patients.

FRIEDMANN,
Ansonia Hotel.

Following this correspondence, it was decided to appoint a board of officers to undertake the investigation contemplated, both by the observation of patients treated by Dr. Friedmann and by certain studies to be made in the hygienic laboratory of the effect of the culture upon the laboratory animals.

A board of officers was convened in accordance with the following letter:

MARCH 8, 1913.

Surg. JOHN F. ANDERSON,
United States Public Health Service,
Director Hygienic Laboratory, Washington, D. C.

SIR: A board of medical officers is hereby convened to make such investigations as may be practicable of the tuberculosis remedy recently announced by Dr. Friedrich Franz Friedmann.

Detail for the board: Surg. John F. Anderson, Director Hygienic Laboratory, chairman; Passed Asst. Surg. A. M. Stimson, Hygienic Laboratory, recorder.

The board will hold a meeting in New York March 9 for conference with Dr. Friedmann and for observing his methods of use of the preparation. The board will hold such subsequent meetings in New York as may be necessary to determine the efficacy of this remedy in the treatment of tuberculosis, and the board or each member will make such trips from Washington to New York and return as may be required in carrying out these investigations.

There is inclosed herewith correspondence had with Dr. Friedmann, in which it is stated that the department, through the Public Health Service, will enter into any reasonable arrangement for an investigation of the preparation in question. After the necessary arrangements shall have been made, the board will receive cultures of the organism used for studies in the Hygienic Laboratory, and the recorder of the board will associate himself with Dr. Friedmann in New York for such time as may be necessary to learn the method of preparation and use of the new remedy and to observe its effects on any cases of tuberculosis to whom it may be administered. Should it be deemed advisable by the board to arrange for admittance to hospital of cases of tuberculosis, the matter should be taken up with the bureau and the necessary recommendations made.

While on this detail your status will be that of special temporary duty, and upon completion of the duty enjoined you will rejoin your station in Washington, D. C.

Respectfully,

RUPERT BLUE,
Surgeon General.

The expenses incurred in carrying out the foregoing instructions are hereby authorized.

SHERMAN ALLEN,
Assistant Secretary.

The board held its first meeting in New York City on March 9, 1913, and arranged for an interview with Dr. Friedmann for the same day. At this meeting Dr. Friedmann delivered to the board a culture of an organism claimed by him to be the one used by him for the preparation of his vaccine; he declined to make known the method of preparation of the vaccine from the culture. At this meeting arrangements were completed for the treatment in certain hospitals in New York City by Dr. Friedmann of persons suffering from tuberculosis.

Arrangements were made for the treatment of patients in Mount Sinai Hospital, Bellevue Hospital, Montefiore Home, and Seton Hospital. Through the cooperation of the above-named institutions a sufficient number of cases of tuberculosis, both medical and surgical, in various stages of the disease, was placed at our disposal, but the board early exposed a reluctance on the part of Dr. Friedmann to treat even the limited number finally given the treatment. While we have not an exact record of the number of patients selected for treatment, we do know that not half of those selected were treated. This was especially the case with patients at the Montefiore Home and at Seton Hospital. At considerable expense and labor a number—at least 20—of incipient cases of pulmonary tuberculosis were brought from Bedford to the former institution for treatment, but Dr. Friedmann declined to administer the treatment to them.

About this time our insistence on Dr. Friedmann for a more rapid progress in his demonstration became so urgent that he finally declared himself willing to treat a series of 100 cases in a single hospital if such arrangements could be made. Accordingly 100 patients

in various stages of the disease, including both medical and surgical cases, were selected for treatment at Seton Hospital, and although Dr. Friedmann had positively agreed to treat that number, he actually only administered the treatment to 17. He gave as his reason a lack of sufficient amounts of vaccine, but from what we now know of the ease with which it can be prepared, this was not the true reason. Moreover, he at that time had ample vaccine, as was shown by the treatment immediately after of a considerable number of patients elsewhere.

The evident reluctance on the part of Dr. Friedmann to treat a larger number of patients under our supervision and his refusal to give second treatments to those declared by him to be ready for such treatment became so accentuated that on April 15 the following letter was sent by registered mail to Dr. Friedmann:

APRIL 15, 1913.

DR. FRIEDRICH FRANZ FRIEDMANN,
Hotel Narragansett, Providence, R. I.

SIR: We regret to have to invite your attention to the halting progress in your demonstration of the alleged curative value of your remedy for tuberculosis. Only 94 of the patients accepted by you as suitable for such test have been treated by you. In order to avoid undue prolongation of your demonstration and to avoid unnecessary delay in advising the public of the judgment that we may be able to form of the value of your treatment, we are forced to limit our clinical studies to the number already treated under our observation in the hospitals in New York City.

From conversations with you it is understood that some of these patients are now ready for a further injection of your remedy. In their interest and for the reasons given for limiting our clinical observations to those already treated, we feel that these patients should now be seen by you with the view of giving such additional injections of your remedy as may, in your judgment, be necessary to effect a cure. We should be pleased, therefore, to have you give this matter your prompt attention and inform us regarding the same at an early date.

We may be communicated with in writing addressed either to Dr. A. M. Stimson, Hotel Martinique, New York City, or to Dr. John F. Anderson, Director Hygienic Laboratory, Washington, D. C.

Respectfully,

JOHN F. ANDERSON,
Director Hygienic Laboratory, Chairman of the Board.

No reply was received to this letter, although soon after a certain number of cases were given a second treatment.

The frequent absence of Dr. Friedmann from New York City during this period greatly interfered with the investigation. His general attitude of suspicion, his lack of sympathy with the studies, his secretiveness and vacillation, so at variance with his expressed willingness "to place at the disposal of the Government investigators all the facts at my (his) command and afford them every aid to prepare a comprehensive and impartial report," further greatly added to the difficulties.

About May 1, 1913, it was deemed wise to make public a progress report of the investigation because so many requests were being received by the Public Health Service for information as to the results of the investigation and because certain reports had appeared in the press purporting to be expressions of opinion on the part of the board. This report was published in the Public Health Reports of May 16, 1913, and stated that—

> Without presenting in detail the condition of patients under observation, we are in a position to state that the effects so far observed do not justify that confidence in the remedy which has been inspired by widespread publicity.

The investigations made by the board consisted of the clinical observations of medical and surgical cases of tuberculosis treated by Dr. Friedmann, and of certain laboratory studies of a culture of an organism given to the board by Dr. Friedmann. In addition, certain studies were made of cultures made by us from the material used by him for the treatment of patients.

Although numerous reports have appeared in the American and European literature of investigations by others of the claims of Dr. Friedmann, we have not deemed it necessary to review them here, but have confined this report to the studies made by ourselves. It may, however, be stated that the reports of other investigators have been almost uniformly against the validity of the claims of Dr. Friedmann.

It is a pleasure for us to make acknowledgment of many courtesies and assistance to the board by representatives of the New York City Department of Health, the staff and authorities of Mount Sinai, Bellevue, and Seton Hospitals, and of the Montefiore Home; to Surg. Lavinder for assistance in some of the clinical studies; and especially to Passed Asst. Surg. Leake for his services in the laboratory studies.

Respectfully submitted.

JOHN F. ANDERSON,
Director Hygienic Laboratory, Chairman of the Board.
A. M. STIMSON,
Passed Assistant Surgeon, Recorder of the Board.

PART II.

SUBJECT MATTER OF THE INVESTIGATION.

The matter before the board for investigation consisted of the statements made by Dr. Friedmann before the Berlin Medical Society and published in the Berliner Klinische Wochenschrift, Nos. 47 and 49, 1912; the results of treatment of 88 cases by Dr. Friedmann under our observation; and our observations on the culture of bacteria presented to us by Dr. Friedmann, and said by him to be used in a certain way, not described, in the preparation of his remedy.

It is realized that the public may have judged Dr. Friedmann's methods on the basis of the extravagant claims for his treatment which appeared at times in the lay press. These claims we would not be justified in attributing to Dr. Friedmann.

The most significant statements contained in Dr. Friedmann's article as translated from the German appear to us to be the following:

"I have tested many and various avirulent cultures for curative purposes, including those derived from man and made avirulent by certain measures, but have found that the curative results were only slightly gratifying. This was changed instantly when I made use of an *avirulent tubercle strain* which I had secured several years ago, but which became *completely changed in its action only recently.* Formerly this strain *was unsuitable* for *therapeutic use in man.* Only after I was enabled to remove the *last trace of virulence* by suitable cultivation and passage did I make use of the preparation on people."

From this paragraph we infer the following three claims:

1. The organism is a tubercle bacillus.
2. It was formerly not entirely free from virulence.
3. The change which made it suitable for therapeutic use has been a recent one.

His further claims were:

4. "The preparation has shown itself completely harmless even in large doses by every method of administration."
5. "The treatment consists of intramuscular injections, one, two, or three, seldom more."
6. "Repeated at various intervals."
7. "Success or failure are dependent upon the complete resorption of the preparation."
8. "There must develop at the site of injection an infiltration from the size of a nut to that of a small apple."

9. "Which disappears gradually in the course of the following weeks and months."

10. "As long as this tissue remains and while the gradual resorption goes on, the cure progresses."

11. "Only when and while the injected substance is completely taken up and remains in the body does the specific curative effect appear in response thereto, but in this case it does so regularly in a very short space of time, in the most noticeable manner, and with constant progression."

12. "As a *result of a single injection* we often see bone and joint fistulæ of years' duration become clean and close up, scrofulous skin lesions become covered with young sound skin, large hard gland tumors become materially smaller, tubercular abscesses flatten out and cicatrize, chronic scrofulous eczema permanently heal, and, last but not least, cases of *lung tuberculosis* cease their complaints and lose their *physical signs* of disease."

13. "On the other hand, whenever the resorption of the substance is incomplete, wherever the deposit at the point of injection *undergoes a partial breaking down* after weeks or even sometimes months from obscure causes and begins *to discharge*, or even removes itself from the body in the form of *an abscess*, in these cases the cure *often but not always* remains stationary, and one would *accomplish nothing in such cases by further injection*, but would subject the patient only to a *new discharging infiltration or abscess* without doing him any good."

14. "In this manner I formerly had failures in many cases, or at least partial incomplete cures. I do not desire to conceal the great imperfections of my former methods, nor their difficulties."

15. "For instance, I found that in those cases where the *Pirquet reaction was commonly negative or nearly negative*, in cases of consumption of a progressive character, in severe or multiple tubercular bone lesions, especially in cases of progressive tuberculosis propagated by the circulation, the first injection was followed without exception by a *rapid, complete resorption*, with only a small remaining infiltration. Only after the second or third injection in such cases did specific hypersusceptibility manifest itself in the form of a considerable infiltrate."

16. "On the other hand, if the cutaneous reaction is *very strongly positive* and the case is not a very light one no complete cure will follow a simple subcutaneous or intramuscular injection."

17. "Following the intravenous introduction of the remedy, which aside from transient fever and depression is always well borne, even in large doses, there is *often* observed an immediate result with quickly commencing healing, and then, however, as if cut off, an absolute cessation of the curative process."

18. "But still another great difficulty appeared in the further treatment of cases *previously injected intravenously with large doses.* It consists in the fact that by this treatment the patients have acquired the power of completely dissolving the remedy, and that large doses administered subcutaneously or intramuscularly become immediately dissolved without causing any considerable infiltrate or significant curative effect."

19. "I therefore concluded to unite the advantages offered by each method of introduction by combining the methods. And as a matter of fact the *results of the simultaneous method were such* that now *abscesses were completely avoided*, that beautiful infiltrations were formed and well absorbed gradually, and that correspondingly the *curative effects* could be described as very gratifying."

20. "The sovereign form of administering the remedy is and remains the subcutaneous or intramuscular."

21. "The combination with the intravenous treatment can have for its object only the preparation of the body to receive the subcutaneous treatment."

22. "It is, however, possible to break up with certainty the specific hypersusceptibility by purely subcutaneous methods, namely, by intermittent treatment with certain *specific bacterial products prepared by me.*"

23. "In those cases of *bone and joint tuberculosis* in which the preparation is resorbed and cure follows, relapses do not occur. In fistulæ firm scars gradually becoming pale and without tenderness are found. With the exception of one hopeless case with total destruction of the pelvis, peritonitis, and extensive amyloid, and 2 cases of 75-year-old women with dry caries, all 12 cases of bone fistulæ treated by me have been cured."

24. "Cases of pulmonary tuberculosis when the destruction has not progressed altogether too far show almost without exception *a reduction of the manifestations* after resorption of the remedy."

25. "Since the intramuscular injection *never causes focal reaction*,"

26. "One *never observes hemoptysis* as a *consequence of or following the injections.* Rather when this has previously existed it usually disappears."

27. "The first symptom which regularly disappears and remains absent is *night sweating.* Except in cases of severe mixed infection the *fever also diminishes very rapidly.* A long series of purely subjective symptoms disappears very early."

28. "Also progressive loss of flesh is commonly arrested shortly after the beginning of treatment and the patient *gains almost always.*"

29. "In no case was it necessary for a patient to quit work on account of the treatment. Many who for months had been unfit for

work were able to go back to work *a few weeks* after the first injection."

30. "Under the influence of the injection, cough and expectoration disappeared."

31. "At the same time the auscultatory phenomena, such as rales, became better gradually and disappeared."

32. "In those cases of tubercular skin disease which are probably often due to the bovine bacillus, * * * the specific hypersusceptibility is often very marked and thereby the taking hold of the remedy is made difficult. *The result is obtained in these cases, however, by the simultaneous method of injection.*"

33. "After the preparation had shown itself harmless within the widest limits in *man and animals*, and after the progressive and *permanent* cures in man were beyond question, I made use of the remedy for purposes of protective inoculation in children. So far 335 children from 1 hour to 3 years of age have been inoculated. Although the oldest series were inoculated more than a year ago, not the slightest trace of beginning scrofula or tuberculosis has appeared in any case."

34. "In contrast to these weakly virulent bacilli" (experiments of Orth and Rabinowitsch), "the completely avirulent bacilli which enter into the composition of the preparation used by me on man, are *never to be found* in the *guinea pig body even after a short time.* It is to be emphatically stated that my preparation is completely *harmless* for guinea pigs; even if one injects several times the dose used for man, the animals are found altogether sound, if killed years afterwards."

35. "These animals never show cavitation following virulent injection."

36. "Although they *do not possess full immunity against* the severe artificial infection, still while untreated animals infected with tuberculosis die on the average after 110 days, they are kept alive 363 days, near a year, by a *single therapeutic injection of this remedy.* And in the same way a single immunizing injection is sufficient to preserve the life of the animal previously treated and subsequently injected with highly virulent human tubercle bacilli, more than four times as long as the control; that is, the animal only infected with human tubercle bacilli."

In the discussion repeated demands were made upon Dr. Friedmann for a statement of the exact nature of his remedy. He still refrained from a definite statement, but his language leads one to infer that his *bacillus is not of human origin*, but is derived from a *naturally infected turtle*, and is the third which he has isolated, originally of very low virulence, but now absolutely avirulent. In

his communications with us he has not made any more definite statements than are contained in his address.

Dr. Friedmann's presentation and citation of cases constitute a claim of curative property for his preparation. The very few failures reported are invariably explained on the basis of very advanced tubercular processes. There is no tabulation of cases showing the proportion of successes to failures. Hence we are evidently desired to assume that in cases not very far advanced, cures are the rule.

These in brief are the claims which we were to investigate. In this inquiry we have not had the advantage of accurate knowledge concerning the composition of the material used for injection, inasmuch as Dr. Friedmann, contrary to what his communications with us previous to his coming to America had led us to expect, has not divulged the method of preparation. He furnished us with a culture which he said was used in the preparation of his "remedy," and we shall report such observations as we have made upon it.

PART III.

CLINICAL OBSERVATIONS.

Our clinical material for determining the curative properties of Dr. Friedmann's preparation was collected through the courtesy of the authorities of four New York hospitals. We take this opportunity of expressing our deep appreciation of the kindness shown us by the authorities and personnel of Bellevue and allied hospitals, Mount Sinai Hospital, the Montefiore Home for Chronic Invalids, and the Seton Hospital, in affording us access to these cases and their records, and in forwarding in every way the observation of the effects of the treatment upon them.

We observed the treatment of 94 cases, and were prepared to furnish many more for treatment, but owing to Dr. Friedmann's delay in treating these cases for reasons which did not seem to us satisfactory, we were obliged to limit our observations to this number. Five of this number escaped more than a few days' observation and will not be reported upon.

Dr. Friedmann was disposed to criticize our material as being too far advanced in many cases. It is quite true that a large proportion of our pulmonary cases must be described according to the Turban method of classification, as belonging to the third stage. But this does not tell the whole truth, since a good many of these third-stage cases were in excellent general condition, without fever, of good body weight, with little cough and expectoration, and stationary or very slowly progressive lesions. Moreover, a considerable number of incipient or moderately advanced cases were brought at no little expense and inconvenience from a country sanatorium and presented to Dr. Friedmann for treatment, but he refused them on the ground that since they were already doing well, the beneficial effects of the treatment would not be as apparent as in those having more pronounced symptoms. Our surgical cases were not numerous, and some of them were perhaps not adapted for demonstration purposes on account of long duration and considerable destruction of tissue. Still, some of the cures or marked beneficial results reported by Dr. Friedmann were in just such cases. A number of suitable orthopedic cases were awaiting treatment at the time when Dr. Friedmann left New York for Providence, he having postponed their treatment ostensibly for lack of injection material.

Following are brief excerpts from the clinical histories and notes on the clinical material.

ABSTRACT OF CLINICAL HISTORIES.

No. 1. S. B.—Pulmonary tuberculosis, II stage; laryngeal tuberculosis.—Improving when treated. Four years' duration. Pulmonary condition involves one upper lobe. Moist lesions, no cavitation. Infiltration both cords and arytenoids. Nodules on both cords, removed by operation February 18, and lactic acid applied. Gained 11 pounds in two months preceding treatment. General condition, fair; weight, 127 pounds; maximum temperature, 99.5°.

Treated 0.3 c. c. intramuscularly, March 9, 1913. Transient induration.

Treated 0.15 c. c. intramuscularly, May 17, 1913. Transient induration.

RESULT: Ten days after first treatment laryngologist reports marked improvement in larynx, more than he expected as result of operation March 22, 13 days after injection, weight 117 pounds, loss of 10 pounds. Feels poorly. Subsequently began to gain weight and feel better again. Two weeks after the second injection began to feel badly, was feverish and very weak. Coughed much but expectorated little. Throat painful.

Three months and four days after first injection patient is about the same condition as before treatment. Believes the treatment did him no good. Lost weight, which he has regained, lacking 2½ pounds. Physical signs about the same as before treatment, both in lungs and larynx.

SUMMARY: Patient's improvement before treatment did not continue after it. Temporary improvement in laryngeal condition, followed by retrogression in general condition. A special relation between the disease and the treatment seemed to be established, but the patient was not favorably influenced in the end.

March 27, 1914. Seen. Has returned to hospital, but has not been able to work since last last seen. Has been getting worse recently. Throat painful, hurts to swallow, coughs much. Temperature 98° to 102°; weight 109 pounds.

Laryngologist reports "much induration over left half of larynx at site of false vocal cords, both arytenoids infiltrated." Chest signs show extensions of lesion at right apex and beginning involvement of left apex. Loss of weight very apparent.

No. 2. C. H.—Pulmonary tuberculosis, I; floating kidney.—A case of slight involvement at right apex. No cough, no fever. Sputum positive for tubercle bacilli only after 12 examinations and then by antiformin method. Under hospital treatment gained 5½ pounds in the 12 days preceding treatment. Weight at time of treatment, 128½ pounds.

Treatment, 0.2 c. c. intramuscularly, March 9, small nodule palpable for six weeks.

RESULT: Three months later, gained 2 pounds in 18 days following treatment—i. e., at a slower rate than previously. No change in general condition. This case is not regarded as a suitable test case on account of the absence of symptoms, and the very inconclusive physical signs.

No. 3. H. R.—Pulmonary tuberculosis, I; acute pneumonia.—This patient admitted to hospital with symptoms and signs of acute pneumonia of the right upper lobe. Had been sick but a few days. High fever. On being put to bed he improved rapidly, temperature fell to normal and he began to gain weight. Tubercle bacilli in sputum.

Treatment, 0.3 c. c. intramuscularly March 9, 1913; transient infiltration.

RESULT: Continued to improve after treatment as before. Gained 13 pounds in two months. The last five examinations of sputum negative for tubercle bacilli. Has gone to the country and his friends report that he is in fine condition. Physical signs at last examination, same as before treatment, high-pitched expiration right apex, no râles. Still had a little cough when last seen. It is difficult to determine whether the undoubted improvement was due to the treatment or not, as he was gaining rapidly before it.

No. 4. E. J.—Pulmonary tuberculosis, III.—Constant cough one year. Sputum blood tinged at times. Moderate emaciation. Loss of 6½ pounds in seven weeks preceding treatment. Night sweats disappeared after admission to hospital. Cavitation right apex, disseminated lesions right side. A few râles at left apex. Runs irregular temperature to 102°.

Treatment, 0.3 c. c. intramuscularly March 9, pullet's egg infiltration gradually absorbed during following weeks.

