

THE GOMES COMPLEMENT-FIXATION TEST IN CONTACTS OF LEPERS¹

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The subject of complement-fixation with our test by the sera of persons who have been in contact with lepers, has been considered by us for some time in connection with our study of actual cases of leprosy in different stages. On account of the importance of the matter in the control of the disease we now add further observations.

In order to show the sensitiveness of our test we present here a summary of the clinical and bacteriologic examinations of each case, which demonstrates the value of the serological findings. Unfortunately, a great many of our contact-cases could not be followed up year by year, as would be desirable. A great many persons do not understand the importance of such a follow-up. However, those who were educated in sanitary matters came voluntarily to be re-examined, which allowed us to note the significance of the serological phenomena.

In 1930 we observed a case (Case 9) in which there had been a persistently positive Gomes reaction and in which, after the delivery of a child, clinical manifestations of leprosy appeared and the nasal mucus became positive for the bacilli. There were also a number of other individuals whose sera had showed complement-fixation years before, and who later were found to have acid-fast bacilli in the lymph nodes or the nasal mucus. This obliged us to abandon our previous attitude of simple expectation and to interfere therapeutically. However, it is evident that the presence of *Mycobacterium leprae* in the glands, or its occasional elimination, does not always determine the development of actual leprosy. We have had patients with this condition who did not become lepers, protected by the supervision of an anergic state.

At first our study was limited to the action of potassium iodide in activating the serum.² The value of such a procedure was soon

¹This study was made at the Institute of Hygiene, Sao Paulo, Brazil.

²To activate the serum it is necessary to administer potassium iodide in doses of two grams per day for a week.

evident, but the significance of cases that lost their ability to react to the antigen (i.e., became negative) after the use of potassium iodide remained dependent on later observations. Later we obtained proof that such individuals, suffering from some anergic shock, do not become lepers. We are convinced that these conditions should be studied in a greater number of contacts, because success in controlling the disease in the shortest space of time depends on a knowledge of them.

We give below a list of cases that had been in contact with lepers and whose sera fixed complement with an antigen made from a defatted culture of *Streptothrix leproides* Deycke. In this list are included only the cases in which a close follow-up was possible. In 1927, in our first report upon complement-fixation in leprosy, we included the results obtained with the sera of 28 contacts; 7 of these deviated the complement but showed no signs of leprosy, while 2 others were dubious. We noted this fact but left any comments or conclusions for the future. In the years that followed we have studied many contacts, among which the following are of importance:

Case 1.—G. F., male, 34 years, examined 10/11/27. Contact with leprosy wife. No signs of leprosy. Smears of nasal mucus and from lymph nodes negative. Gomes test ++++. After administration of potassium iodide became negative. Still in good health.

Case 2.—A. A., Italian male, 39 years, examined 14/2/27. Contact with leprosy wife. No signs of leprosy. Smears of nasal mucus negative. Gomes test ++++. Second examination on 29/9/27; nasal mucus negative. Clinical re-examination in 1929; in good condition.

Case 3.—J. C., Brazilian male, 22 years, examined 9/2/27. Contact with mother, an active case of leprosy. No signs of leprosy, only slight enlargement of lymph nodes. Smears of nasal mucus negative, even after administration of KI. Gomes test ++. Second examination 1/12/27; nasal mucus and lymph nodes negative. Clinical re-examination in 1929; well.

Case 4.—E. E., Brazilian male, 20 years, brother of Case 3. Contact with leprosy mother. No signs of leprosy. Nasal mucus and left crural lymph node negative. Gomes test ++. Second examination, 1/12/27; nasal mucus negative, Gomes test++.

Case 5.—P. F., Brazilian female, single, 27 years, examined 11/1/27. Contact with sister, an active leper, with whom she used to sleep. No signs of leprosy. Nasal mucus negative, but smears had been positive 11 months before. Gomes test ±. Second examination, 11/3/27; no clinical signs, nasal mucus negative, Gomes test ++. Married in 1929, she now has a son and enjoys good health.