Treatment, 0.15 c. c. intramuscularly May 17, transient infiltration.

RESULT: Three months later. No improvement observed. Some extension of the lesion followed by retrogression to original condition. Febrile temperature continues with temporary respites. Has lost 4½ pounds since treatment. Weight, 86 pounds; tubercle bacilli in sputum.

No. 5. L. R.—Pulmonary tuberculosis, I.—Apparently recovered from a severe cough nine months before treatment, but had been losing weight when admitted and had suffered three days before admission with copious hemoptysis. General condition fairly good. Very scanty physical signs consisting of a variable number of moist râles at right apex and on the left side just above the pericardium at the fourth rib. At some examinations these could not be heard. Had gained 8¾ pounds in the hospital before treatment. Hemoptysis had ceased. Tubercle bacilli present in sputum. Temperature occasionally reaches 101°–102° F.

Treatment, 0.1 c. c. intramuscularly March 9, 1913, small nodule which disappeared in two months.

Treatment, 0.1 c. c. intramuscularly May 17, 1913, developed an infiltrate which was the size of a cherry one month later.

RESULT: April 15, five weeks after injection, had considerable blood spitting. In general there has been slight improvement. Following each injection at a period of three to four weeks, the local site became painful, and at the same time the patient felt very badly in condition. Dr. Friedmann attached importance to this and said that another injection at this time would surely cause abscess formation. Patient gained 3 pounds in three months, that is, at a slower rate than before treatment. Three months after treatment râles could still be heard on coughing at the original site and she was suffering with a new pain in the right chest. Temperature usually under 100°.

The very slight improvement in this favorable case is not as great as would be expected from sanatorium treatment in favorable surroundings for the same length of time.

No. 6. T. Z.—Pulmonary tuberculosis, III.—An unfavorable case of a year's duration, with extensive disseminated infiltration of the left lung and suspected cavitation. Has lost 5½ pounds in two months in the hospital. Febrile temperature when confined to bed.

Treatment, 0.2 c. c. intramuscularly March 9, 1913, followed by induration of long duration, terminating in abscess formation. Still discharging three months later.

RESULT: No improvement; loss of 5½ pounds in three months. Some increase of physical signs at right apex. Fever and subjective symptoms unimproved.

No. 7. B. G.—Pulmonary tuberculosis, III.—Some symptoms about three months following influenza. Disseminated infiltration left lung with probable

cavitation, rough breathing right apex. With rest in bed, gained 7 pounds in 6 weeks, and amelioration of cough and night sweats, but temperature occasionally rises to 101°.

Treatment, 0.3 c. c. intramuscularly March 9, 1913, transient local reaction.

Treatment, 0.15 c. c. intramuscularly May 17, 1913, transient local reaction.

RESULT: Appeared to be improving slowly after the first injection, but after the second injection temperature ran a high course (103° maximum) for three weeks, all symptoms aggravated and patient lost weight. Patient does not desire further treatment. Developed a pleural effusion of small amount of fluid. Physical signs show a slight improvement in lung condition, but the general condition is worse. Fever, maximum 101.2°.

A specific action of the treatment seems probable, but not to the advantage of the patient.

No. 8. W. B.—Tuberculosis of right kidney.—Painful attacks in kidney region one year. Hematuria, 4 months. Painful and frequent micturition. No loss of weight, general condition good. Tuberculin tests positive. Tubercle bacilli in urine from right kidney demonstrated by guinea-pig test. Edema of bladder wall around orifice of right ureter.

Treatment, 0.6 c. c. intramuscularly March 9, 1913, transient local infiltration.

Treatment, 0.5 c. c. intravenously March 9, 1913, three days' fever and depression.

Treatment, 0.3 c. c. intramuscularly May 17, 1913, no subsequent observation.

Following the first treatment, frequency and pain were improved. Tubercle bacilli still present in urine. Later complained of return of pain in kidney, but not on micturition, and of having to get up at night to urinate, which he had not before. The effects of second treatment were not observed, as efforts to locate the patient failed.

SUMMARY: The improvement noted was not greater than is often observed under the influence of rest and diet.

No. 9. S. S.—Pulmonary tuberculosis, II.—States that he has lost 40 pounds in 6 months. Never had hemorrhage. Severe pains in the left chest. Much cough. Temperature, 102° maximum, remittent; weight, 128 pounds; infiltration both apices. Râles only on coughing. No cavitation. Tubercle bacilli in sputum. Pirquet positive.

Treatment, March 17, 1913, intramuscular 0.1 c. c., slight persistent infiltration.

Treatment, May 17, 1913, intramuscular 0.15 c. c., transient infiltration.

RESULT: Three months after first injection, lung condition not significantly changed. Still has rales on coughing. Subjective symptoms about the same, but says he eats and sleeps better, and has not felt feverish. Has left hospital and does not take temperature. When seen his temperature was normal. Attempted to work at his trade of cooper for a few days, but had to give it up. Still has pain in chest. Weighs about 6 pounds more than before.

SUMMARY: The slight improvement in this case is confined to reduction of temperature and gain of weight. It might amply be accounted for by his rest in the hospital.

No. 10. J. R.—Pulmonary tuberculosis, II; pleural effusion.—Had been sick three years. Is about 7 pounds under his best weight. Complains of pain in left chest at times. Much cough and increasing weakness. Is fairly nourished. Suffering from large accumulation of fluid in left chest. Infiltration of right apex. No cavitation. Evidence of bronchitis in lower right lobe posteriorly. Runs fever, maximum temperature, 103°. Has been more acutely sick for two weeks. Pirquet negative. Tubercle bacilli found in sputum only after repeated examination.

Treatment, March 17, 0.2 c.c. intramuscularly, no reaction observed.

Treatment, May 17, 0.25 c.c. intramuscularly, no reaction observed.

RESULT: Obscured by the necessity for repeated thoracocentesis with the removal of large quantities of fluid. Three months after the first injection the patient had regained the condition described by him before the acute attack two weeks before treatment. His temperature was reduced to a maximum of 100.5°. He weighed 3 pounds heavier. Fluid reaccumulates in the left chest. Cough and expectoration are much improved. Has râles on coughing at right apex, and harsh breathing in right lower lobe posteriorly.

SUMMARY: The improvement in this case may be accounted for by his rest in the hospital and the removal of fluid from chest.

No. 11. E. J.—Tubercular tenosynovitis; pulmonary tuberculosis, III.—A history of swelling of the anterior side of the wrist of 2½ months' duration tender but not painful, with limitation of the mobility of the flexer tendons. Increasing cough for year, with loss of weight and pains in the chest. There is partial consolidation of both apices and upper lobes. and fluid in the left chest. Low febrile temperature, much weakness. Weight, 134½ pounds. Swelling of wrist above carpus doughy and tender to pressure. Tubercle bacilli in sputum.

Treatment, March 17, 1913, 0.2 c. c. intramuscularly, transient induration.

Treatment, May 17, 1913, 0.2 c. c. intramuscularly, transient induration.

RESULT: Three months after treatment. The swelling of the wrist was incised at the time of the first injection, a small amount of tissue being removed for laboratory examination, which demonstrated its tubercular nature. At first it appeared that the wrist was becoming worse. The skin became red and more bulging and the patient suffered so much pain that a cast was applied. On removing this cast May 10 the wrist was found much improved, the swelling much reduced. The patient had been doing poorly and was allowed to sleep out doors, whereupon marked improvement occurred, he gained 10 pounds and his temperature was reduced to 100.5° maximum. Three months after the first injection the patient was coughing much and feeling poorly again, but this was apparently due to a rheumatic attack. Pains in the leg and hip of a rheumatic character were favorably influenced by salicylates. The wrist is much improved over its original condition. The lung findings are practically the same as before. After having gained 10 pounds in 6 weeks the patient has commenced to lose again, being now 5 pounds heavier than before treatment.

The physical condition of the lungs is not improved. That of the wrist is improved, but by no means cured. The general condition improved only when the patient slept out doors instead of in the ward. The improvement of the wrist gives the impression of being due to some specific influence.

March, 1914. Died of pulmonary tuberculosis. The wrist had improved as regards pain, redness, and swelling, but never to the extent that it was useful or flexible.

No. 12. S. T. (30 years)—Tuberculosis of the lungs, III.—Known duration, eight months. Loss of about 7 pounds in weight. Cough variable during this period. Eight days before treatment had a copious hemorrhage. Was much prostrated by the direct and psychic effects of his first hemorrhage. Temperature, maximum 100°. Probable cavitation of right upper lobe and infiltration of middle and lower lobe. Slight infiltration left apex. Tubercle bacilli in sputum.

Treatment, March 17, 1913, 0.2 c. c. intramuscularly, transient local reaction.

Treatment, May 17, 1913, 0.25 c. c. intramuscularly, transient local reaction.

RESULT.—The patient's general condition improved as he recovered from the effects of the hemorrhage. General condition and subjective symptoms improved steadily until about May 12, when he complained of returning pains in the chest, a moderate night sweat, and increased expectoration. Following the second injection his subjective complaints improved. Three months after the first injection he feels very well and strong. Has a little cough still, and temperature sometimes reaches 99.3°. Has gained 10 pounds. Has moved to the country and consumes a dozen eggs and 2 quarts of milk daily. There is marked improvement in the physical signs, rales now being very few and confined to the right apex. Evidence of dry cavity remains. The result thus far has been very favorable. A cure has not yet been effected. It would be unfair to compare the patient's present condition with his state immediately before treatment, as he was at that time just recovering from a severe hemorrhage.

March, 1914. Not seen. Writes that he is unable to respond to request to present himself for examination, as he is suffering from stomach trouble. Dr. Rambaud says that this patient became exposed in a storm about March 1, 1914, and suffered a return of his lung trouble. Had a hemorrhage, followed by temperature of 101° to 102°.

No. 13. M. D.—Pulmonary tuberculosis, I.—An old sanitarium case, well trained in taking care of himself, in good general condition, and with small nonprogressive involvement of both apices. Has had four hemorrhages, one being severe. No fever. Slight cough. Was at work daily as an interpreter. Tubercle bacilli in sputum.

Treatment, March 17, 1913, 0.1 c. c. intramuscularly; small, rather persistent nodule formed.

RESULT: Three months later. The patient insists that he feels better than before treatment, although he was doing very well before. Says he is stronger and notices that his breathing is freer. Physical signs have improved to the extent that rales formerly heard without coughing are now elicited only on coughing. Weight about stationary.

March 27, 1914. Seen. In addition to the treatment given by Dr. F., he has had three treatments of the F. F. F. vaccine from Dr. R., one each in July and September, 1913, and one February 27, 1914. None followed by more than local induration. Thinks they did him much good.

On December 22, 1913, had a severe attack of intestinal trouble said to be a "kink" in the bowel, which came near ending fatally, reduced him to 95 pounds weight, and started up his pulmonary trouble anew. He had previously been regarded as cured. Is now gaining and weighs 119 pounds. Weight before attack, 128 pounds. Sputum is positive for tubercle bacilli. Now has considerable cough, not productive, sputum being only about ½ ounce daily. For past week has had hoarseness. Temperature 98°to 99°.

Physical examination shows practically same condition as when first seen. Moderate dullness and moist rales on coughing, at both apices. Loss of flesh ascribed to recent illness is apparent.

No. 14. J. F. R.—Pulmonary tuberculosis, I.—First symptoms noticed two months before treatment, when he had a hemorrhage. Another hemorrhage two or three weeks before treatment. Cough remains. Slight pain in chest at times. No sweats, fever, or loss of weight. Weight, 119 pounds. Some dullness and fine moist rales at both apices. Tubercle bacilli in sputum.

Treatment, March 17, 1913, 0.1 c. c. intramuscularly, transient local reaction.

Treatment, May 17, 1913, 0.2 c. c. intramuscularly, transient local reaction.

RESULT: Had a small hemorrhage following physical exertion about three weeks after treatment. On May 31 and June 16 spit up a little blood. Has

improved greatly in general health; gained 14 pounds; his cough reduced to a little morning and evening. Pains in the chest disappeared, strength and appetite improved. The physical signs are reduced to few râles on coughing only at left apex. Has been working at his trade of jeweler.

SUMMARY: There was undoubtedly marked improvement in this case, but not a positive cure, as shown by the persistent rales and recent blood spitting. An untreated patient in the same ward with more pronounced lesions improved to an even greater extent.

March 28, 1914. Seen. Had a third treatment from Dr. Rambaud in the summer of 1913, followed by local induration and feeling sick for a few days. Has been working steadily as a jeweler. Feels well, has no cough nor expectoration. No blood spitting for seven or eight months. Before sputum disappeared it was reported negative for tubercle bacilli on several examinations. Weight (slot machine, clothed), 143 pounds; temperature, 98.6°; chest signs show no evidence of activity; some dullness and high-pitched expiration remain, and there are inspiratory clicks suggestive of pleural thickening.

No. 15. W. W.—Pulmonary tuberculosis, III.—Duration about two years, following pneumonia. Complains of cough, much weakness on exertion. No night sweats now. Temperature reaches 100°. Is anemic, but fairly well nourished. Weight, 128½ pounds. Infiltration of both apices extending to third rib on right side and fifth rib on left. Many coarse and fine moist rales. Is short of breath.

Treatment, March 17, 1913, 0.2 c. c. intramuscularly, no reaction noted.

Treatment, May 17, 1913, 0.2 c. c. intramuscularly, no reaction noted.

RESULT: Patient claims that he caught cold from a draft. He ran high fever with more cough and loss of weight. Shortly before the second injection he had improved somewhat, his temperature reaching a maximum of 99.4°, and his sputum being reduced in amount. His weight remained practically stationary. Following the second injection he writes that he is worse again. Temperature reaches 102°. His strength is less, and he has lost a few pounds weight. At the time of receiving the second injection, the lung condition was practically the same as before treatment on the right side but much improved on the left, where the signs pointed more to an acute bronchitis than tubercular involvement. Previous to this, when patient was feeling so badly, the lung signs also were aggravated in extent and severity.

SUMMARY: The patient felt worse following each injection and ran high fever. The first time he attributed this to catching cold, but has no explanation of the second time. He has apparently derived no benefit from the treatment.

March 31, 1914. Seen. Is now bedridden in the terminal stage of tuberculosis, emaciated, gasping for breath, coughing incessantly, raising large quantities of sputum, and running a fever. Says he dates his decline from the second injection.

No. 16. A. B.—Pulmonary tuberculosis, III.—An attack of pneumonia in December, 1912. Cough since getting worse. No hemorrhage or night sweats. Slight pain in chest between shoulder blades. Loss of about 20 pounds in weight. Infiltration right apex to fourth rib anteriorly and lower angle of scapula behind. Infiltration of the left apex. Temperature maximum, 101.4°. Tubercle bacilli in sputum. Weight, 115 pounds.

Treatment, March 17, 1913, 0.2 c. c. intramuscularly; no reaction observed.

This patient failed progressively following the injection, and it seemed at a more rapid rate than would have been expected. Developed tuberculosis of the larynx, with almost complete aphonia. The lung signs show progress of the disease, with suspected cavitation and new involvement of the left base. Fever high (103°); loss of weight since treatment, about 23 pounds.

SUMMARY: In this case, if the treatment did not actually have an unfavorable influence, it certainly exercised no restraining effect on the progress of disease and the involvement of new areas. The case was unfavorable, although of recent development.

Subsequently died.

No. 17. J. M., 21 years—Pulmonary tuberculosis, II.—Three months' duration; cough; loss of weight; recent night sweats, which stopped before treatment began. Weight, 126½ pounds. Sputum blood streaked. Tubercle bacilli in sputum. Pirquet positive; infiltration right apex to third rib. Febrile temperature, maximum 102°.

Treatment, March 17, 1913, 0.1 c. c. intramuscularly; slight local reaction.

RESULT: Two weeks after treatment had hemorrhage, 12 ounces, and more or less on following days. General condition worse. Higher temperature, 103.4°. On account of continued bleeding, artificial pneumothorax was performed April 11, resulting in control of hemorrhage and immediate reduction of temperature to a maximum of 99°. It was thought necessary to repeat this operation. When last seen the patient was feeling poorly and running fever again. The signs were obscured by compression of the lung. Patient escaped further observation.

SUMMARY: No conclusions justifiable, except that, contrary to Dr. Friedmann's statement that hemoptysis is not observed as a consequence of or following treatment, a copious hemorrhage did occur for the first time two weeks after treatment.

No. 18. K. H.—Pulmonary tuberculosis, III.—Coughing for only a few months. Some weakness, but no very marked symptoms. No hemorrhage. Infiltration of right apex, and disseminated moist lesions of left lung. No cavitation. General appearance good.

Treatment, March 17, 1913, 0.2 c. c. intramuscularly; transient infiltration.

March 26, 1914. Seen at her home. States that she has lost health progressively since receiving the treatment. Has been confined to bed since September. Increasing cough, expectoration, chest pains, night sweats, and fever. Is now confined to bed, emaciated, and in the terminal stage of the disease.

No. 19. E. S., 30 years—Pulmonary tuberculosis, III.—Cough for one year, productive three months. Lost 15 pounds in 10 months. Night sweats six weeks past. Much weakness and shortness of breath. Temperature febrile, reaching 103°. Tubercle bacilli in sputum. Infiltration right apex and small area in lower lobe. Extensive consolidation left upper lobe with cavitation.

Treatment, March 17, 1913, 0.2 c. c. intramuscularly, transient local reaction.

RESULT: Some subjective improvement in first month, then patient began to sleep outdoors, resulting in great improvement of general health. Cough less, breathing freer, temperature reduced, and gain of weight. June 9–10 had copious hemorrhage, resulting in return of symptoms. No significant change in lung condition. Fever, 101°. Very short of breath. Artificial pneumothorax performed for relief of hemorrhage.

Subsequently died.

No. 20. B. R., 40 years—Pulmonary tuberculosis, III.—Sick a year and a half. Lost 18 pounds, which he has recovered in a sanatorium. Hemorrhage three months before treatment. Improves greatly under the sanatorium care, but gets worse on return to the city. Infiltration both apices on right to fourth rib, on left to second rib. Suspected cavity on right side. Moist râles plentiful. No fever; tubercle bacilli in sputum.

Treatment, March 17, 1913, 0.1 c. c. intramuscularly; large infiltration, ending in abscess formation.

RESULT: Six weeks after the injection the local site became painful, and at the same time the patient, who had been feeling better, began to feel worse even than before treatment. He subsequently improved again to a quite noticeable extent, but about June 10 developed an ischio-rectal abscess, which required operation. Before this complication was feeling much improved and had gained 7 pounds. The lung signs show improvement at the left apex where râles are no longer heard. This case exhibits the phenomenon of simultaneous development of pain at the site of injection and the general symptoms becoming worse. Until the development of the ischio-rectal abscess the progress of the patient was satisfactory in spite of the fact that the injection resulted in abscess formation.

March 24, 1914. Seen. In sanatorium. Condition in all respects similar to that before treatment. Sputum still contains tubercle bacilli. Chest signs indicate extension of the lesion on the left side to a significant extent at the same time that the right-side lesion has become less active.

No. 21. K. S., 43 years—Pulmonary tuberculosis, III.—History of ischio-rectal fistula seven years ago, with several operations resulting in cure. Had pulmonary condition four and one-half years. Some hemorrhages four and two years ago. Temperature subfebrile for a long time. Infiltration both upper lobes, possible cavitation.

Treatment, March 17, 0.1 c. c. intramuscularly; large infiltration; gradually resorbed. May 17, 1913, 0.15 c. c. intramuscularly; transient reaction.

RESULT: No significant change in lungs, except reason for increased suspicion of cavity. Has lost 4 pounds in three months. Says his cough is somewhat lighter, but that he is weaker.

March 24, 1914. Seen. Still in sanatorium. Condition in all respects similar to that before treatment. Tubercle bacilli in sputum. Lung signs the same as before.

No. 22. G. G., 32 years—Pulmonary tuberculosis, III.—Sick nine months Lost about 12 pounds, now gaining slowly. Temperature, 100.4° maximum. Has much pain in chest on coughing. Disseminated moist lesions in right lung and a few rales and suspected cavity at left apex.

Treatment, March 17, 1913, 0.2 c. c. intramuscularly, transient reaction.

Treatment, May 17, 1913, 0.2 c. c. intramuscularly, transient reaction.

RESULT: Three months later. Patient had a temporary amelioration of subjective symptoms following the first injection and also improved after the second. Three months after the first injection he stated that his cough was better, pain gone, and he was stronger. His temperature reaches 100°. The lung signs are about the same as before although the lesion at the left apex appears to be drier. He has lost about 4 pounds weight.

March 25, 1914. Seen in sanatorium. Since last seen has had a fistula in ano, which was operated upon with good result. Coughs excessively and expectorates much. Lately temperature has been reaching 100° at times. No copious hemorrhages, but occasional blood-stained sputum. Weighs 17 pounds less than before treatment. Lung signs practically the same as before treatment.

No. 23. J. A.—Pulmonary tuberculosis, III; tubercular epididymitis.—Cough five and one-half years. Used to have fever and sweats. Temperature now subfebrile with occasional jumps to 102°. Weight about stationary; extensive involvement of left lung; large cavity; pleural adhesions and catarrh; right apex shows some infiltration. Bilateral epididymitis of one year's duration, large, hard, with a small sinus discharging slightly.

Treatment, March 17, 1913, 0.2 c. c. intramuscularly, transient induration.

Treatment, May 17, 1913, 0.15 c. c. intramuscularly, transient induration.

RESULT: After three months no improvement. Sinus still discharges; left spermatic cord has recently become hard and swollen. Lung condition unchanged; maximum temperature 101°; sharp remissions.

March 24, 1914. Seen in sanatorium. Weighs about 5 pounds more than before treatment, but otherwise unimproved. Lung signs unchanged. The sinus leading to the testicle is still open and discharging, and the left testicle and cord have become more involved than when last seen.

No. 24. E.—Tuberculosis of wrist.—Case not observed more than a few days.

No. 25. R. R., 24 years.—Pulmonary tuberculosis, III.—More than two years' duration; doing well under hospital care. Temperature always under 100°. Well nourished; healthy appearing; weight about stationary. Impaired resonance; right apex; few rales. Evidence of old pleurisy left side. Cavitation left upper lobe, with generally distributed moist rales left side. Tubercle bacilli in sputum.

Treatment, March 17, 1913, 0.2 c. c. intramuscularly, terminating in small abscess.

RESULT: After some temporary subjective improvement the symptoms returned with increased severity. Coincident with the appearance of soreness at the site of injection the patient began to feel worse generally. Three months after injection cough is worse than before treatment and sputum harder to raise, though large in amount. Temperature reaches 100.6°. Lung signs practically the same. No rales now heard at right apex. Has gained 4 pounds.

March 25, 1914. In sanatorium. Condition in all respects similar to that before treatment.

No. 26. E. L., 24 years—Pulmonary tuberculosis, III.—Sick a few months. Now improving in weight, but not otherwise. Temperature, 98°–100°. Has night sweats; cavitation right upper lobe, with catarrh. Dry infiltration left apex. General condition appears fairly good.

Treatment, March 17, 1913, 0.1 c. c. intramuscularly, persistent nodule.

RESULT: No improvement, except relief of pain in chest, and gain of 7 pounds weight. There was some temporary improvement in subjective symptoms. Lung condition practically unchanged. Temperature frequently 100.8°. Pulse averages more rapid than before treatment. Now nearly always over 100.

March 24, 1914. Still in hospital. Has been confined to bed for past two months with fever and aggravation of pulmonary symptoms. Temperature, 103° frequently. Chest signs indicate extension of the lesion. Weighs about 9 pounds less than before treatment.

No. 27. A. R., 27 years—Pulmonary tuberculosis, III.—Over three years' duration. Early hemoptysis. Temperature, subfebrile. Weight about stationary; impaired resonance right lung, with cavitation; slight involvement left apex.

Treatment, March 17, 0.1 c. c. intramuscularly, transient induration; treatment May 17, 0.15 c. c. intramuscularly, resulted in abscess.

RESULT: Three months after first injection the condition of the patient is apparently worse than before injection. Temperature, 101.2° maximum; has lost 5 pounds. Lung signs practically the same as before. Cough and expectoration worse. At the site of injection there is a painful discolored swelling discharging sero-pus. The patient states that the pain in her chest is better, but that in other respects she feels worse.

March 24, 1914. Seen in sanatorium. Now in bed constantly; diarrhea not responding to medication for two months. A few weeks ago was running fever of 103°, now 100° maximum. Large amount of sputum containing tubercle bacilli. Lung signs somewhat increased since last examination. Has lost 15 pounds since treatment.

No. 28. D. W.—Pulmonary tuberculosis, III.—Duration, one and one-half years; blood-streaked sputum June, 1912; condition now stationary; temperature, always under 100°; infiltration of both apices, suspected cavitation on the left posterially. Treatment, March 17, 1913, 0.1 c. c. intramuscularly, transient reaction; May 17, 1913, 0.15 c. c. intramuscularly, large induration.

RESULT: Temporary improvement in subjective symptoms, with return to former condition; upon examination shows reduction in the number of râles. No gain in weight. Recently at the site of injection a swelling tender to pressure has developed; temperature runs in general lower than before, 99.4° maximum. Sputum occasionally blood streaked.

March, 1914. Not seen. Gone to Europe.

No. 29. E. M.—Pulmonary tuberculosis, I.—Cough three years; hemorrhages at various times; last time eight months before treatment; temperature mostly normal; occasionally rises to 101; infiltration both apices, no cavitation; general condition good.

Treatment, March 17, 0.1 c. c. intramuscularly, transient reaction; May 17, 0.3 c. c. intramuscularly, followed by a small abscess.

RESULT: Temporary improvement in the subjective symptoms; lesion appears dryer; three months after treatment patient feeling worse than before; cough and expectoration worse; increased weakness; several small hemorrhages; temperature, 99.4 maximum. Slight loss of weight.

March 27, 1914. Seen. Feels poorly. Has every two weeks or so a hemorrhage of 2 to 6 ounces. Highest temperature, 102. Has pain in chest which she never had before Friedmann treatment. Cough bad, but unproductive. No sweats. Objectively patient is worse than before treatment. The lesion has extended and become more active.

No. 30. S. S., 45 years—Pulmonary tuberculosis, III.—Sanatorium case of long duration, slowly progressive; gain of 21 pounds in the past six months; patient fat and robust looking; tubercle bacilli not found. Temperature between 99 and 100; hemorrhage seven months ago; infiltration of both apices; pleuritic involvement left base.

Treatment, March 17, 1913, 0.1 c. c. intramuscularly, followed by large abscess. Still discharging two months later.

RESULT: No change in subjective symptoms except feels a little stronger; temperature, maximum 99.6. The lung signs after temporary increase have returned to practically what they were before treatment.

March 27, 1914. Seen at home. Has lost weight and is evidently thinner than before; has pain in chest and tires easily. Does not cough much. Has spit a little blood twice since last seen. Temperature, 99.6–99.8°. Lung condition apparently somewhat improved since treatment.

No. 31. C. G.—Tuberculosis of knee joint.—Swelling of right knee 12 years, not tender or painful. Wore plaster cast or leather brace several times. Operated one and one-half years ago. Two months ago the swollen knee was incised and pus evacuated. Sinuses posteriorly now discharge sero-pus. About 35° of flexion possible. Swelling of knee joint 2 cm. over healthy knee. Attempt at flexion painful. Tenderness on pressure. X ray shows moderate destruction of articular surfaces of femur anteriorly.

Treatment, 0.1 c. c. intravenously, March 19, 1913; transient high fever.

Treatment, 0.5 c. c. intramuscularly, March 19, 1913; persistent induration.

Treatment, 0.7 c. c. intramuscularly, April 27, 1913; large persistent induration.

RESULT: No change following first injection. After second injection improvement in range of motion. Knee could be flexed about 75° as against 35°, and less pain. The patient was able to walk a few steps. On leaving hospital

for less favorable surroundings the swelling increased and the range of motion was reduced again. The discharge from the sinus continued.

SUMMARY: This case, judging from the X-ray findings, was very suitable for a demonstration of the curative effects claimed by Dr. Friedmann, being much less severe than some in which he reports cures. Some improvement occurred, although the sinuses did not heal. Indications three months later are that the improvement will not be permanent.

No. 32. F. S.—Tubercular gland of neck.—Duration one year. Before treatment, gland 1 inch in length. Patient has cough, pain in throat, and frequent headaches, but no physical evidence of pulmonary or laryngeal tuberculosis. General condition good.

Treatment, 0.5 c. c. intramuscularly, March 19, 1913, caused a large infiltrate, which finally formed an abscess and still discharged three months after treatment.

RESULT: Some diminution of size of gland occurred, but it fluctuates in size from time to time. The general health of the patient has improved and the subjective symptoms mentioned are much better. This was three months after treatment.

No. 33. F. G.—Tuberculosis of knee joint.—History of a fall five years ago, followed by swelling and pain in left knee, which was injured. A cast was applied for two weeks, followed by resumption of function. Five months ago a cast was again applied, since which she has not walked. Has pain on attempting to stand or walk. Cast was removed before treatment and not reapplied, patient remaining in bed or wheel chair. Affected knee measures 37 cm.; well knee, 35 cm.; bony, landmarks obliterated; flexion possible to about 70°, extension to 120°; atrophy of thigh and leg muscles. No fistulæ. Pain and tenderness on manipulation. X ray shows extensive destruction of articular surfaces.

Treatment, 0.2 c. c. intravenously and 0.5 c. c. intramuscularly, March 19, 1913; transient high fever; locally large infiltrate, discharge of pus.

Treatment, 0.5 c. c. intramuscularly, April 27, 1913; painful for several days.

RESULT: No objective change in condition of knee. Patient suffered more pain in knee immediately following second injection. Subsequently the pain and tenderness became less, although attempts at bending caused pain. No functional improvement up to three months following injections.

No. 34. L. T., 14 years old—Tuberculosis of knee joint.—Swelling of right knee of three years' duration; only slightly painful. Has worn cast at intervals and had worn one for eight months up to a few days before treatment. Before it was applied patient could walk about without much pain and could bend knee to about 70°. X ray shows periarticular infiltration and some rarifaction of the condyles. Just before treatment the knee could be bent about 40°. It was 6 cm. larger than the well knee and was painful and tender. Atrophy of thigh and leg.

Treatment, 0.2 c. c intravenously, March 19, 1913; transient high fever, epistaxis.

Treatment, 0.5 c. c. intramuscularly, March 19, 1913; terminated in discharging pus.

RESULT: Flexion of the knee increased up to the point it had been at when the cast was applied eight months before. When last seen (three months later) there was tenderness and swelling the same as before treatment, and the patient and his mother did not consider the case improved. March, 1914, information from mother that patient did not improve; was operated upon, and a cast applied, which has been worn continuously since. No pain is complained of and the general health is unchanged.

No. 35. M. L., 16 years old—Tuberculosis of knee joint.—Has had swelling and some stiffness of left knee for three or four years. Up to the time of admission was working as a delivery man daily, walking a great deal. Had pain in knee only after a hard day's work, when the swelling is most marked. X ray shows involvement of the tuberosity and one-third of articular surface of tibia and foci in the internal condyle. The knee is 1½ cm. larger than the other and can be bent to a right angle.

Treatment, 0.1 c. c. intravenously, March 19, 1913; marked febrile transient reaction.

Treatment, 0.5 c. c. intramuscularly, March 19; transient induration.

Treatment, 0.5 c. c. intramuscularly, April 27; transient induration.

RESULT: Gained a few degrees (5—10°) flexion of the knee during his stay in hospital, also gained 21 pounds. The knee still hurts him and swells after being about on it. The improvement is insignificant and could be readily accounted for by the rest secured in hospital. The case was a favorable one for functional cure, judging from those which Dr. Friedmann reports.

March 29, 1914. Seen at home. Since leaving the hospital has been working at inside work, being too lame to continue his outside work. For the past two months has had more pain in the knee. The joint is movable to the same extent as before treatment, but lateral passive movements of the patella are more limited. The enlargement is the same as before, as is the tenderness on pressure.

No. 36. M. A.—Tuberculosis of knee and shoulder joint—Pulmonary tuberculosis.—Trouble with knee and shoulder 13 years. Used knee, however, with little discomfort up to two years ago, when a cast was applied. Two months ago coughed up a little blood and has had some cough since. Knee joint is swollen (4 cm.); hard, except internally where it is somewhat doughy; the bony outlines are obliterated, and the range of motion is about 15°. The shoulder joint is apparently ankylosed. Atrophy of muscles of shoulder, arm, thigh, and leg. Knee joint very tender to pressure and forced flexion is very painful. The lungs exhibit infiltration of both apices. X ray shows dislocation upward of the shoulder, and fungoid proliferation obscuring the knee joint.

Treatment, 0.1 c. c. intravenously, March 19, 1913; transient febrile reaction.

Treatment, 0.5 c. c. intramuscularly, March 19; transient induration.

Treatment, 0.5 c. c. intramuscularly, April 27, 1913.

RESULT: Eight days after injection patient had pulmonary hemorrhage, after which a systolic apical heart murmur was heard. The shoulder joint remained unchanged, as did the lung condition. The knee joint, became perceptibly softer and its range of motion increased to 35 or 40°. It became also less tender to the touch. The circumference was not reduced.

SUMMARY: The improvement in this case was not greater than could have been expected from the substitution of rest in bed for ambulant treatment with a cast. A hemorrhage occurred after the injection, but can not be definitely attributed to it. No improvement in the shoulder joint was to be expected, and little in the knee.

No. 37. M. L., age 3—Tuberculosis of shoulder and hip joint.—Hip joint affected since age of 11 months, when a cast was applied, which, except for intervals of a few days, has been on continuously. Removed before treatment, and not reapplied. During the intervals when the cast was removed the patient could walk, but soon complained of pain. Could not sit squarely on a chair, but sat on the edge with leg hanging down. Shoulder affected about the same time. Child complained of much pain when clothes were put on or off and arm handled. X ray shows destruction of the head of the femur and disloca-

tion upward. The head of the humerus is largely absorbed, but bony ankylosis is not apparent. Motion is very restricted in both joints and causes pain, especially in the shoulder. There is atrophy of the muscles surrounding the joints. Pirquet reaction strongly positive.

Treatment, 0.2 c. c. intravenously, March 19, 1913; transient febrile reaction.

Treatment, 0.5 c. c. intramuscularly, March 19; persistent small induration.

March 30, 1914. Seen. In addition to the injections recorded above, has received two intramuscular injections from Dr. Rambaud, July 7 and October 30, 1913. Now has no pain in the joints; general condition good; has grown normally. Walks well, though with decided limp, and touching only the toes on the affected side, the shoe having a thick sole. Sits more squarely on a chair than before, but most of the motion of the thigh is accomplished by tilting the pelvis. Can raise right hand above head with some difficulty.

The improvement in this case is suggestive of a specific action of the remedy. The effect of prolonged immobilization in a cast must, however, be taken into account.

No. 38. S. Z.—Tuberculosis of hip joint.—Duration, four years. Operated two years ago for supposed dislocation, he says. Cast then applied which has been kept on since; only removed a few days before treatment. Motion of the hip is limited to about 20°. Pressure on the joint anteriorly causes pain. Muscular atrophy of thigh. No shortening. X ray shows extensive proliferation of acetabulum and head of femur.

Treatment, March 19, 1913, 0.2 c. c. intravenously; marked febrile reaction.

Treatment, March 19, 0.5 c. c. intramuscularly; transient infiltration.

Treatment, May 17, 0.7 c. c. intravenously; transient infiltration.

March 29, 1914. Is doing well. Walks with a slight limp. Flexion of thigh possible to about 45° before tilting of the pelvis occurs. No pain or tenderness. Muscles of thigh on affected side have developed so that there is now but 4 cm. difference. Obviously a good result, but whether due to immobilization or to the Friedmann treatment is not apparent.

No. 39. H. R.—Tubercular glands of neck.—Glands have increased in size during the past six months. Three weeks before treatment they were incised and pus liberated. Mass as large as a lemon matted together; semifluctuating; the skin purplish and excoriated.

Treatment, March 19, 1913, 0.05 c. c. intravenously; transient febrile reaction; 0.3 c. c. intramuscularly; persistent nodule.

Treatment, May 17, 0.15 c. c. intramuscularly; transient infiltration.

Result: Shortly after the first injection the skin broke down and a profuse discharge of pus occurred. Two months after the first injection the wound discharged slightly, and the granulations had a healthy appearance, without the purplish discoloration of the skin commonly observed. Three months after the first injection the wound was entirely healed, and the scar of a healthy color and not attached deeply. There are two glands to be felt under the sterno-mastoid—one the size of a plump almond, the other of a bean. General condition excellent. Patient had measles during the period of observation.

Summary: The result in this case is very good. The remaining glands suggest that cure is not complete.

March, 1914. Patient not seen, but relatives state that the neck has remained well and the patient is in good health.

No. 40. B. T.—Tuberculosis of wrist joint and of lungs, II.—More than three years ago was operated upon for ileocecal tuberculosis, resection, and colostomy. A ventral hernia followed and the scar has broken down at times; now healed, but very thin. Eight months ago, swelling of wrist. Placed in cast for

past four months. Aspirated one month ago and iodoform and glycerin injected. The wrist joint distended with fluid; landmarks obliterated; no redness; slightly tender. Passive motion possible. Wasting of hand and arm. Infiltration of both apices of the lungs. Duration of pulmonary condition indefinite. Patient up and about, but in rather poor general condition.

Treatment, March 19, 1913, 0.2 c. c. intravenous, marked febrile reaction; 0.5 c. c. intramuscular, no reaction.

RESULT: Three days later an area of necrosis had developed in the scar of the colostomy wound, and a discharge of pus occurred. The wrist became redder. The patient's temperature rose and continued high, and he was confined to bed. Eight days after the injection the patient was allowed to be up and about the ward, but was in poor condition. Had lost 15 pounds weight. There was no change in the wrist. The sinus in the abdominal scar discharged slightly. Four days later, there being no improvement in the wrist, Dr. Gerster aspirated it, removed pus, irrigated with carbolic, and injected iodoform and glycerin. On April 3 the patient's condition was poor; had much cough, high fever, and complained of headache. Following this stiffness of the neck appeared and the symptoms of tubercular meningitis. Patient died in coma April 10. No autopsy could be obtained. Before death spinal fluid was removed, which contained tubercle bacilli. No growth was obtained on media, but a guinea pig inoculated with the spinal fluid died of tuberculosis in 16 days.

SUMMARY: The development of tubercular meningitis secondary to pulmonary and other tubercular involvement is not rare, hence in this case we are not justified in attributing this fatal issue to the Friedmann treatment. Owing to the lighting up of the process in the old scar and the increased redness of the wrist, which resembled a focal reaction, the suspicion arises that dissemination of the bacteria may have been due to the treatment. At any rate it is evident that the treatment was powerless to prevent the involvement of tissues hitherto free from tuberculosis.

No. 41. E. McG.—Tubercular glands of neck.—More than two years ago enlarged glands on the right side of the neck were removed and found to be tubercular. Enlargement involving the glands of both sides of the neck has been proceeding for more than a year. Patient in excellent general condition and gaining weight. The glands are matted together, forming a mass on the right side, 4½ by 3½ cm. in measurement, on the left 8 by 4½ cm. The left submaxillary region is occupied by a mass, and smaller masses are palpable in both supraclavicular regions. A distinct and disfiguring bulging of the neck is evident.

Treatment, March 19, 0.2 c. c. intravenously, marked febrile reaction; 0.35 c. c. intramuscularly, deep induration lasted more than a month.

Treatment, May 17, 0.4 c. c. intramuscularly, transient induration.

RESULT: The patient observed a dimunition in size of the masses within a few days of the first injection. In about three weeks the glands were definitely marked out, the masses being lobulated instead of matted. Some of the glands were definitely softer than before. One month after injection a very marked diminution in the size of the glands was evident. They were freely movable and flatter than before. In a letter written three months after the first injection the patient states that the diminution in size of the glands has been progressive.

SUMMARY: While a cure has not been effected as yet, the progress of the case has been very satisfactory, and the improvement is such as is not commonly observed.

No. 42. J. L.—Tubercular tenosynoritis.—This patient escaped observation, being obliged to return home to care for her children.

No. 43. D. D.—Tuberculosis of knee joint.—Developed two and one-half years ago following a fall. Knee held rigidly by spastic muscles at angle of 90°. Joint very hard. Attempted motion causes pain. Swelling amounts to 1½ inches.

Treatment, March, 19, 1913, 0.2 c. c. intravenous, marked transient febrile reaction with epistaxis; 0.6 c. c. intramuscular, no reaction observed.

Treatment, April 27, 0.6 c. c. intramuscular, followed by slight rise of temperature, 100.8°.

RESULT: When last observed, about six weeks after the first injection, the joint was definitely softer than before and could be moved passively in an arc of some 20°. It was less painful. Patient had been kept in bed without apparatus.

No. 44. B. G., 14 years—Pulmonary tuberculosis, II.—More or less cough since pertussis at age of 3 years. Pneumonia in March, 1910. Frequent examination of sputum negative until February 28, 1913, when positive. Slowly progressing lesions. No fever. Pirquet positive. Signs consist solely of variable moist rales in lower lobes. No hemorrhages, but occasional blood-streaked sputum.

Treatment, March 22, 1913, 0.1 c. c. intramuscularly, resulting in formation of small abscess.

RESULT: No change in patient's condition observed. Has gained 3½ pounds in about three months; is a growing child. No subjective improvement. The discharge at point of injection continued two months after treatment. Sanatorium conditions.

March, 1914. Subjective symptoms have been the same since treatment. Has gained 11 pounds in past year. Coughs a little during the day and has only a small amount of sputum, which has been negative for tubercle bacilli in all recent examinations. Complains of pricking pains in the chest at times. Physical examination shows conditions practically unchanged; moist rales still audible at the bases.

No. 45. A. L., 13 years—Pulmonary tuberculosis III.—Coughing two months or more. No hemorrhage or night sweats; lost weight; had fever. Temperature reaches 102°, sharply remittent. Extensive lesions of both upper lobes, with probable cavitation on left side. Tubercle bacilli in sputum. Treatment, March 22, 1913, 0.2 c. c. intramuscularly; transient local reaction.

RESULT: About three months after treatment, subjectively a little better. Temperature runs lower; maximum 100°. Respirations and pulse slower. Physical signs indicate progress of the disease. Cavitation on right side probable. No gain in weight. Patient had but one injection. The spread of disease process was not halted, but some symptoms were temporarily improved; was under sanatorium conditions; constantly in open air. Subsequently died of tuberculosis.

No. 46. C. C., 25 years—Pulmonary tuberculosis, II.—Cough of two months' duration. Lost 11 pounds since last summer (1912). Night sweats in January, none since. Blood-streaked sputum in January. Cough slight. Temperature sometimes reaches 102°. Tubercle bacilli in sputum. Gained 5 pounds in two weeks before injection. Infiltration of both upper lobes, more active on right side.

Treatment, March 22, 1913, 0.15 c. c. intramuscularly; transient reaction.

RESULT: For first few weeks, subjective symptoms improved. Had a small hemorrhage April 16 and subsequently felt badly; ran fever. Escaped further observation; went away to the country. Subsequently died of tuberculosis.

No. 47. T. B.—Lupus of face—Tubercular glands of neck.—Lupus of one year's duration, beginning as papules on left cheek and nose; slowly progressive. Had tubercular glands at angle of jaw three years ago, which broke down, discharged pus, and healed; now has enlarged glands in the submental and submaxillary region. Lupus involves isolated areas on nose and cheek and upper lip. Pathological diagnosis made from material from septum.

Treatment, March 22, 0.1 c. c. intramuscularly; marked febrile reaction, formed infiltration, which eventuated in abscess.

Treatment, March 22, 1913, 0.1 c. c. intravenously; marked febrile reaction.

RESULT: After about three months no decided change could be determined. Some tuberculous elevations had decreased in size, while others had increased. The submental glands broke down and still continue to discharge. The site of injection was occupied by a purplish scar, which broke down and discharged intermittently.

SUMMARY: Here is an instance where the simultaneous injection failed to prevent abscess formation. No significant curative effect took place.

March 29, 1914. Seen at home. No significant improvement having followed the Friedmann treatment, the patient consulted a private physician, under whose care the condition improved greatly. Without apparent reason, three weeks ago it suddenly began to get worse again and is now more extensive than at the time of treatment.

No. 48. E. H., 17 years—Pulmonary tuberculosis, II.—Cough three years. Early hemorrhages; none since. Lost 10 pounds in two years before admission. Fever at first only. Complains of weakness. Temperature now seldom reaches 99.5°. Gained weight recently. Tubercle bacilli in sputum. Pirquet positive. Infiltration left upper lobe. General condition fairly good.

Treatment, March 22, 1913, 0.15 c. c. intramuscularly; local infiltration delayed six weeks.

RESULT: Early improvement in subjective symptoms, followed by their return, and gradual improvement again. One month after the injection the physical signs indicated progress of the lesion. Three months after injection some improvement observable. Cough practically disappeared. Expectorates once or twice a day. Temperature subnormal. Weight stationary since treatment. Signs show less moisture; few rales except on coughing. Sanatorium conditions much of the time.

SUMMARY: Improvement could be readily accounted for by excellent surroundings.

No. 49. F. E., 17 years—Pulmonary tuberculosis, II.—Four years' duration. One early hemorrhage and one since. Improved to arrested condition two years ago. Since then slowly progressive. Does well while at rest; under sanatorium conditions; has fever on attempting to return to work. Temperature now normal to 99°; has gained only 2 pounds in two years. Tubercle bacilli found in sputum only after many examinations. Infiltration of both apices and left lung to the lower end of the scapula.

Treatment, March 22, 1913, 0.2 c. c. intramuscularly; large lasting induration.

RESULT: Three months after injection feels the same as before treatment; temperature, maximum 100°; usually subnormal; a very small hard nodule at the sight of injection. Physical examination shows no significant change in condition.

March 16, 1914. Seen. Condition practically the same as last year. Is in sanatorium. Has gained only 7 pounds in the past year, and most of that since coming to the sanatorium. Cough and expectoration slight. Sputum contains tubercle bacilli. Chest signs practically the same as before.

No. 50. M. V., 11 years—Pulmonary tuberculosis, I.—Uncertain duration; cough recently productive. Hemoptysis about March 1. Sweats at night, but runs practically normal temperature. Attends school and considers her health good. Slight infiltration left apex. Tubercle bacilli in sputum. Pirquet positive.

Treatment, March 22, 1913, 0.1 c. c. intramuscularly; large induration, terminating in discharge of pus.

RESULT: Three months later condition the same as before treatment. No subjective or objective improvement.

March 23, 1914. Seen. Patient is a growing child and has gained about 18 pounds in the past year. Recently, however, she has been losing and her health has not been as good. Her temperature while seldom over 99° occasionally reaches 100°. Her cough has became worse recently. Daily sputum, one-eighth cup; tubercle bacilli present. A recent examination of the larynx shows marked infiltration and thickening of the false cords, probably tubercular. The laryngeal involvement is recent. Chest signs show extension of the lesion at the left apex, a new pleural involvement at the base, and a suspicion of involvement at the right apex. Patient in worse condition than before treatment.

No. 51. C. V., 32 years—Lupus and pulmonary tuberculosis.—Case escaped further observation.

No. 52. M. McF., 41 years—Pulmonary tuberculosis, II.—Cough for eight months; considerable loss of weight. Sputum blood streaked at times; weak and short of breath. Temperature under 100°. Has had hemorrrhage; much improved by recent treatment. Infiltration of right apex and left base.

Treatment, March 22, 1913, 0.2 c. c. intramusclarly; transient local reaction.

RESULT: Patient gained about 11 pounds in weight; subjective symptoms much improved; lung examination shows no change of existing lesions and suspected involvement of the left apex, which was apparently free before. Sputum still contains tubercle bacilli.

SUMMARY: The improvement in general condition and subjective symptoms in this case has not been accompanied by improvement in the physical signs. Patient has been under sanatorium conditions.

No. 53. J. F., 26 years—Pulmonary tuberculosis, III.—Sick about six years. Hemorrhage one year ago. No night sweats; loss of about 10 pounds weight; temperature normal. Dry cavity in right apex, fine moist rales left apex, and small area lower lobe. In hospital has gained weight to practically the point normal for him. Tubercle bacilli in sputum.

Treatment, March 22, 1913. 0.1 c. c. intramuscularly; infiltration resulted in abcess.

RESULT: Three months later he had lost the pain in the chest which formerly troubled him a good deal; had lost about 2 pounds weight. No rales heard at the right apex; signs of dry cavity remain. Rales in the left lung heard only on coughing. In spite of abcess formation, some improvement in signs and symptoms occurred. Tubercle bacilli still found in sputum.

March, 1914. Not seen. On reliable information patient is working on express wagon, handling light packages. His weight, January 17, 1914, was 106 pounds, about the same as when treated, and his chest examination showed evidence of new involvement of the left apex. The sputum contained tubercle bacilli September 16, 1913.

No. 54. M. G., 26 years—Pulmonary tuberculosis, III.—Known duration, nine months. Has gained 14 pounds in hospital. Temperature normal; infiltration of both upper lobes; sputum positive for tubercle bacilli.

Treatment, March 22, 1913, 0.2 c. c. intramuscularly; transient reaction.

Treatment, May 17, 1913, 0.15 c. c. intramuscularly; transient reaction.

RESULT: Three months after treatment pain in the chest has entirely disappeared; other symptoms remain the same. Appetite is poor; has lost 7 pounds. Temperature, maximum, 99°. Physically the rales are much fewer than before treatment. Tubercle bacilli still present in the sputum.

March, 1914. Not seen. Said to be in sanatorium.

No. 55. P. I., 2 years—Lupus and tubercular glands of neck.—Glands swollen for seven months. Lupus on face, size of 10 cent piece, of uncertain but long duration. Gland measures 1½ by ¾ inches; fluctuation in the upper part; skin red.

Treatment, March 22, 1913, 0.1 c. c. intravenously; 0.5 c. c. intramuscularly; transient febrile general reaction; persistent small nodule locally.

RESULT: Gradual significant reduction in the size of the lupus area. The gland shows no reduction in size. The improvement in the lupus condition is remarkably good, while the gland has not improved at all.

No. 56. C. K., 28 years—Pulmonary tuberculosis, III.—Sick about 1 year. Early hemorrhage; blood-streaked sputum since then at times. Temperature seldom over 100°; gaining weight slowly; infiltration of right apex and entire left upper lobe; no cavitation; tubercle bacilli in sputum.

Treatment, March 22, 1913, 0.1 c. c. intramuscularly; transient infiltration.

Treatment, May 17, 1913, 0.2 c. c. intramuscularly; transient infiltration.

RESULT: Patient states that pain in the chest from which he formerly suffered had entirely gone. Temperature on the average lower than before, but sometimes reaches 100.2°. Weight stationary; physical signs show no significant change three months after treatment. Subsequently died of tuberculosis.

No. 57. N. V., 20 years—Pulmonary tuberculosis, II.—Sick only a few months. Has much cough and large amount of expectoration; temperature under 100°; infiltration of left apex to third rib.

Treatment, March 22, 0.1 c. c. intramuscularly; transient reaction.

RESULT: Marked improvement in subjective symptoms; feels stronger; cough is much reduced; temperature, maximum, about 99°; weight stationary; has had some blood-streaked sputum; physical examination shows reduction in the number of rales. Tubercle bacilli still found in sputum.

March, 1914. Not seen; has gone to Italy.

No. 58. J. G., 36 years—Pulmonary tuberculosis, III.—Duration about five years; lost about 35 pounds in the first year; has regained much of that since. Copious hemorrhage four years ago and one year ago; no night sweats for a long time. Cough severe; temperature never over 100°; weight now practically stationary. Infiltration of right apex to third rib and entire left upper lobe; no cavitation. Tubercle bacilli in sputum.

Treatment, March 22, 1913, 0.1 c. c. intramuscularly; transient reaction.

Treatment, May 17, 1913, 0.2 c. c. intramuscularly; transient reaction.

RESULT: Immediately following the first injection the patient complained of feeling worse and coughing more. About the middle of April began to feel better, cough and strength being improved. Just before the second injection began to feel poorly again, his subjective symptoms having returned. Objectively there has been no significant change in the patient's condition, although he has gained about six pounds weight in 10 weeks. His temperature is running slightly lower; maximum 99°.

No. 59. J. F., 31 years—Pulmonary tuberculosis, II.—Duration about a year; in past eight months has gained about 8 pounds. Temperature 99½° maximum; infiltration of both apices to third rib; tubercle bacilli in sputum.

Treatment, March 22, 1913, 0.1 c. c. intramuscularly; transient reaction.

RESULT: Patient states, three months after treatment, that he is a little stronger, appetite is better, and cough less troublesome. Objectively there is no change in his condition; weight stationary; temperature, maximum, 99°. Tubercle bacilli in sputum.

No. 60. C. K., 43 years—Pulmonary tuberculosis, III.—Indefinite beginning three or four years ago. Loss of weight; very short of breath; occasional blood-streaked sputum; cough not severe; temperature always under 100°. Infiltration right apex to third rib; left apex to fourth rib with cavity. Tubercle bacilli in sputum. Has gained about 18 pounds during the last year.

Treatment, March 22, 1913, 0.1 c. c. intramuscularly; transient reaction.

Treatment, May 17, 1913, 0.15 c. c. intramuscularly; transient reaction.

RESULT: Three months after treatment patient stated that he felt a little stronger than before and his shortness of breath was somewhat relieved; had gained three pounds in weight; temperature, maximum, 99½°. No change in physical signs. Tubercle bacilli in sputum.

March 23, 1914. Seen in hospital. Condition essentially the same as before treatment, except that about five months ago he developed an eczema, apparently tubercular, of the wrist, which has resisted local treatment. Constantly under sanatorium conditions.

No. 61. W. B. Pulmonary tuberculosis, III.—Sick three years; an advanced case with cavitation; night sweats and fever.

Treatment, March 22, 0.2 c. c. intramuscularly; slight local reaction.

RESULT: During the six weeks of observation the patient did not improve; physical signs indicated progress in the lung lesions.

No. 62. F. O., middle age—Tuberculosis of the kidney and epididymis.—Patient had had left kidney removed one year previously. When treated was in a condition of uremia and practically hopeless. Treatment desired by family as last resort.

Treatment, March 22, 1913, 0.1 c. c. intramuscularly.

RESULT: Following the treatment the patient became progressively worse, temperature rising to 103°, and he died in coma.

REMARKS: This patient being in a hopeless condition no blame can be attached to the treatment for his death.

No. 63. H. L., 13 years—Lupus of face.—History of sore on face since 2 years of age. Areas about 2½ by 1 inch, irregularly oblong, red, elevated, shiny, and scaly.

Treatment, March 22, 0.1 c. c. intravenously; marked febrile reaction.

Treatment, March 22, 0.6 c. c. intramuscularly; infiltration developed into a large painful abscess, which was opened in order to relieve the pain. Dr. Friedmann said that it was a great mistake to open the abscess and renounced any responsibility for the cure.

Treatment, May 17, 0.2 c. c. intramuscularly.

RESULT: At the time of the second injection the edges of the lesion show a pale margin suggestive of epithelialization not observed before.

March, 1914. Patient's mother seen, who says that the condition of her son's face is just the same as before treatment.

No. 64. F. M., 34 years—Lupus of face.—Duration, seven years. Very extensive; resistant to all treatment. Covers face from eyebrows to chin, and both cheeks to within 1 inch of the ears. Septum perforated. The greater part of this area consists of red scar tissue, but the edges are elevated and tubercular. There is considerable moisture.

Treatment, March 22, 1913, 0.5 c. c. intramuscularly; persistent infiltration.

Treatment, May 17, 1913, 0.3 c. c. intramuscularly; abscess formation.

RESULT: No decided change is noticeable. Appearance varies from day to day according to how recently the surface has been mechanically cleansed of secretion, scales, etc. Three months after treatment it seems that more patches of whitish scar tissue are visible, but the thick tubercular parts are not improved and one new patch has developed. The abscess resulting from the second injection became so painful that at the patient's request it was opened, a large amount of pus being liberated.

March, 1914. Patient not located, but a hospital nurse who has seen him within a month says that he was unimproved.

No. 65. G. L., 31 years—Tubercular sinus following removal of kidney.—The kidney operation was followed by sinuses, which closed up partially, only to break down again. Suffers also from frequency of urination. General condition poor. Slight pulmonary involvement probable.

Treatment, March 22, 1913, 0.3 c. c. intramuscularly; large induration; gradually disappeared.

RESULT: Three months later condition not improved. Dicharge from sinuses continues. Urinates very frequently, and now has blood mixed with urine.

March 23, 1914. Seen in hospital, where he has been readmitted after attempting to work in the kitchen of a steamship. Has been sick all the time. The sinuses in his back have never healed. Was operated upon in January, 1914, the sinuses being opened up and curetted. Must pass urine every 15 minutes or so. Phenol sulphonphthalein test, 40 per cent excreted in two hours. Runs an irregular temperature, reaching 101° maximum.

No. 66. T. S., 29 years—Pott's disease of the spine—Pulmonary tuberculosis, I.—States that he has been ill only one and one-half months, with cough and pain and deformity of the spine. Temperature normal. Tubercle bacilli not found in sputum. Impaired percussion note, and high-pitched expiration, both apices; no rales. Marked deformity of spine, the angulation being at about the fifth dorsal vertebra.

Treatment, March 22, 1913, 0.15 c. c. intramuscularly; transient reaction.

Treatment, May 17, 1913, 0.15 c. c. intramuscularly; transient reaction.

RESULT: About a month after the first injection a cold abscess developed near the lower end of the sternum. The patient says that the severe pains which he formerly had in the thorax are entirely gone; he coughs less and his appetite is much increased. Two months after first injection the angulation of the spine had increased. The cold abscess was opened and pus evacuated, which reaccumulated. Lung condition unchanged. Three months after first injection the patient said that the Friedmann treatment had relieved his pain but not otherwise improved him. He was operated upon for the relief of the rapidly increasing deformity of the spine.

No. 67. P. A., 25 years—Pulmonary tuberculosis III.—Sick two years following pneumonia and pleurisy. Pleural adhesions contracting caused dextrocardia, and patient complains chiefly of shortness of breath. Temperature, subfebrile, under 101°. Cough and expectoration moderate. Cavitation right apex; few rales; left apex dull, but no rales; right base covered by thickened pleura.

Treatment, March 29, 1913, 0.25 c. c. intramuscularly; transient induration.

Treatment, May 17, 1913, 0.2 c. c. intramuscularly; transient induration.

RESULT: Up to the time of second treatment no change observed. About the time of second injection temperature began to run higher, and by the end of three months from the first injection the patient's condition was definitely worse. The left lung gave evidence of recent progressive involvement. The temperature daily reached 102°. There was severe pain in the left chest; the patient was weaker and had lost weight. Subsequently died of tuberculosis.

No. 69. A. D., 48 years—Pulmonary tuberculosis, III.—Duration nine years; slowly progressive; weight practically stationary; temperature normal or subfebrile; copious hemorrhage June, 1912. Patient well nourished; weight, 145 pounds; infiltration both upper lobes; pleuritic rubs right base; suspected cavitation right apex.

Treatment, March 29, 1913, 0.1 c. c. intramuscularly; persistent induration.

Treatment, May 17, 1913, 0.15 c. c. intramuscularly; transient reaction.

RESULT: Three months later patient says she feels worse; more cough sputum, night sweats, and pain. Sputum blood tinged; slight loss of weight. Temperature, maximum, 100°. Lung signs show definite increase, undoubted cavitation of right apex.

March 24, 1914. Seen in sanitorium. General condition somewhat worse than before treatment; lost about 12 pounds. Has had blood spitting at times and been confined to bed off and on. No fever. Sputum, daily, two ounces; contains tubercle bacilli. Chest signs indicate increased area of involvement since treatment.

No. 70. M. R.—Pulmonary tuberculosis, II.—Duration, three years; early hemorrhage and night sweats; cough and expectoration moderate; frequent attacks of vomiting; has gained about 8 pounds in six months. Temperature, subfebrile; dry lesions both upper lobes; moist rales right base; no cavitation.

Treatment, March 29, 1913, 0.1 c. c. intramuscularly; transient reaction; May 17, 0.15 c. c. intramuscularly.

RESULT: Patient continued to have vomiting attacks, which were finally controlled by lavage and diet. Result of treatment obscured by vomiting, which reduced the patient very much and was suspected of being due to diaphragmatic pleurisy. Lung signs practically the same as before treatment.

No. 71. D. W., 18 years—Pulmonary tuberculosis, III.—Sick one year; early hemorrhage; weight stationary; cough moderate; temperature under 101°; infiltration of right apex and left upper lobe; rales on coughing only, except near angle of scapula.

Treatment, March 29, 1913, 0.5 c c. intramuscularly; transient infiltration.

RESULT: Three months later, cough now returning after temporary improvement; feels stronger; temperature as before; lung signs show no rales at right apex; increased rales at left apex; rales in left axilla only on coughing; gained 13 pounds.

March, 1914. Not seen. Said by his mother to be in a sanatorium and doing well. Recent photograph indicates good general condition.

No. 72. I. F., 41 years—Pulmonary tuberculosis, III.—Uncertain duration. Severe hemorrhage last August and two before that; much cough and expectoration morning and night; gain of 8 pounds in last three months; temperature usually under 100°; dullness right side to fourth rib and lower angle of scapula; moist rales posteriorly; dullness left apex.

Treatment, March 29, 1913, 0.15 c. c. intramuscularly; transient reaction.

Treatment, May 17, 1913, 0.2 c. c. intramuscularly; transient reaction.

RESULT: Had severe hemorrhage June 12. Three months after treatment patient notices no difference in condition; temperature 100.4°, maximum. Lost 3 pounds following hemorrhage. Lung shows signs of greater activity in tubercular process in increase of number and area of rales. Died January 19, 1914, of pulmonary hemorrhage.

No. 73. S. K., 22 years—Pulmonary tuberculosis, II, Tuberculosis of elbow joint.—Pulmonary condition, 2½ years' duration. Early hemorrhages; cough and expectoration slight; tubercle bacilli scanty and seldom found; infiltration

both apices. Pain and swelling in the left elbow began 1½ years ago; opened spontaneously. Necrotic bone removed 4½ months ago; treated with bismuth subnitrate and pronounced cured, although a small sinus remained, discharging two or three drops daily. Extension of arm incomplete; flexion possible to about 80°. Dr. Friedmann injected a guinea pig with material from the sinus and the animal developed tuberculosis.

Treatment, March 29, 1913, 0.5 c. c. intramuscularly; slow resorption.

Result: Patient said that his general health seemed to be greatly improved following the first injection; he was much stronger and his cough disappeared. On May 17, when he was to have received the second injection, he was suffering from a severe hemorrhage. Nearly 3 months after the injection subjective symptoms were improved; the elbow was unchanged; still a slight discharge from sinus; lost a few pounds following the hemorrhage; râles were more numerous at the right apex than before.

March 31, 1914. Seen at home. Unable to work since treatment. In June, 1913, began to have trouble with left foot. Diagnosed as tubercular bone disease, and operated upon with good temporary result. Later abcesses developed and he must now undergo another operation for removal of carious bone. Still has sinus at the old site at the elbow, which discharges. Joint can be flexed better than before, nearly to a normal extent. No cough, but brings up some sputum without coughing which is sometimes blood tinged. Chest signs essentially the same as before treatment.

No. 74. S. R., 19 years—Pulmonary tuberculosis, III.—Two and a half years' duration. Severe hemorrhage one month ago; now has very little cough; temperature under 101°; gained 13 pounds in a year; cavitation right upper lobe; impaired resonance left upper lobe; no rales except on coughing.

Treatment, March 29, 1913, 0.3 c. c. intramuscularly; infiltration slowly resorbed.

Result: Nearly three months after treatment patient felt the same as before; temperature ran a little lower, maximum 100°; weight about stationary; greater moisture of lesions indicated by rales.

March 24, 1914. Seen in sanatorium. Condition essentially the same as before treatment, except that the physical signs indicate extension of the lesion in the left upper lobe and increased activity.

No. 76. M. W., 57 years—Pulmonary tuberculosis, III.—Duration four years. Early loss of 25 pounds; weight stationary for two years. Temperature normal. Complains of excessive cough; great shortness of breath. Generally distributed involvement of right lung and of upper lobe of left lung; no cavitation; few moist rales, but mostly sonorous and sibilant rales.

Treatment, March 29, 1913, 0.2 c. c. intramuscularly; transient reaction.

Treatment, May 17, 1913, 0.15 c. c. intramuscularly; transient reaction.

Result: Nearly three months after treatment patient says that he has less pain in the chest than formerly, and on the whole feels somewhat better. Temperature mostly subnormal; 99.4° maximum; weight stationary; lung signs practically the same as before, minus the bronchitis. Died March 14, 1914, of uremia.

No. 8–1. D. H., 24 years—Pulmonary tuberculosis, II, Tuberculosis of knee joint.—Pulmonary condition, six years' duration; slowly progressive; good general appearance; well nourished; maximum temperature 100.5°; slight hemorrhage four months ago; cough and expectoration slight; general distributive lesions both lungs; no cavitation. Left knee swollen and somewhat painful 1½ years following injury; full range of motion possible; can walk, but goes upstairs with some difficulty.

Treatment, April 6, 1913, 0.6 c. c. intramuscularly; transient reaction. Same date, 0.5 c. c. intravenously; marked febrile reaction.

Treatment, May 18, 1913, 0.5 c. c. intramuscularly, causing swelling, which appears about to discharge.

RESULT: Very marked improvement in subjective symptoms; 2½ months after treatment the patient has gained about 7 pounds; temperature frequently 99.3°; states that cough is very slight and sputum about one-third of former amount. The knee very seldom is painful. Physical examination shows no significant change in the lung conditions, and the knee is not objectively improved. The patient is still very short of breath. Treatment caused marked psychic impression.

March, 1914. Not seen; said to be at a sanatorium.

No. S–2. R. L., 5 years—Tuberculosis of hip joint.—Uncertain duration; confined to bed seven weeks previous to admission to hospital; extension with weights practiced for last four weeks; child suffers no pain; has no fever; looks well and comfortable. General condition excellent. Difficult to ascertain whether the limitation of motion is due to ankylosis or muscular spasm. Some pain caused by manipulation of joint.

Treatment, April 6, 1913, 0.7 c. c. intramuscularly; persistent infiltration.

Treatment, April 6, 0.5 c. c. intravenously; severe febrile reaction.

RESULT: June 21, 1913, hip joint more painful; as soon as the weight on the extension apparatus is removed the child cries with pain. The case now seems to be getting worse.

March 23, 1914. Not improved. It has been necessary to have extension apparatus constantly applied. Since January has been running fever, frequently 101°, maximum 103°.

No. S–3. F. B., 4 years—Tuberculosis of knee joint.—Duration uncertain, but supposed to be a recent case. No muscular atrophy; knee joint swollen; intensely tender; practically no motion possible on account of muscular spasm; general condition good.

Treatment, April 6, 1913, 0.5 c. c. intramuscularly, slowly resorbed. Same date, 0.5 c. c. intravenously; severe febrile reaction.

June 21. No improvement noted; motion still rigidly limited.

March 23, 1914. Patient left hospital, but was obliged to return again, the knee being rigid in a flexed position on readmission. The condition is now essentially that described before treatment, except that the knee is somewhat more swollen. Extension apparatus now used.

No. S–4. W. C., 5 years—Tuberculosis hip joint.—Duration probably less than a year; motion limited by muscular spasms; atrophy of corresponding leg; general condition good.

Treatment, April 6, 1913, 0.5 c. c. intramuscularly; persistent infiltration; later abscess. Same date, 0.3 c. c. intravenously; severe febrile reaction.

RESULT: June 21, no improvement having occurred, a brace has been fitted to the child, who is able to walk about on it.

March 23, 1914. Ambulant extension splint continuously applied. Condition of joint essentially the same as before treatment. General condition not as good. The infiltration at the point of injection eventuated in an abscess, the scar of which now remains.

No. S–5. L. L., 16 years—Pulmonary tuberculosis, III.—Duration, two years. Although an advanced case, the general condition is excellent; no cough, expectoration, or fever; weight stationary; tubercle bacilli in sputum. Generally

distributed moist lesions of entire left lung, with probable cavitation and some accumulation of fluid in the pleura; moist infiltration right apex.

Treatment, April 6, 1913, 0.2 c. c. intramuscularly; transient infiltration.

RESULT: June 21, patient states that she feels much stronger than before treatment; gained about 5 pounds. No rales are now heard at the right apex and the left lung is distinctly drier.

SUMMARY: This patient has shown considerable improvement.

March, 1914. Not seen; has gone to Europe.

No. 8–6. C. L., 47 years.—Pulmonary tuberculosis III.—Two years' duration. Slowly progressive case; fairly well nourished; considerable cough and expectoration; temperature 100.5° maximum; weight stationary; tubercle bacilli in sputum; disseminated moist lesions in left lung, especially upper lobe; cavitation in the right upper lobe.

Treatment, April 6, 1913, 0.1 c. c. intramuscularly; transient reaction.

RESULT: Suffered considerably with diarrhea for a few weeks following injection. Patient coughs a great deal and raises more sputum; otherwise feels better than before treatment. Temperature, maximum, 99.8°. Has gained 7 pounds. Lung lesions seem to be somewhat drier than before; this was three months after treatment.

March 23, 1914. Seen. Constantly in sanatorium. Her general condition is somewhat better than before treatment. The lesions are drier and expectoration less.

No. 8–7. N. McK., 18 years—Pulmonary tuberculosis, III.—Known duration only a few months. Pulmonary condition stationary; gaining weight gradually; temperature normal; tubercle bacilli in sputum; general condition appears excellent; disseminated lesions in left chest and right apex.

Treatment, April 6, 1913, 0.2 c. c. intramuscularly, eventuating in discharge of pus.

RESULT: No change in condition observable, except that rales no longer heard at right apex; has lost about 4 pounds. About one month after injection had hemorrhage of about 6 ounces, followed by a fever for a few days. This was the first hemorrhage she ever had.

No. 8–8. A. H., 16 years—Pulmonary tuberculosis, I.—Onset about five months before treatment. Incipient case. Practically no symptoms; excellent general condition. Gaining weight. Tubercle bacilli not demonstrated. Dullness in upper lobe left lung posteriorly with a few fine friction rales.

Treatment, April 6, 1913, 0.2 c. c. intramuscularly; eventuating in abcess formation; perhaps determined by an injury.

RESULT: June 21, patient feels the same as before treatment and physical condition is unchanged.

No. 8–9. R. L., 29 years—Pulmonary tuberculosis, III.—Known duration about two months. Progressive case, with fever sometimes to 104°. Much cough; blood-streaked sputum; losing weight; tubercle bacilli positive in sputum; disseminated moist lesions in left lung with suspected cavitation in lower lobe; isolated areas of rales at right apex and in right axilla.

Treatment, April 6, 1913, 0.2 c. c. intramuscularly; transient infiltration.

RESULT: Three months later. After some temporary subjective improvement patient began to fail, and is now distinctly worse; confined to bed; temperature nearly 103° every day; much cough; excessive night sweats. Subsequently died of tuberculosis.

No. 8–10. M. A., 18 years—Pulmonary tuberculosis, II.—Duration about six months; moderately advanced case; the only symptom is a slight cough. Gen-

eral appearance excellent; is gaining weight; lung signs consist of a few scattered rales in the right upper and middle lobe. There is no expectoration and tubercle bacilli have not been demonstrated.

Treatment, April 6, 1913, 0.2 c. c. intramuscularly, eventuating in discharge of pus.

RESULT: June 21, feels the same as before treatment; gained about 3 pounds; lung signs unchanged, except that there is suspicion now of cavitation in the middle lobe.

March, 1914. Seen the 29th. Feels well and is at work winding lace on cardboard. No hemorrhages. Cough same as before; little or no sputum. No fever. Weight about the same. Was in hospital 10 months and discharged "arrested." Lung signs show less moisture than when first seen; a suspicion of cavity remains as before, and dry crackles are heard not only on the right but also on the left side.

No. S–11. C. D., 32 years—Pulmonary tuberculosis, III.—Duration about six months; an unfavorable rapidly progressive case with fever, emaciation; disseminated lesions in both lungs; large cavity in left lower lobe.

Treatment, April 6, 1913, 0.1 c. c. intramuscularly; transient reaction.

Treatment, May 18, 1913, 0.1 c. c. intramuscularly; transient reaction.

RESULT: Patient said that she felt better and stronger. Physical examination showed no improvement, except reduction in the number of rales in the right lung. Subsequently died of tuberculosis.

No. S–12. S. Y., 24 years—Pulmonary tuberculosis, II.—Five years' duration; moderately advanced case; now practically stationary; normal temperature; lost weight slowly; infiltration of both apices extending to the third rib on the right side, and the angle of the scapula on the left; no cavitation. Tubercle bacilli in sputum.

Treatment, April 6, 1913, 0.2 c. c. intramuscularly; persistent infiltration.

RESULT: June 21, patient has been running high temperature, recently to 100.3°; has lost about 5 pounds; lung signs, if anything, are better, the area of rales being reduced.

March 25, 1914. Seen in sanatorium. Condition in all respects about the same as before.

No. S–13. C. D., 29 years—Pulmonary tuberculosis, III.—Duration about a year. Advanced case; progressive. In fair general condition without fever; moderate cough and expectoration; weight much below normal, but practically stationary for several months; infiltration of right apex and middle lobe; disseminated moist lesions of left upper lobe with cavitation.

Treatment, April 6, 1913, 0.2 c. c. intramuscularly; persistent infiltration.

RESULT: Three months later, thinks herself improved, especially in strength; weight stationary; lung signs show disappearance of rales at right apex, otherwise no change.

No. S–14. M. B., 19 years—Pulmonary tuberculosis, III.—Duration about eight months; advanced case, progressing slowly; poor general condition; daily rise of fever, at times to 102°; losing weight; infiltration of right upper lobe with cavitation; evidence of old pleurisy at right base; some rales at right base at apex.

Treatment, April 6, 0.2 c. c. intramuscularly; transient reaction.

Treatment, May 18, 1913, 0.2 c. c. intramuscularly; transient reaction.

RESULT: No significant change in subjective symptoms; patient lost about 9 pounds. Still ran fever to 102°. June 21, recent hemorrhage 3 ounces, first she ever had. Physical examination showed fewer rales than previous examinations; probable collection of fluid in right pleural cavity. Subsequently died of tuberculosis.

No. 8–15. E. L., 22 years—Pulmonary tuberculosis, I.—Gradual onset, two years before treatment. General condition excellent. Favorable case; improving; has had hemorrhage within a few weeks. Temperature normal; slight loss of resonance at right apex; no rales.

Treatment, April 6, 1913, 0.1 c. c. intramuscularly, terminating in abscess formation on May 5.

RESULT: No change subjectively or objectively. April 11, had slight hemorrhage. May 18, another. Some loss of weight followed the hemorrhage, but three months after treatment she was regaining her weight.

No. 8–16. M. B., 33 years—Pulmonary tuberculosis, III.—General condition poor; weight stationary; usually low fever; occasional rise to 101°. Several small hemorrhages; infiltration of right apex and in the right axilla; disseminated moist lesions throughout left lung.

Treatment, April 6, 1913, 0.1 c. c. intramuscularly; transient reaction.

Treatment, May 18, 1913, 0.1 c. c. intramuscularly; persistent nodule.

RESULT: Three months later patient says she feels somewhat stronger; sleeps better and has better appetite. Temperature, maximum, 99.3°, seldom reached. Weight stationary; physical signs same as before, except that no rales now heard at the right apex.

No. 8–17. M. K., about 30 years—Pulmonary tuberculosis, I.—An advanced, rapidly progressive case; hectic fever; loss of weight; infiltration of right upper lobe; disseminated lesions in left lung with cavitation in upper lobe.

Treatment, April 6, 1913, 0.1 c. c. intramuscularly; transient reaction.

RESULT: Patient continued to get worse and died on May 12, 1913. No influence of the treatment either for better or worse could be determined.

No. 8–18. B. B., 14 years—Pulmonary tuberculosis.—Onset August, 1911. This case is described as a cured case. Has absolutely no symptoms; fat and appears in good health. Lung signs: Slight dullness at left apex.

Treatment, April 6, 0.1 c. c. intramuscularly, eventuating in discharge of pus May 18.

RESULT: Aside from the abscess formation no effect of the treatment was noted.

March, 1914. Not seen. A friend says she is in good health.

DISCUSSIONS OF CLINICAL OBSERVATIONS.

Phthisiologists will appreciate how difficult it is to express the condition of a patient or the results of treatment in a tabulated statement. They understand moreover the pitfalls which beset the investigator in obtaining the material on which such a tabulation is based. Nevertheless such a concise presentation is of value in giving at a glance a survey of numerous observations, and we have prepared the following table for that purpose. The following observations are essential to an understanding of what we mean by the various headings:

1. The "number of treatments" refers to the number of times treatment was given, not necessarily to the number of injections, since at the first treatment in some of the cases, chiefly extrapulmonary, two injections were given, one intramuscularly, and one intravenously, as will be seen by consulting the case histories.

2. By "result unusually good" we mean simply that the improvement noted was of such a degree as is not commonly observed in the general run of cases. In no single case was this improvement such that it could not be paralleled in the experience of any physician having extensive acquaintance with tuberculosis.

3. By "result unusually bad" we mean that the course of the disease following treatment was distinctly worse than would be expected in the general run of cases. Here again we must concede that no single case taken by itself would be unparalleled in an extensive experience.

4. Under the caption "usual result" we have grouped those cases in whom the disease in our judgment ran a course which would be expected without special treatment under the conditions obtaining for each individual patient. Some of these got a little better, some a little worse, and some, as might have been foreseen, died of their disease. In some of these cases, abscesses, which did not appreciably affect the condition of the patient, developed at the site of the intramuscular injection.

The classification of pulmonary cases is the Turban-Gerhardt, which is based on the extent of the lesion, and does not take into account the resistance or general condition of the patient, or his expectancy of life. As has been stated, some of our third-stage cases were persons of uncommonly robust appearance, with lesions of low activity and slow progress, and were not, as Dr. Friedmann hastily assumed them to be from casual inspection of their chest diagrams, "dying cases," although the outlook for a cure in this class of patients with ordinary methods of treatment is admittedly very poor.

TABLE I.

PULMONARY CASES, STAGE I.

Serial number.	Number of treatments.	Result unusually good.	Result unusually bad.	Usual result.	Months observed.	Remarks.
S18	1	.....	.....	+	12	Healed case before treatment. Abscess from injection.
2	1	.....	.....	+	3	
S8	1	.....	.....	+	3	Abscess from injection.
3	1	+	.....	.....	.....	Acute condition, rapidly improving when treated.
13	4	.....	.....	+	12	Pulmonary condition, considered cured, returned after intercurrent illness.
50	1	.....	.....	+	12	Recent laryngeal involvement. Abcess from injection.
S15	1	.....	.....	+	3	Hemorrhage before and after treatment. Abscess from injection.
5	2	.....	.....	+	3	Hemorrhage before and after treatment.
14	3	+	.....	.....	.....	Hemorrhage before and after treatment. Is now apparently an arrested case.
29	2	.....	.....	+	12	Hemorrhage before and after treatment. Abscess from injection.

TABLE I—Continued.

PULMONARY CASES, STAGE II.

Serial number.	Number of treatments.	Result unusually good.	Result unusually bad.	Usual result.	Months observed.	Remarks.
1	2	.....	.....	+	12	Laryngeal complication. General condition worse following each injection.
9	2	.....	.....	+	3	
10	2	.....	.....	+	3	
17	1	.....	.....	+	3	First hemorrhage 2 weeks after treatment.
14	1	.....	.....	+	12	Abscess followed injection.
46	1	.....	.....	+	3	Subsequently died of tuberculosis.
48	1	.....	.....	+	3	
49	1	.....	.....	+	12	
52	1	.....	.....	+	3	
57	1	.....	.....	+	3	
59	1	.....	.....	+	3	
70	2	.....	.....	+	3	
S11	2	.....	.....	+	3	Knee-joint complication, subjectively improved.
S10	1	.....	.....	+	12	Abscess from injection.
S12	1	.....	.....	+	12	

PULMONARY CASES, STAGE III.

4	2	.....	.....	+	3	
6	1	.....	.....	+	3	Abscess from injection.
7	2	.....	.....	+	3	Much aggravation of symptoms followed second injection.
12	2	.....	.....	+	12	Was doing well when exposed in storm, and return of symptoms followed.
15	2	.....	+	.....	12	Rapid increase of disease followed second injection.
18	1	.....	+	.....	12	Rapid increase of disease followed injection.
16	1	.....	+	.....	3	Died of tuberculosis. Rapid increase of disease and laryngeal involvement followed injection.
19	1	.....	.....	+	3	Died of tuberculosis.
20	1	.....	.....	+	12	Abscess from injection.
21	2	.....	.....	+	12	
22	2	.....	.....	+	12	Ischio-rectal abscess developed after injection.
*23	2	.....	.....	+	12	See also under genito-urinary tuberculosis.
25	1	.....	.....	+	12	Abscess from injection.
26	1	.....	.....	+	12	
27	2	.....	.....	+	12	Abscess from second injection.
28	2	.....	.....	+	3	
30	1	.....	.....	+	12	Abscess from injection.
45	1	.....	.....	+	3	Died of tuberculosis.
53	1	.....	.....	+	12	Abscess from injection.
54	2	.....	.....	+	3	
56	2	.....	.....	+	3	Died of tuberculosis.
58	2	.....	.....	+	3	
60	2	.....	.....	+	12	Intractible eczema developed since injection.
61	1	.....	.....	+	1½	
67	2	.....	.....	+	3	Died of tuberculosis. Involvement of new areas followed injection.
69	2	.....	.....	+	12	
71	1	.....	.....	+	3	
72	2	.....	.....	+	3	Died of pulmonary hemorrhage.
74	1	.....	.....	+	12	
76	2	.....	.....	+	3	Died about one year later of uremia.
S5	1	+	.....	.....	3	
S6	1	.....	.....	+	12	
S7	1	.....	.....	+	3	First hemorrhage 1 month after treatment. Abscess from injection.
S9	1	.....	.....	+	3	Died of tuberculosis.
S11	2	.....	.....	+	3	Do.
S13	1	.....	.....	+	3	
S14	2	.....	.....	+	3	Died of tuberculosis. First hemorrhage followed injection.
S16	2	.....	.....	+	3	
S17	1	.....	.....	+	3	Died of tuberculosis.

TABLE I—Continued.

TUBERCULOSIS OF BONES AND JOINTS.

Serial number.	Number of treatments.	Result unusually good.	Result unusually bad.	Usual results.	Months observed.	Remarks.
73	1	.....	.....	+	12	Also pulmonary, second stage, hemorrhage before and after injection. New involvement of bone after injection.
31	2	.....	.....	+	3	Temporary improvement after second injection.
33	2	.....	.....	+	3	Abscess from first injection.
34	2	.....	.....	+	12	Abscess from second injection. Joint subsequently operated.
35	2	.....	.....	+	12	
36	2	.....	.....	+	3	Also pulmonary, first stage, hemorrhage before and after injection.
37	3	+	.....	.....	12	Effect of prolonged immobilization not eliminated. Case apparently cured.
38	2	+	.....	.....	12	Same remarks as above case.
43	2	.....	.....	+	1½	
40	1	.....	+	.....	¾	Strong evidence of focal reaction. Meninges became involved. Died 3 weeks after injection.
82	1	.....	+	.....	12	Pain increased after injection.
83	1	.....	.....	+	12	
84	1	.....	.....	+	12	
11	1	.....	.....	+	12	Died of pulmonary tuberculosis. Bone condition seemed favorably influenced.
66	2	.....	+	.....	3	Pain less, but bone destruction more rapid after injection.

LUPUS.

47	1	.....	.....	+	12	Abscess from injection.
55	1	+	.....	.....	3	Lupus area improved remarkably. Associated lymph node involvement not influenced.
63	2	.....	.....	+	12	Abscess from first injection.
64	2	.....	.....	+	3	Abscess from second injection.

TUBERCULOSIS OF LYMPH NODES.

32	1	.....	.....	+	3	General health improved. Abscess from injection.
39	2	+	.....	.....	12	Healing of sinus unusually prompt and smooth. Deep glands remained enlarged.
41	2	+	.....	.....	3	Rapid reduction in size of nodes.

GENITO-URINARY TUBERCULOSIS.

8	2	.....	.....	+	3	
65	1	.....	.....	+	12	
62	1	.....	.....	+	.....	Died in a few days. Hopeless when treated.
23	2	.....	.....	+	12	

We propose to discuss this table briefly and then to discuss certain features of our observations which, being largely of the nature of impressions, are less susceptible of tabulation, although we believe of no less value in forming our final conclusions.

The great majority of cases are seen to fall in the column "usual result," and call for little comment. Many of these cases claimed relief from one or another subjective symptom during the first few weeks following treatment, but in nearly all cases this improvement was merely temporary and was unaccompanied by discoverable objective changes. Other physicians who saw these cases were willing to dismiss this subjective improvement at once as due to psychic

influence. However, as there is at hand no absolute proof that this improvement may not have been attributable to some action on the toxic substances which play a part in tuberculosis, we prefer not to attempt to decide this question. It is a well-known fact that tuberculous patients are similarly affected at the outset by almost any new form of treatment to which they are subjected. The same remarks we believe are applicable to minor grades of objective improvement noted in some of the patients recorded in the column under consideration.

The "result unusually good" column presents eight cases for discussion. Details are given in the case histories. Results like these are undoubtedly seen occasionally, though not commonly, after the ordinary methods of treatment. If these cases represented a majority of the "not altogether too far advanced cases" we should be quite justified in attributing to the remedy very significant and promising curative properties. They actually represent only a small minority of such cases in our series, and collectively can only be regarded as suggestive of specific action.

The cases headed "result unusually bad," six in number, are equally inconclusive, but also give the impression of specific activity of the remedy, in this case to the detriment of the patient. The pulmonary cases were of the third stage, and the fact that they rapidly grew worse shortly after the treatment may perhaps be regarded as mere coincidence, although the change was very striking to the observer. The bone and joint cases under this heading contribute stronger evidence of specific and pernicious activity on the part of the remedy, case No. 40 in particular.

Viewing these cases as a whole, they made upon us the impression that some agent specifically related to tuberculosis was at work. In the majority of cases this was evidenced only by subjective changes for the better or worse, and by minor and transient changes in the physical signs which might be in either direction.

To consider now in some detail certain of the claims made by Dr. Friedmann, we will refer to the numbered paragraphs at the beginning of this report (see Part II, p. 11) in which these claims are presented.

Paragraph 4. We have evidence that the material injected was harmful of itself, inasmuch as it produced abscesses or inflamed and discharging lesions in approximately one-fourth of the persons injected. These did not, however, appear to influence the general health, and are of slight importance in this connection, although from what is said of these lesions in paragraph 13 (see p. 12) it would appear that their appearance is regarded by Dr. Friedmann as a bar to successful treatment. It will be noted that they were most

frequent in the most benign class of cases, those which are most amenable to successful treatment by our present methods. While the injections did not appear to be directly harmful beyond abscess production, there was sufficient evidence of their being indirectly injurious when injected into certain tuberculous persons, to make the indiscriminate administration of the material to such subjects a matter of very dubious propriety. Moreover, we were unable to determine any rule by which it could be foreseen in what class of patients this action was most likely to take place. We can not, therefore, subscribe to the unmodified statement of Dr. Friedmann cited in paragraph 4. The question is naturally suggested also, why, if the material is completely harmless, is it necessary to so carefully regulate the dosage, and why may not the combined intravenous and intramuscular injection be made in every case?

Paragraph 12 (see p. 12). Our observations do not bear out all of the claims made in this paragraph. None of our bone and joint cases with fistulæ has been healed. It is true that some of our lymph node cases did improve remarkably and are very significant of favorable specific action. The results in the pulmonary cases do not confirm the claim made by Dr. Friedmann.

Paragraph 13 (p. 12) we can confirm, inasmuch as no case in which an abscess formed could be classified in the "result unusually good" column.

Paragraphs 15 and 16 (p. 12). We have insufficient data on which to determine the facts relating to the minutiæ of these claims. It is suggested by these statements that the reactions, local and general, resulting from successive injections may be very different. This appears to be so. Several of our patients who were subjectively improved after the first injection became subjectively and objectively worse following the second. Some patients developed abscesses from the first injection, and others only after the second.

The claims of paragraph 19 (p. 13) can be definitely refuted. Abscess formation was prevalent following the "simultaneous" injections in about the same proportion as after the intramuscular alone.

The claims of paragraphs 23 and 24 (p. 13) have already been dealt with.

Paragraph 25 (p. 13) can not be unreservedly indorsed. Increased activity of existing lesions following the injections was so frequently observed as to be almost the rule. It was not of the explosive character described as following an overdose of tuberculin. In one case there must remain the strong suspicion that the injection lighted up old areas of infection to the extent of determining metastasis to hitherto uninvolved areas (case 40).

Sufficient evidence will be found in Table I to disprove the remarkable assertions of paragraph 26 (p. 13). Hemorrhages, in some cases the first which the patient had ever suffered from, were frequently seen after the injections.

Paragraph 27 (p. 13) can be partially confirmed. We had too few cases with night sweating shortly before treatment to contribute any evidence on this point. On the average the temperature of the patients was running somewhat lower a few months after the treatment than immediately before it, but striking reductions were not seen, and in a number of cases the fever was higher, especially following the second injection. In a majority of cases subjective improvement was noted by the patients, which was usually only temporary.

On the average the gain in weight in these patients was less than a pound during the three months following treatment (c.f., par. 28).

Some of our patients were in condition to do light work a few weeks after treatment, but none who was not able to do so before was fit to undertake severe labor, which is the class of work done by most of the patients Dr. Friedmann reports upon (par. 29 and elsewhere in his article).

Paragraphs 30 and 31 (p. 14) can receive only partial confirmation from our observations. It is true that in some cases cough and expectoration were lessened or even disappeared, and some improvement in auscultatory signs occurred, but this was not the typical course. Such cases were exceptional and were balanced by others in which the symptoms and signs were increased.

Some reference must be made to the methods of injection and the dosage employed by Friedmann in treating the patients. The mere technic employed was in general adequate but not scrupulous, although some glaring exceptions were accidentally observed. Intravenous injections were given commonly in the veins at the bend of the elbow, occasionally in children in the external jugular. The intramuscular injections were made about an inch posterior to the great trochanter of the femur, with some show of pains in selecting the exact spot. Two bottles of the preparation were at hand, one for intravenous and the other for intramuscular use. On at least one occasion it was observed that they became unwittingly confused, without, however, causing any unusual symptoms in the patient. As regards dosage, but two factors were observed by Friedmann with what appeared to be any consistence, and in several cases through forgetfulness they were ignored. These were pulmonary involvement and hemorrhage, the former apparently constituting a contraindication to the intravenous injection and the latter calling for only minimal doses. This naturally suggests the question, Why, if

the substance is entirely harmless, is it necessary to discriminate as to the dosage? Why can not intravenous injections be given to pulmonary cases and maximum doses to patients who have had bleeding?

The reactions following the intravenous injections were invariably severe, with headache, malaise, and high fever, which passed off in the course of two or three days. The local manifestations, after intramuscular injection, varied from the mere mark of the needle through various grades of induration to abscess formation, as noted in the case histories and table of summaries.

CONCLUSIONS ON THE CLINICAL OBSERVATIONS.

The preparation used by Dr. Friedmann in our cases was not entirely harmless, inasmuch as it frequently produced abscesses or discharging lesions at the site of injection. Moreover, there is presumptive evidence that it may cause damage to a tuberculous person. For this reason we believe that its promiscuous injection into tuberculous patients is unjustifiable.

There is evidence that this preparation exerts a specific action when injected into persons suffering from tuberculosis, which in the majority of cases treated with the number of injections which our patients received is insufficient to materially alter the course of the disease, in a small minority of cases redounds to the patient's advantage, and in another small minority results in definite injury.

The nature of the claims, the cases cited, and the general tone of Dr. Friedmann's article are such as to create the impression that his methods represent a great advance over previous methods of treating tuberculosis. The observations here recorded do not bear out this impression.

It is realized that the claim will be made that our patients did not receive as protracted a course of treatment as might have been administered if they had been continuously under Dr. Friedmann's care, and that had they received more treatments the results might have been different. To this claim we can answer: First, that many of the brilliant results which he reports in his article, and which we must assume to be representative, were obtained with but one or two injections; second, that the failure of our patients to receive further treatments was due to Dr. Friedmann's negligence, unprofessional conduct, and commercial greed, primarily, and secondarily to the alarm engendered on the part of the health authorities locally responsible by the unfavorable course taken by the disease in certain patients, apparently as a result of the injections.

PART IV.

LABORATORY STUDIES.[1]

CULTURAL.

In the experiments with the Friedmann culture several different "strains" were used from time to time, in addition to the one turned over to the board by Dr. Friedmann on March 9, 1913, and designated hereafter as FFF. These other strains were two grown from the material used by Dr. Friedmann for intravenous injection, one from the material for intramuscular injection, one recovered after passage through an experimental animal, and one recovered from the abscess at site of intramuscular injection in a patient treated by Dr. Friedmann. No noteworthy differences in characteristics or rapidity of growth were seen between the original strain (FFF) and the others after the first few generations, nor in morphology and staining reactions. Of the four strains obtained directly from Dr. Friedmann, two showed contamination and were isolated with difficulty. These two were from a vaccine for intravenous injection obtained March 19, 1913, and from one for intramuscular injection obtained March 22, 1913. The contaminating organism in both cases was a small staphylococcus.

The following media were used for the cultivation of the Friedmann bacillus:

Three per cent glycerin agar (taken as the standard for carrying over the various strains and for animal inoculations).
Five per cent glycerin agar.
Five per cent glycerin potato.
Plain egg medium (Dorset).
Glycerin egg medium (Lubenau).
Blood serum.
Five per cent glycerin broth.
Plain agar.
Three per cent glycerin gelatin.
Plain gelatin.

To compare with Friedmann's bacillus, several other acid-fast organisms were grown—namely, human, bovine, and avian tubercle bacilli, fish tubercle bacillus, frog tubercle bacillus, Moeller's grass bacillus, butter bacillus, milk bacillus, margarine bacillus, dung

[1] We are indebted to Passed Asst. Surg. Leake for the performance of much of the work involved in these studies.

bacillus, bacillus of nasal secretion, smegma bacillus, and 10 strains of the chromogenic leprosy bacillus, with two strains of the bacillus of rat leprosy. No marked correspondence was noted between any of these and the Friedmann bacillus. The latter grew in general more rapidly and in less nodular fashion than the different varieties of tubercle bacilli, and produced less pigment than the other organisms of the acid-fast group.

Morphologically and in staining reaction the Friedmann bacillus showed considerable variation. This variation was not regular in relation to the age of the culture and the medium used or to the period of inoculation when recovered from animals, but smears from any one tube or from one site were fairly uniform in appearance. In general the morphology was indistinguishable from that of tubercle bacilli and the grouping was often characteristic of the pathogenic organism. Bent and beaded forms were more common in smears from animals than in those from cultures. In length the bacilli measured from 1 to 11 micra and in breadth from one-fourth to three-fourths of a micron. All were Gram positive, and, with weak decolorizing agents such as Gabbet's stain, all were acid fast, but prolonged application of the stronger means of decolorization, such as acid followed by alcohol or combined with it in Czaplewski's or Ebner's fluids, resulted in a great proportion of the bacteria losing the original stain—about 95 per cent after an 18-hour treatment with Czaplewski's acid alcohol and practically 100 per cent after one hour in Ebner's fluid. A similar but not so marked tendency to decolorization was noted in all the strains of human, bovine, and avian tubercle bacilli examined, and all the other acid-fast organisms lost their stain in general even more rapidly. As with the Friedmann bacillus, this decolorization varied in different methods of manipulation, precluding its establishment as an absolute differential point.

On the glycerin media the bacillus grew readily at 37°, 27°, 20°, and 15°, and, after nursing, more profusely at 40° than at any of the lower temperatures. The rapid growth at this high temperature was maintained for only a few days, and soon after subcultures showed no growth. At 0° there was a questionable growth of all the strains in 10 days, but marked in 20 days. At this temperature glycerin egg did not prove as suitable a medium as glycerin agar. The moistness of the cultures grown at low temperatures (20°, 15°, and 0°) is in marked contrast to the dry appearance of those grown at higher temperatures, irrespective of the dryness of the media. This was noted by Friedmann in regard to his first turtle bacillus.[1] After several months' cultivation at low temperatures all of our

[1] Centralblt. f. Bakt., Orig., Bd. 34, Heft 7, p. 650.

strains persisted in giving a moist growth through successive generations at 37°. We have found the organism viable for a long time—after 10 months at 15°. Paraffined cotton plugs were commonly used to prevent drying out, though some tubes were capped with tin foil or plugged with corks, and some were simply stoppered with cotton in the ordinary way.

With favorable media and temperatures growth was visible in 24 hours, and luxuriant after a week, but sometimes tubes planted with material from animals experimentally inoculated would show no change after a week or 10 days, colonies being found a week later. This may have been due partly to change in environment and partly to the sparsity of bacilli viable on the culture medium, as ordinary transplants which showed the more rapid growth were heavily inoculated as a rule.

Glycerin egg proved to be the most favorable culture medium, but glycerin agar was used for routine transplants on account of its uniformity and the ease with which the bacillary mass was separated from its surface. The growth on blood serum and plain egg was disappointingly sparse. Growth was scant on plain agar and plain gelatin, but all the media containing glycerin showed good growth. At the higher temperatures this was dry, finely granular at first, becoming nodular after a few days. It was nearly white in color, slightly yellowish on glycerin egg and glycerin potato. The egg cultures at 0° were uniformly of a pinkish cream tint. Over the water of condensation in glycerin agar tubes and on the surface of glycerin broth cultures a pellicle is rapidly formed which in a week extends for 1 centimeter upward on the glass, the fluid remaining clear. This pellicle is also nearly white and wrinkled, becoming heavily rugous after 10 days. The appearance on solid media did not resemble that of human or bovine tubercle bacilli closely; the growth was more rapid, whiter in color even in old cultures, softer, and less dense. The apparent nodules were at first only rugæ in the superficial pellicle, the growth at the summit being but little thicker than at the base. In old broth cultures there was a distinct difference in odor between the Friedmann flasks and the flasks inoculated with tubercle bacilli; this was appreciated by all observers, but the description of the odors varied widely, some terming the odor of the FFF culture sweet and some sour.

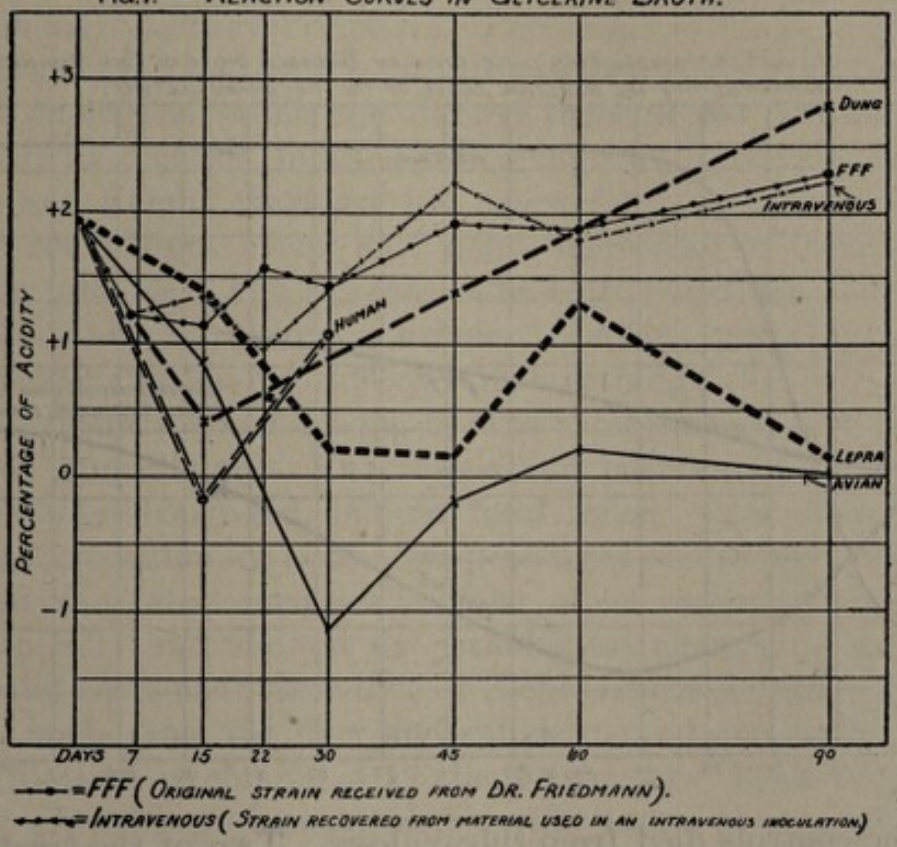
The Smith reaction curve in glycerin bouillon showed nothing to distinguish this bacillus from others of the acid-fast group. Six flasks each, of two strains, were inoculated and compared with other organisms. The result is shown in the accompanying chart (fig. 1). The second chart (fig. 2) gives three curves, one compounded from the two Friedmann curves in the preceding chart and the other two

from the different human and bovine curves, respectively, given by Theobald Smith.[1] The 90-day end point which differentiates human strains from bovine, as found by Grund,[2] is also indicated. Grund found that after 90 days the different types of bovine strains had, in general, a lower acidity than 1.5 per cent and the human types a higher. The methods of cultivation and titration described by Grund were used.

ANIMAL INOCULATIONS.

The animal experiments continued over 14 months; 180 guinea pigs, 30 rabbits, 16 monkeys, and 8 tortoises have been used. The

FIG. 1.— REACTION CURVES IN GLYCERINE BROTH.



animals were weighed weekly, and the temperatures of some were taken daily or twice daily.

The usual dose was 10 mg., this giving, when suspended in 1 c. c. of physiological saline solution, an emulsion apparently about as dense as that used by Dr. Friedmann in New York. Necropsies were made on all animals, those surviving being chloroformed at the conclusion of the period of observation.

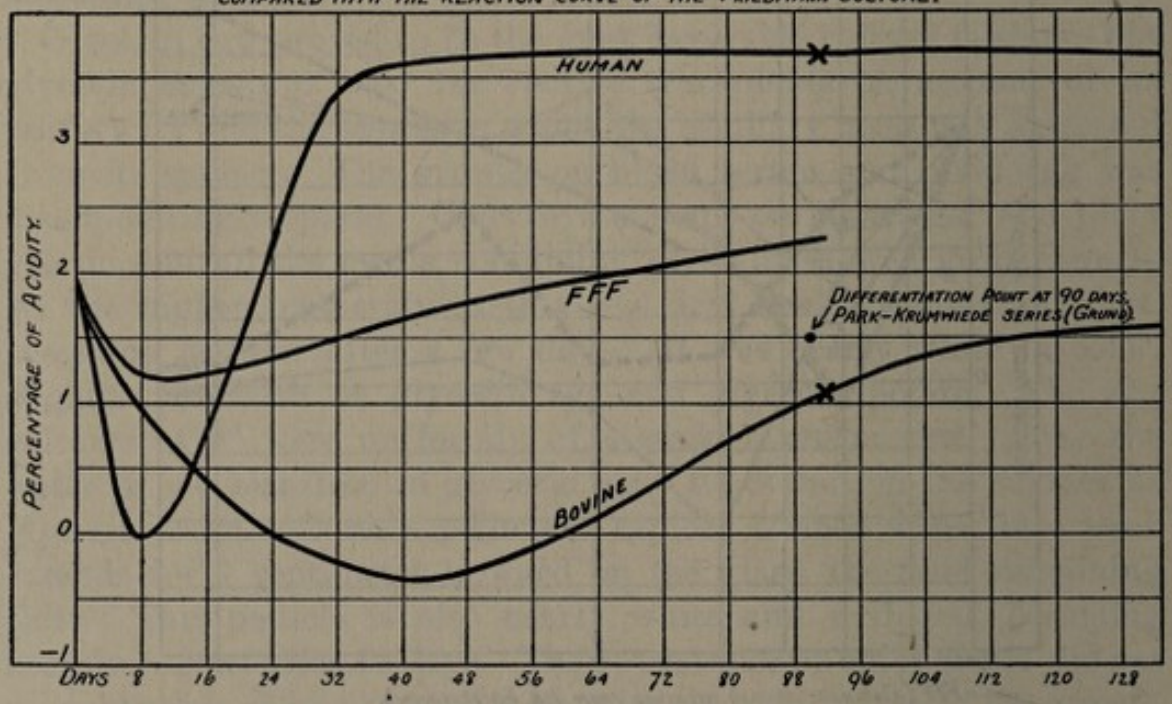
Six of the tortoises were *Chrysemys picta* (one of the variety marginata) and two were land tortoises, Cistudo or Emys. They were

[1] Journal Medical Research, vol. 23, p. 185.
[2] Idem, vol. 25, p. 358.

inoculated intraperitoneally with various acid-fast bacilli, four with Friedmann's organism, one with lepra bacilli, one with human tubercle bacilli, and one with bovine tubercle bacilli, one being kept uninoculated as a control. None of the tortoises developed tuberculosis, most of them living over a year after inoculation.

Nine monkeys received the Friedmann bacillus, intramuscularly in part, intravenously in part, and some by both methods. An interval of 31 to 47 days was allowed to elapse between treatments. Seven were kept uninoculated as controls. Before the first inoculation the presence or absence of tuberculosis was deduced from the cutaneous (v. Pirquet) and ophthalmic (Calmette) tests and from thoracic percussion. Three of the Friedmann-treated monkeys and

FIG. 2.— CURVES COMPOUNDED FROM THOSE GIVEN BY THEOBALD SMITH IN JOUR. MED. RES., OCT. 1910, COMPARED WITH THE REACTION CURVE OF THE FRIEDMANN CULTURE.



one of the controls died from tuberculosis. Two of the treated animals apparently had tuberculosis before treatment—at the time of the first examination. The other treated animal which died and the control apparently contracted tuberculosis during the period of observation. None of the other monkeys showed tuberculosis at autopsy, though slight pleural adhesions were found in some, both treated and controls. There was nothing significant in the weight charts, save, in the monkeys which died of tuberculosis, a gradual decline before death.

Temperature reactions (of about a degree Centigrade) were more uniformly observed after intravenous inoculation than after intramuscular, and were more common in both series after second and third treatments than after the first. Only one of the monkeys was artificially inoculated with tuberculosis; this animal was turned over

to the laboratory through the courtesy of Dr. Gerald Webb, of Colorado Springs, who gave it 400 living tubercle bacilli subcutaneously 70 days before the treatment was begun here. At the time of the first Friedmann inoculation there was a papule at this site. This monkey received three "simultaneous" treatments—that is, inoculations with Friedmann's bacillus, both intravenously and intramuscularly, and reacted in temperature each time. At autopsy an intense tubercular peritonitis was found; the three naturally infected monkeys died of pulmonary tuberculosis. One other monkey died in a manner worthy of mention. The protocol follows:

Monkey No. 22: 3–17–1913, cutaneous tuberculin test, right thigh, negative; 3–19–1913, conjunctival tuberculin test (1 drop 1 per cent tuberculin alt), right eye, negative. Percussion of lungs shows nothing abnormal; 3–21–1913, 2 p. m., 10 milligrams FFF suspended in 1 c. c. physiological saline and filtered through No. 588 Schleicher and Schüll Faltenfilter, injected into a vein of the right calf. Temperature and weight chart are not noteworthy. 5–2–1913, epileptiformlike convulsions every half hour, increasing in frequency to every five minutes. The attacks begin with twitching of limbs on left. 5–3–1913, convulsions continue. Monkey becoming progressively weaker and having difficulty in breathing. 3 p. m.—As animal was evidently about to die, he was chloroformed and necropsy performed immediately. The vessels and membranes of the brain were somewhat congested, but no focal lesions were discovered in cerebrum, cerebellum, or pons after prolonged sectioning. The lungs were also somewhat congested. The other organs were normal macroscopically and showed no pathological changes after Zenker fixation and eosin-methylene-blue or Ziehl-Gabbet staining. Smears, however, made from the liver and spleen showed extracellular acid-fast bacilli, some in clumps of 15 micra diameter. Tubes of glycerin agar and glycerin egg inoculated from the tissues gave no growth.

It is to be especially noted that the tuberculin tests made before inoculation with the Friedmann culture were negative in each instance; nevertheless, clumps of acid-fast bacilli were found at autopsy in the liver and spleen.

The rabbits were all inoculated subcutaneously with .01 milligram of a 46-day culture of bovine tubercle bacilli. The suspension used (1 c. c. per dose) was entirely clear macroscopically, but smears showed an even distribution throughout the suspension of 10 to 30 acid-fast organisms in each microscopic field. Five of these rabbits were kept as controls and received no Friedmann inoculation. Seven received Friedmann bacilli before the bovine injection—two getting two intravenous treatments, 60 and 30 days, respectively, before the bovine, three receiving the first intravenous and the second intra-

muscular on the same dates, and two receiving only the first intravenous treatment. Eleven were treated with the Friedmann bacillus 30 days after the bovine injection; various amounts of FFF, from 0.001 milligram to 1,000 milligrams, were given intramuscularly. Seven rabbits died of intercurrent disorders not pertinent to the experiment. All of the 23 other rabbits were allowed to die with typical pulmonary tuberculosis save two, which were chloroformed 363 days after inoculation with bovine tubercle bacilli. The protocols of these two follow.

Rabbit No. 1.—3–21–1913; 10 milligrams FFF suspended in 1 c. c. physiological saline solution passed through No. 588 S. & S. filter paper and injected into an ear vein. No temperature reaction during seven days observation. 4–2–1913; the same dose repeated. 5–20–1913; 0.01 milligram bovine tubercle bacilli injected subcutaneously in the belly wall. The weight was taken weekly and showed a gradual increase up to 4–25–1914, then a slight decline. 5–18–1914, chloroformed. Necropsy.—There is a small brownish abscess at the site of the bovine inoculation. The lungs are somewhat reddened but no definite lesions could be made out macroscopically; Zenker fixed sections show small areas of infiltration with epithelioid cells. The other organs are normal. Smears from the lung fail to show acid-fast bacilli but these are relatively numerous in smears from the site of the bovine inoculation.

This is the nearest approach to apparent immunization by the Friedmann bacillus that we have encountered in any of our animals. However, this can by no means be counted as absolute because, in the first place, rabbit No. 30 of the control series showed even less local change at the site of inoculation on necropsy; this control rabbit died with pulmonary tuberculosis 267 days after the bovine inoculation and neither macroscopically nor in smears could any trace of abscess formation or acid-fast organism be found at the site. In the second place, in all the rabbits actual tubercle bacilli were infrequent in smears and sections from the lung, no matter how intense the tubercle process appeared in situ and histologically. In the third place, to judge from beginning epithelioid infiltration, beginning decrease of body weight, and the weight charts of the other rabbits, this animal (No. 1) would not have lived more than 2 months.

Rabbit No. 11.—5–20–1913, 0.01 milligram bovine tubercle bacilli subcutaneously. 6–19–1913, 0.001 milligram FFF, 9-day culture, suspended in 1 c. c. saline solution, into muscles of right thigh. No local reaction from the FFF injection. Weight increased till three months before death, when it fell gradually. 5–18–1914, chloroformed.

Necropsy.—There is no trace of the inoculation at either site. Both lungs are completely shot through with 1 mm. tubercles, not more than 2 mm. apart at any place. There are a few stercoraceous or parasitic pockets in the intestine with firm fibrous walls—almost cartilaginous. The cortices of both kidneys contain many small tubercles. Thirty minutes search through three smears from the lungs disclosed only seven tubercle bacilli while in smears from the kidney lesion they were more easily found—5 in 5 minutes. Zenker fixed sections of the lung showed typical miliary tubercles with necrotic center, giant cells and epithelioid cells containing rare tubercle bacilli, and only a slight fibrolastic reaction at the periphery.

It is evident that this rabbit could not have lived more than 10 days, or 373 days from the date of inoculation with bovine tubercle bacilli.

The rabbits survived the inoculation with bovine tubercle bacilli as follows:

Control series (no FFF given).—No. 26, 133 days; No. 27, 211 days; No. 28, 265 days; No. 30, 267 days; No. 29, 303 days. Average, 236 days. Average deviation (from the arithmetical mean), 51 days.

Curative series (FFF after bovine).—No. 12, 137 days; No. 14, 139 days; No. 16, 154 days; No. 21, 159 days; No. 23, 174 days; No. 24, 176 days; No. 25, 178 days; No. 18, 191 days; No. 19, 200 days; No. 17, 204 days; No. 11, 373 days (estimate). Average, 190 days. Average deviation, 38 days.

Prophylactic series (FFF before bovine).—No. 8, 129 days; No. 4, 146 days; No. 6, 146 days; No. 5, 177 days; No. 2, 200 days; No. 9, 276 days; No. 1, 423 days (estimate). Average, 214 days. Average deviation, 63 days.

It is thus seen that even including the two treated rabbits which survived the year the control rabbits survived infection with tubercle bacilli, on the average, better than those which received Friedmann bacilli. The average deviations were computed as an index as to whether rabbits No. 1 and No. 11 should be considered as chance items falling within the extremes of reasonable variation or as indicating, in their cases, specific and unusual resistance to tubercle infection. These deviations as computed would indicate that the former is undoubtedly the case with rabbit 11, while rabbit 1 might possibly be considered as showing some specific immunity. It may be noticed, however, that even including these two animals the average deviation of the prophylactic series exceeded that of the controls by a less amount than that by which the latter exceeded the average deviation of the curative series, so that rabbit 1 may, with equal propriety, be regarded as a chance variant.

The guinea pigs were inoculated with the Friedmann bacillus subcutaneously, intramuscularly, and intraperitoneally. Their weight charts showed no significant difference from those of controls kept under identical conditions. About 50 per cent of the guinea pigs inoculated intraperitoneally had a temperature elevation of a degree

or more 24 to 96 hours afterwards. There were no temperature reactions in the subcutaneous series, but persistent nodules appeared at the site of inoculation which became abscesses in about 50 per cent (27 out of 55); acid-fast bacilli were found in smears from these lesions up to 128 days after inoculation. Other acid-fast organisms—the avian tubercle bacillus, butter bacillus, the dung bacillus, frog tubercle bacillus, grass bacillus, lepra bacillus (chromogenic), margarine bacillus, milk bacillus, the bacillus of nasal secretion, the smegma bacillus—were also injected subcutaneously into 36 guinea pigs, producing about the same sort of local reaction, going on to abscess formation uniformly in the dung bacillus, lepra bacillus, margarine bacillus, and bacillus of nasal secretion, but clearing up without discharge in all the pigs inoculated with the butter bacillus and grass bacillus. No distant lesions were found at autopsy except occasional involvement of the lymph nodes draining the site of inoculation. One guinea pig inoculated with the bacillus of nasal secretion died on the fifth day with the local abscess; acid-fast bacilli were also found—without lesions—in the organs generally and in the heart's blood.

Several attempts to exalt the virulence of the Friedmann bacillus by passage through a series of guinea pigs fell short; the proliferation in the tissues was not marked, the number of bacilli recoverable decreasing in each successive animal unless resort was had to cultivation on artificial media. It was noted, however, that tendency to abscess formation was increased by this passage. When sterile butter was added to the subcutaneous injection (five guinea pigs) large abscesses were produced in all the animals, though the butter alone produced practically no reaction (five guinea pigs). Intraperitoneally, the addition of the butter caused the formation of abscesses and tubercle-like lesions of the peritoneum, as well as the adhesions which were caused by FFF alone. Butter alone caused no pathological changes.

Acid-fast bacilli were found in some of the butter-FFF intraperitoneal series killed 96 days after inoculation, as well as in one which died in 33 days, showing a more intense process.

Intramuscular injections were better absorbed than subcutaneous, going on to abscess formation and breaking down in only 22 per cent (6 out of 27).

To gain some approximation of the minimal lethal dose intraperitoneally 11 pigs were inoculated with varying amounts and with cultures of different ages. The pig receiving 14 mg. survived, also all three receiving 40 mg. Two of the three 60 mg. pigs died, one of the three 80 mg., and the single guinea pig receiving 100 mg. Death in all was acute, and the pathological picture was that of a fibrino-purulent peritonitis, with the omentum matted and congested.

The pus cells were intensely phagocytic, and smears from the peritoneum and liver showed the acid-fast bacilli in intracellular and extracellular masses; but in smears from the lung and kidney they were almost entirely extracellular. Glycerin agar tubes planted from the heart's blood, lung, and peritoneum gave an acid-fast bacillus corresponding to the Friedmann bacillus in pure culture.

Subsequent to treatment many of the guinea pigs, as well as untreated controls, were inoculated subcutaneously with bovine tubercle bacilli. A summary of these animals, showing treatment and length of life after the bovine inoculation, follows:

Series I.—10 mg. FFF subcutaneously 14 days before inoculation with 0.8 mg. bovine tubercle bacilli: No. 6 survived 37 days; No. 7 survived 38 days; No. 5 survived 39 days; No. 1 survived 45 days; No. 8 survived 46 days; No. 4 survived 48 days; No. 2 survived 51 days; No. 9 survived 51 days; No. 10 survived 52 days; No. 3 survived 99 days; average, 51 days.

Controls (receiving only the bovine inoculation).—No. 64 survived 53 days; No. 63 survived 56 days; No. 66 survived 58 days; No. 65 survived 59 days; No. 62 survived 63 days; average, 58 days.

Series II.—10 mg. FFF subcutaneously 21 days and intramuscularly 7 days before inoculation with 0.8 mg. bovine tubercle bacilli: No. 18 survived 32 days; No. 12 survived 42 days; No. 16 survived 43 days; No. 14 survived 45 days; No. 13 survived 58 days; No. 15 survived 62 days; No. 17 survived 66 days; average, 48 days.

Control (receiving only the bovine inoculation).—No. 87 survived 68 days.

Series XIV:

(*a*) 10 mg. FFF subcutaneously 95 days, intramuscularly 81 and 74 days before inoculation with 0.05 mg. bovine tubercle bacilli: No. 24 survived 45 days; No. 28 survived 52 days; No. 23 survived 60 days; No. 25 survived 87 days; No. 27 survived 89 days; average, 67 days.

(*b*) 10 mg. FFF subcutaneously 95 days, intramuscularly 74 days before inoculation with 0.05 mg. bovine tubercle bacilli: No. 31 survived 60 days; No. 29 survived 61 days; No. 30 survived 99 days; average, 73 days.

(*c*) 10 mg. FFF subcutaneously 95 days, intramuscularly 66 days before inoculation with 0.05 mg. bovine tubercle bacilli: No. 34 survived 59 days; No. 35 survived 127 days; No. 33 survived 140 days; average, 109 days.

(*d*) 10 mg. FFF subcutaneously 95 days before inoculation with 0.05 mg. bovine tubercle bacilli: No. 38 survived 40 days; No. 39 survived 55 days; No. 49 survived 59 days; No. 50 survived 62 days; average, 54 days.

(*e*) 10 mg. FFF intraperitoneally 95 days before inoculation with 0.05 mg. bovine tubercle bacilli: No. 58 survived 52 days; No. 59 survived 59 days; No. 51 survived 66 days; No. 52 survived 99 days; average, 69 days.

Average for all of Series XIV, 72.2 days.

Controls.—0.05 mg. bovine tubercle bacilli alone: No. 171 survived 63 days; No. 174 survived 75 days; No. 172 survived 101 days; No. 175 survived 114 days; average, 88 days.

Average for all treated pigs, 61.8 days.

Average for all controls, 71 days.

Thus not only for the whole number, but for each series taken separately, the control pigs survived infection with bovine tubercle longer than the pigs treated with Friedmann's bacilli. The average

deviation (15.4 days for the controls, and 17.6 days for the treated animals) would not indicate much greater variation in the latter than in the former, but certain pigs are seen to have lived unusually long, thus pig 3 lived about twice as long as the others of the same series, and pigs 35 and 33 outlived all the rest. Part of the immunity exhibited by pig 33 may be due to the fact that she was pregnant at the time of inoculation with bovine tubercle bacilli, and gave birth 38 days thereafter. Though she died from tuberculosis, the lesions were less extensive than usual.

It may here be pointed out that treatment with the Friedmann bacillus would seem to have some specific effect on tubercular infection in the guinea pig, as was shown by the hypersusceptibility manifested by almost all the animals. Thus in Series I all of the treated animals died before any of the controls, and in Series II all the treated animals, save No. 3, died before the single control. The average length of survival, showing hypersusceptibility as compared with the controls, agree with the results in rabbits.

The behavior of the Friedmann organism after inoculation in some of the animals is shown in the following protocols:

Guinea pig No. 41, weight 300 grams, 3–21–1913, 1 milligram of FFF suspended in 1 c. c. physiological saline solution inoculated subcutaneously in the belly wall. This produced a local swelling, which persisted during the week of observation. The temperature on successive days following the inoculation was 38.8, 38.8, 39.0, 39.2, 39.2, 39.2, 38.8. 3–28–1913, chloroformed. No lymphatic enlargement or other abnormalities were found save the 1 cm. abscess at the site of injection, consisting of semisolid, somewhat cheesy pus. This pus contained masses of acid-fast bacilli, a large part of which were intracellular; no other organisms were seen. Sections from the abscess wall fixed in Zenker's fluid, imbedded in paraffin, and stained with eosin-methylene blue and hematoxylin-eosin show typical chronic inflammatory tissue extending partially into the abdominal muscles. In some of the sections, however, a tendency to tubercular degeneration is seen, with necrotic center, phagocytic epithelioid and giant cells, small round cell infiltration, and a circumscribing overgrowth of young connective tissue. Eosinophilic cells are frequent, and in some sections pus cells are very numerous. Glycerin agar cultures planted from the pus give a growth typical of the Friedmann organism, but growing in the first generation only after two weeks incubation.

Guinea pig No. 36, weight 300 grams, 3–21–1913, 10 mg. FFF in 1 c. c. saline injected subcutaneously into the abdominal wall. This injection caused a persistent local swelling; 3–29–1913, weight 300 grams. 4–5–1913, weight 310 grams. 4–12–1913, weight 340 grams. 4–19–1913, weight 350 grams. Chloroformed. Necropsy: Abscess 1 cm. in diameter at site of injection, containing fluid pus. Other organs normal. Smears from the abscess show acid-fast organisms, mostly intracellular and disintegrated. A smear from the liver shows acid-fast bacilli, many extracellular and intact, but for the most part within large mononuclear cells and partly fragmented. A smear from the spleen gives a similar picture, but the bacilli are less numerous. Only two acid-fast bacilli, and these extracellular, were seen in a smear from the lung.

Guinea pig No. 163, weight 315 grams. 5–12–1913, 14 milligrams FFF (8-day culture), suspended in 0.5 c. c. physiological saline solution intraperitoneally. No reaction was noticed, other than a slight loss of weight at first. The pig was weighed weekly and after 12 days began to gain steadily, with only one period of loss, 1–24–1914, reaching 695 gms. on 4–18–1914. 5–18–1914, weight 675 gms. Chloroformed. Necropsy: Well nourished. Generalized intestinal adhesions and abscess in duodeno-pancreatic region. No glandular involvement. A smear from the pus in the abscess shows granular detritus and short unbeaded acid-fast bacilli, from which no growth was obtained on glycerin agar. Sections of the abscess wall show centrally the necrotic area containing disintegrating cells and rare acid-fast bacilli. The outstanding picture in the next peripheral layer is one of pus-cell infiltration; there are, however, some epithelioid and lymphoid cells, and some of the epithelioid cells have merged but no typical giant cells were seen. The bacilli were found in pus cells, but not in the epithelioid cells. Connective tissue formation predominates to the outside.

Guinea pig No. 11, weight 300 grams, 3–21–1913, 10 milligrams FFF (8-day culture on glycerin agar) in 1 c. c. physiological saline solution inoculated subcutaneously in the belly wall. 3–22, swelling at the site of inoculation. 3–23, swelling larger. 3–31, swelling slightly less marked. 4–4, 30 mg. FFF (10-day culture on glycerin agar) in 3 c. c. physiological saline solution inoculated into muscles of the right thigh. 4–5, no marked local reaction. 4–6, considerable swelling, tender at the site of the intramuscular inoculation. 4–11, scrawny; nasal discharge. Marked swelling at the intramuscular site, very small nodule at the subcutaneous site. 4–28, better. No remains of subcutaneous injection; 1 cm. swelling at the intramuscular site; no glandular involvement. 5–13, thickening persists; no glands. 5–31, some thickening of right thigh. No more notes are recorded on this pig, except the necropsy. He was kept in the same room with pigs which had been inoculated with tubercle bacilli, but in a different cage, disinfected before use and on a higher level. Opportunities for infection must have been minimal. 9–22–13, dead. Necropsy: Caseous glands in right groin. Liver and spleen enlarged, showing numerous tubercles. Lungs tubercular. Acid-fast bacilli present in smears from these organs. The cultures planted were lost.

In the autopsy of about 10,000 guinea pigs in this laboratory no instance of spontaneous tuberculosis or cage infection has been found. This fact, together with the apparent primary focus in the right groin at necropsy, would almost certainly imply that the tubercular process in guinea pig No. 11 arose from the Friedmann inoculation.

SUMMARY OF LABORATORY STUDIES.

The organism used by Dr. Friedmann is an acid-fast bacillus, morphologically similar to the tubercle bacillus. Culturally, the organism may be distinguished from organisms heretofore recognized as tubercle bacilli.

Some of the cultural characteristics can be artificially modified.

It is relatively but not completely avirulent and apparently may in very rare cases cause a tubercular process on inoculation. (Guinea pig No. 11.)

Inoculation with the Friedmann bacillus in the doses used caused as a rule hypersusceptibility to bovine tuberculosis in the guinea pig and rabbit, the treated animals dying earlier, on the average, than the untreated.

In a few instances the animals which received the Friedmann culture were apparently somewhat resistant to infection, but all showed evidence of tuberculosis at autopsy (guinea pigs Nos. 3, 33, 35, and rabbit No. 1).

Neither curative nor protective action against natural or inoculation tuberculosis was shown in monkeys.

Acid-fast organisms were repeatedly found in previously healthy guinea pigs over 100 days after treatment with the Friedmann organism. Dr. Friedmann claimed they "are never found in the guinea pig body, even after a short time."

The material used by Dr. Friedmann for the treatment of human beings was found to be at times contaminated with staphylococci.

PART V.

GENERAL CONCLUSIONS.

The claims made by Dr. Friedmann for his method of treating tubercular infections are, in brief, that, by means of injections of a living acid-fast organism, harmless of itself, he is able to cure cases of tuberculosis, pulmonary or otherwise, which have not already advanced to that hopeless stage where death is imminent. From the manner of presenting these claims and from the fact that successes only and not failures are reported, the reader of these claims is bound to assume that such results are the rule; in other words, that a sovereign remedy for tuberculosis has at length been discovered, and incidentally that a method has been devised for the administration of living acid-fast organisms which avoids abscess formation, a complication which has hitherto limited their employment.

The results of the investigation here reported do not confirm the claims made by Dr. Friedmann. We find, in brief, that the preparation used by him is not strictly devoid of dangerous properties of itself, still less so when injected into tuberculous subjects; that the favorable influencing of tuberculous processes by his methods is certainly not the rule, and that if we are to ascribe to the Friedmann treatment the improvement noted in a few cases, we are equally bound to impute to it the serious retrogression observed in other cases; and finally that the phenomenon of abscess formation has not been avoided by Dr. Friedmann's methods.

We find that the organism used by Dr. Friedmann differs in important cultural characteristics from any heretofore recognized tubercle bacillus.

The subcutaneous and intramuscular inoculation of animals with the Friedmann organism caused the formation of abscess in over 25 per cent of the animals treated.

The treatment of animals with the Friedmann organism—rabbits and guinea pigs—either before or subsequent to infection with virulent tubercle bacilli, is followed, as a rule, by an increased susceptibility to the disease.

Inoculation of monkeys with the Friedmann culture did not show either curative or protective action in those animals against tuberculosis.

SUMMARY.

The claim of Dr. F. F. Friedmann to have originated a specific cure for tuberculosis is not substantiated by our investigation.

The claim of Dr. F. F. Friedmann that the inoculation of persons and animals with his organism is without harmful possibilities is disproved.

HYGIENIC LABORATORY BULLETINS OF THE PUBLIC HEALTH SERVICE.

The Hygienic Laboratory was established in New York, at the Marine Hospital on Staten Island, August, 1887. It was transferred to Washington, with quarters in the Butler Building, June 11, 1891, and a new laboratory building, located in Washington, was authorized by act of Congress March 3, 1901.

The following *bulletins* [Bulls. Nos. 1–7, 1900 to 1902, Hyg. Lab., U. S. Mar.-Hosp. Serv., Wash.] have been issued.

*No. 1.—Preliminary note on the viability of the *Bacillus pestis*. By M. J. Rosenau.

No. 2.—Formalin disinfection of baggage without apparatus. By M. J. Rosenau.

*No. 3.—Sulphur dioxid as a germicidal agent. By H. D. Geddings.

*No. 4.—Viability of the *Bacillus pestis*. By M. J. Rosenau.

No. 5.—An investigation of a pathogenic microbe (*B. typhi murium* Danyz) applied to the destruction of rats. By M. J. Rosenau.

*No. 6.—Disinfection against mosquitoes with formaldehyde and sulphur dioxid. By M. J. Rosenau.

†No. 7.—Laboratory technique: Ring test for indol, by S. B. Grubbs and Edward Francis; Collodium sacs, by S. B. Grubbs and Edward Francis; Microphotography with simple apparatus, by H. B. Parker.

By act of Congress approved July 1, 1902, the name of the "United States Marine-Hospital Service" was changed to the "Public Health and Marine-Hospital Service of the United States," and three new divisions were added to the Hygienic Laboratory.

Since the change of name of the service the bulletins of the Hygienic Laboratory have been continued in the same numerical order as follows:

*No. 8.—Laboratory course in pathology and bacteriology. By M. J. Rosenau. (Revised edition, March, 1904.)

†No. 9.—Presence of tetanus in commercial gelatin. By John F. Anderson.

*No. 10.—Report upon the prevalence and geographic distribution of hookworm disease (uncinariasis or anchylostomiasis) in the United States. By Ch. Wardell Stiles.

*No. 11.—An experimental investigation of *Trypanosoma lewisi*. By Edward Francis.

*No. 12.—The bacteriological impurities of vaccine virus; an experimental study. By M. J. Rosenau.

*No. 13.—A statistical study of the intestinal parasites of 500 white male patients at the United States Government Hospital for the Insane; by Philip E. Garrison, Brayton H. Ransom, and Earle C. Stevenson. A parasitic round worm (*Agamomermis culicis* n. g., n. sp.) in American mosquitoes (*Culex sollicitans*); by Ch. Wardell Stiles. The type species of the cestode genus *Hymenolepis;* by Ch. Wardell Stiles.

*No. 14.—Spotted fever (tick fever) of the Rocky Mountains; a new disease. By John F. Anderson.

*No. 15.—Inefficiency of ferrous sulphate as an antiseptic and germicide. By Allen J. McLaughlin.

*No. 16.—The antiseptic and germicidal properties of glycerin. By M. J. Rosenau.

*No. 17.—Illustrated key to the trematode parasites of man. By Ch. Wardell Stiles.

*No. 18. An account of the tapeworms of the genus *Hymenolepis* parasitic in man, including reports of several new cases of the dwarf tapeworm (*H. nana*) in the United States. By Brayton H. Ransom.

*No. 19.—A method for inoculating animals with precise amounts. By M. J. Rosenau.

*No. 20.—A zoological investigation into the cause, transmission, and source of Rocky Mountain "spotted fever." By Ch. Wardell Stiles.

*No. 21.—The immunity unit for standardizing diphtheria antitoxin (based on Ehrlich's normal serum). Official standard prepared under the act approved July 1, 1902. By M. J. Rosenau.

*No. 22.—Chloride of zinc as a deodorant, antiseptic, and germicide. By T. B. McClintic.

*No. 23.—Changes in the Pharmacopœia of the United States of America. Eighth decennial revision. By Reid Hunt and Murray Galt Motter.

No. 24. The International Code of Zoological Nomenclature as applied to medicine. By Ch. Wardell Stiles.

*No. 25.—Illustrated key to the cestode parasites of man. By Ch. Wardell Stiles.

*No. 26.—On the stability of the oxidases and their conduct toward various reagents. The conduct of phenolphthalein in the animal organism. A test for saccharin, and a simple method of distinguishing between cumarin and vanillin. The toxicity of ozone and other oxidizing agents to lipase. The influence of chemical constitution on the lipoytic hydrolysis of etheral salts. By J. H. Kastle.

*No. 27.—The limitations of formaldehyde gas as a disinfectant with special reference to car sanitation. By Thomas B. McClintic.

*No. 28.—A statistical study of the prevalence of intestinal worms in man. By Ch. Wardell Stiles and Philip E. Garrison.

No. 29.—A study of the cause of sudden death following the injection of horse serum. By M. J. Rosenau and John F. Anderson.

†No. 30.—I. Maternal transmission of immunity to diphtheria toxine. II. Maternal transmission of immunity to diphtheria toxine and hypersusceptibility to horse serum in the same animal. By John F. Anderson.

†No. 31.—Variations in the peroxidase activity of the blood in health and disease. By Joseph H. Kastle and Harold L. Amoss.

†No. 32.—A stomach lesion in guinea pigs caused by diphtheria toxine and its bearing upon experimental gastric ulcer. By M. J. Rosenau and John F. Anderson.

*No. 33.—Studies in experimental alcoholism. By Reid Hunt.

†No. 34.—I. *Agamofilaria georgiana* n. sp., an apparently new roundworm parasite from the ankle of a negress. II. The zoological characters of the roundworm genus *Filaria* Mueller, 1787. III. Three new American cases of infection of man with horsehair worms (species *Paragordius varius*), with summary of all cases reported to date. By Ch. Wardell Stiles.

†No. 35.—Report on the origin and prevalence of typhoid fever in the District of Columbia. By M. J. Rosenau, L. L. Lumsden, and Joseph H. Kastle. (Including articles contributed by Ch. Wardell Stiles, Joseph Goldberger, and A. M. Stimson.)

†No. 36.—Further studies upon hypersusceptibility and immunity. By M. J. Rosenau and John F. Anderson.

†No. 37.—Index-catalogue of medical and veterinary zoology. Subjects: Trematoda and trematode diseases. By Ch. Wardell Stiles and Albert Hassall.

No. 38.—The influence of antitoxin upon post-diptheritic paralysis. By M. J. Rosenau and John F. Anderson.

†No. 39.—The antiseptic and germicidal properties of solutions of formaldehyde and their actions upon toxines. By John F. Anderson.

†No. 40.—1. The occurrence of a proliferating cestode larva (*Sparganum proliferum*) in man in Florida, by Ch. Wardell Stiles. 2. A reexamination of the type specimen of *Filaria restiformis* Leidy, 1880=*Agamomermis restiformis*, by Ch. Wardell Stiles. 3. Observations on two new parasitic trematode worms: *Homalogaster philippinensis* n. sp., *Agamodistomum nanus* n. sp., by Ch. Wardell Stiles and Joseph Goldberger. 4. A reexamination of the original specimen of *Tænia saginata abietina* (Weinland, 1858), by Ch. Wardell Stiles and Joseph Goldberger.

†No. 41.—Milk and its relation to the public health. By various authors.

†No. 42.—The thermal death points of pathogenic microorganisms in milk. By M. J. Rosenau.

†No. 43.—The standardization of tetanus antitoxin (an American unit established under authority of the act of July 1, 1902). By M. J. Rosenau and John F. Anderson.

No. 44.—Report No. 2 on the origin and prevalence of typhoid fever in the District of Columbia, 1907. By M. J. Rosenau, L. L. Lumsden, and Joseph H. Kastle.

†No. 45.—Further studies upon anaphylaxis. By M. J. Rosenau and John F. Anderson.

No. 46.—*Hepatozoon perniciosum* (n. g., n. sp.); a hæmogregarine pathogenic for white rats; with a description of the sexual cycle in the intermediate host, a mite (*Ielaps echidnimus*). By W. W. Miller.

No. 47.—Studies on thyroid: I. The relation of iodine to the physiological activity of thyroid preparations. By Reid Hunt and Atherton Seidell.

No. 48.—The physiological standardization of digitalis. By Charles Wallis Edmunds and Worth Hale.

No. 49.—Digest of comments on the United States Pharmacopœia. Eighth decennial revision for the period ending December 31, 1905. By Murray Galt Motter and Martin I. Wilbert.

No. 50.—Further studies upon the phenomenon of anaphylaxis. By M. J. Rosenau and John F. Anderson.

No. 51.—Chemical tests for blood. By Joseph H. Kastle.

No. 52.—Report No. 3 on the origin and prevalence of typhoid fever in the District of Columbia (1908). By M. J. Rosenau, Leslie L. Lumdsen, and Joseph H. Kastle.

No. 53.—The influence of certain drugs upon the toxicity of acetanilide and antipyrine. By Worth Hale.

No. 54.—The fixing power of alkaloids on volatile acids and its application to the estimation of alkaloids with the aid of phenolphthalein or by the Volhard method. By Elias Elvove.

No. 55.—Quantitative pharmacological studies; adrenalin and adrenalinlike bodies. By W. H. Schultz.

No. 56.—Milk and its relation to the public health. (Revised edition of Bulletin No. 41.) By various authors.

No. 57.—I. The presence of tubercle bacilli in the circulating blood in clinical and experimental tuberculosis. By John F. Anderson. II. The viability of the tubercle bacillus. By M. J. Rosenau.

No. 58.—Digest of comments on the Pharmacopœia of the United States of America (eighth decennial revision) and the National Formulary for the period ending December 31, 1906. By Murray Galt Motter and Martin I. Wilbert.

No. 59.—The oxidases and other oxygen catalysts concerned in biological oxidations. By Joseph Hoeing Kastle.

No. 60.—A study of the anatomy of Watsonius (n. g.), Watsoni of man, and of 19 allied species of mammalian trematode worms of the superfamily Paramphistomoidea. By Ch. Wardell Stiles and Joseph Goldberger.

No. 61.—Quantitative pharmacological studies: Relative physiological activity of some commercial solutions of epinephrin. By W. H. Schultz.

No. 62.—The taxonomic value of the miscroscopic structure of the stigmal plates in the tick genus *Dermacentor*. By Ch. Wardell Stiles.

† No. 63.—Digest of comments on the Pharmacopœia of the United States of America (eighth decennial revision) and the National Formulary (third edition) for the calendar year ending December 31, 1907. By Murray Galt Motter and Martin I. Wilbert.

No. 64.—Studies upon anaphylaxis with special reference to the antibodies concerned. By John F. Anderson and W. H. Frost.

No. 65.—Facts and problems of rabies. By A. M. Stimson.

No. 66.—I. The influence of age and temperature on the potency of diphtheria antitoxin. By John F. Anderson. II. An organism (*Pseudomonas protea*) isolated from water, agglutinated by the serum of typhoid-fever patients. By W. H. Frost. III. Some considerations on colorimetry, and a new colorimeter. By Norman Roberts. IV. A gas generator in four forms, for laboratory and technical use. By Norman Roberts.

† No. 67.—The solubilities of the pharmacopœial organic acids and their salts. By Atherton Seidell.

No. 68.—The bleaching of flour and the effect of nitrites on certain medicinal substances. By Worth Hale.

No. 69.—The effects of restricted diet and of various diets upon the resistance of animals to certain poisons. By Reid Hunt.

No. 70.—A study of melting point determinations with special reference to the melting point requirements of the United States Pharmacopœia. By George A. Menge.

No. 71.—1. Some known and three new endoparasitic trematodes from American fresh-water fish. By Joseph Goldberger. 2. On some new parasitic trematode worms of the genus *Telorchis*. By Joseph Goldberger. 3. A new species of *Athesmia* from a monkey. By Joseph Goldberger and Charles G. Crane.

† No. 72.—I. Report on an outbreak of typhoid fever at Omaha, Nebr. (1909–1910), by L. L. Lumsden. II. The water supply of Williamson, W. Va., and its relation to an epidemic of typhoid fever. By W. H. Frost.

No. 73.—The effect of a number of derivatives of choline and analogous compounds on the blood pressure. By Reid Hunt and R. de M. Taveau.

No. 74.—Digitalis standardization and the variability of crude and of medicinal preparations. By Worth Hale.

No. 75.—Digest of comments on the Pharmacopœia of the United States of America (eighth decennial revision) and the National Formulary (third edition) for the calendar year ending December 31, 1908. By Murray Galt Motter and Martin I. Wilbert.

No. 76.—The physiological standardization of ergot. By Charles Wallis Edmunds and Worth Hale.

No. 77.—Sewage pollution of interstate and international waters with special reference to the spread of typhoid fever. By Allan J. McLaughlin.

No. 78.—Report No. 4 on the origin and prevalence of typhoid fever in the District of Columbia (1909). By L. L. Lumsden and John F. Anderson. (Including articles contributed by Thomas B. McClintic and Wade H. Frost).

No. 79.—Digest of comments on the Pharmacopœia of the United States of America (eighth decennial revision) and the National Formulary (third edition) for the calendar year ending December 31, 1910. By Murray Galt Motter and Martin I. Wilbert.

No. 80.—Physiological studies in anaphylaxis. Reaction of smooth muscle from various organs of different animals to proteins. (Including reaction of muscle from nonsensitized, sensitized, tolerant, and immunized guinea pigs.) By William H. Schultz.

No. 81.—Tissue proliferation in plasma medium. By John Sundwall.

No. 82.—I. Method of standardizing disinfectants with and without organic matter. By John F. Anderson and Thomas B. McClintic. II. The determination of the phenol coefficient of some commercial disinfectants. By Thomas B. McClintic.

No. 83.—I. Sewage pollution of interstate and international waters with special reference to the spread of typhoid fever. II. Lake Superior and St. Marys River. III. Lake Michigan and the Straits of Mackinac. IV. Lake Huron, St. Clair River, Lake St. Clair, and the Detroit River. V. Lake Ontario and St. Lawrence River. By Allan J. McLaughlin.

No. 84. Digest of comments on the Phamacopœia of the United States of America (eighth decennial revision) and on the National Formulary (third edition) for the calendar year ending December 31, 1910. By Murray Galt Motter and Martin I. Wilbert.

No. 85.—Index catalogue of medical and veterinary zoology. Subjects: Cestoda and cestodaria. By Ch. Wardell Stiles and Albert Hassall.

No. 86.—Studies on typhus. By John F. Anderson and Joseph Goldberger.

No. 87.—Digest of comments on the Pharmacopœia of the United States of America (eighth decennial revision) and on the National Formulary (third edition) for the calendar year ending December 31, 1911. By Murray Galt Motter and Martin I. Wilbert.

No. 88.—Method for determining the toxicity of coal-tar disinfectants, together with a report on the relative toxicity of some commercial disinfectants. By Worth Hale.

No. 89.—Sewage pollution of interstate and international waters with special reference to the spread of typhoid fever. VI. The Missouri River from Sioux City to its mouth. By Allan J. McLaughlin.

No. 90.—Epidemiologic studies of acute anterior poliomyelitis. I. Poliomyelitis in Iowa, 1910. II. Poliomyelitis in Cincinnati, Ohio, 1911. III. Poliomyelitis in Buffalo and Batavia, N. Y., 1912. By Wade H. Frost.

No. 91.—I. The cause of death from subdural injections of serum. By Worth Hale. II. Some new cholera selective media. By Joseph Goldberger.

No. 92.—Gaseous impurities in the air of railway tunnels. By Atherton Seidell and Philip W. Meserve.

No. 93.—Digest of comments on the Pharmacopœia of the United States of America (eighth decennial revision) and on the National Formulary (third edition) for the calendar year ending December 31, 1912. By Murray Galt Motter and Martin I. Wilbert.

No. 94.—I. Collected studies on the insect transmission of *Trypanosoma evansi*. By M. Bruin Mitzmain. II. Summary of experiments in the transmission of anthrax by biting flies. By M. Bruin Mitzmain.

No. 95.—Laboratory studies on tetanus. By Edward Francis.

No. 96.—1. Report of investigation of coastal waters in the vicinity of Gulfport and Biloxi, Miss., with special reference to the pollution of shellfish. By R. H. Creel. 2. A comparison of methods for the determination of oxygen in waters in presence of nitrite. By Elias Elvove. 3. Some new compounds of the choline type; (III) including preparation of monoacetate of *α*, *B* dioxy-*B*-methyl butane. By G. A. Menge. 4. The detection of white phosphorus in matches. By Earle B. Phelps. 5. The chemical composition of rubber in nursing nipples and in some rubber toys. By Earle B. Phelps and Albert F. Stevenson. 6. The analysis of thymol capsules. By Atherton Seidell. 7. Seasonal variation in the composition of the thyroid gland. By Atherton Seidell and Frederic Fenger. 8. Note on a new apparatus for use with the Winkler method for dissolved oxygen in water. By Hyman L. Shoub. 9. The pharmacological action of some serum preservatives. By Carl Voegtlin.

No. 97.—1. Some further siphonaptera. 2. A further report on the identification of some siphonaptera from the Philippine Islands. 3. The taxonomic value of the copulatory organs of the females in the order siphonaptera. By Carroll Fox.

No. 98.—Digest of comments on the pharmacopœia of the United States of America (eighth decennial revision) and on the National Formulary (third edition) for the calendar year ending December 31, 1913. By Murray Galt Motter and Martin I. Wilbert.

No. 99.—The Friedmann treatment for tuberculosis: A report of the board appointed for its investigation. By John F. Anderson and Arthur M. Stimson.

In citing these bulletins bibliographers and authors are requested to adopt the following abbreviations: Bull. No. ——, Hyg. Lab., Wash., pp. ——.

The service will enter into exchange of publications with medical and scientific organizations, societies, laboratories, journals, and authors. ALL APPLICATIONS FOR THESE PUBLICATIONS SHOULD BE ADDRESSED TO THE "**Surgeon General, U. S. Public Health Service, Washington, D. C.,**" EXCEPT THOSE MARKED (*) AND (†).

The publications marked (*) are no longer available for distribution by the Surgeon General of the Public Health Service. Copies of those marked (†) may, however, be obtained from the Superintendent of Documents, Government Printing Office, Washington, D. C., who sells publications at cost, and to whom requests for publications thus marked should be made.

ADDITIONAL COPIES
OF THIS PUBLICATION MAY BE PROCURED FROM
THE SUPERINTENDENT OF DOCUMENTS
GOVERNMENT PRINTING OFFICE
WASHINGTON, D. C.
AT
10 CENTS PER COPY