Case 6.—D. P., Italian male, widower, 61 years. Skin and sensations normal. Rhinitis present. Gomes test +. Nasal mucus negative, but was positive a

month before, when he had contact with a leprous woman. Re-examined 29/5/29; skin and nerves normal, vague pains in limbs, nasal mucus negative, Gomes test ++. Antileprosy treatment started.

Case 7.—P. R., male, adult, examined 19/4/27. Contact with leprous woman. No signs of leprosy. Nasal mucus negative. Gomes test ++.

Case 8.—M. S., Brazilian woman, 30 years. Contact with leprous husband and son. Hypoesthesia on the right leg. Nasal mucus negative. Gomes test negative, becoming ++ 17 days later, after administration of KI.

Case 9.—A. R., female. Contact with leprous husband. No signs of leprosy, but a persistent Gomes test (+) in previous examinations. In January, 1930, she had a child, and in August she presented a hypoesthetic patch on the right foot, and the nasal mucus was positive.

Case 10.—M. T. Contact with leper. Presented areas of insensibility. Nasal mucus negative. Gomes test negative, becoming + after KI.

Case 11.—M. A. S., Negro girl, 15 years. Contact with leprous sister. Years ago had a circinate lesion on the left eyebrow, without sensory changes. Nasal mucus and skin negative. Gomes test +++.

Case 12.—F. G., Italian male, married, 47 years. Contact with leprous daughter. No signs of leprosy. Nasal mucus negative, but 5 years before this was positive. Gomes test ±.

Case 13.—S. P., Italian male, married, 58 years. Does not admit contact with a leper but came voluntarily for a special examination, which is suspicious of a family case. Presents vague pain in right shoulder, a pigmented patch on right leg, normal sensation, enlarged lymph nodes. Nasal mucus negative. Gomes test +++.

Case 14.—E. P., Italian male, 38 years, brother of Case 13. Skin and nerves normal. Had rhinitis, but nasal mucus negative. Gomes test +++.

Case 15.—J. P., Italian male, 36 years, brother of Cases 13 and 14. Presented only rhinitis; nasal mucus negative. Gomes test ++.

Case 16.—D. U., Italian male, 38 years, brother-in-law of Cases 13, 14, and 15. No signs of leprosy. Nasal mucus negative. Gomes test ++.

Case 17.—J. B., Brazilian, widow, 49 years, examined 14/1/31. Contact with a sister of a leper. No signs of leprosy. Nasal mucus negative. Gomes test ++.

Case 18.—M. C., Brazilian female, single, examined 16/1/31. She was a nurse in a leper asylum. Loss of sensation on right leg and pain in the feet. Nasal mucus negative, but several years ago atypical acid-fast organisms were found. Gomes test +++.

Case 19.—S. M., boy 11 years, examined 17/1/31. Contact with leprous brother. No signs of leprosy. Nasal mucus negative. Gomes test +++.

Case 20.—F. M., girl, 18 years, sister of Case 19. No signs of leprosy. Nasal mucus negative. Gomes test negative, becoming positive (++++) after administration of KI. In one inguinal lymph node acid-fast bacilli were found. Received antileprosy treatment.

Case 21.—M. F. N., boy, 11 years, examined 19/1/31. Contact with leprous mother. Two achromic patches in the gluteal region, with disturbed sensation.

Nasal mucus negative. Gomes test + + +. Received antileprosy treatment.

Case 22.—A. G., boy, 11 years, examined 19/1/31. Contact with leprous mother. No signs of leprosy. Nasal mucus negative. Gomes test +.

Case 23.—A. P., Brazilian girl, 14 years, examined 21/1/31. Contact with leprous mother. No signs of leprosy. Nasal mucus negative. Gomes test + + + +. After administration of KI still + + + +.

Case 24.—E. P., Brazilian female, 20 years, single, examined 10/2/31. Contact for 8 years with a leprous woman friend. No signs of leprosy. Nasal mucus negative. Gomes test + + + + after taking KI.

Case 25.—R. C., girl, 14 years, examined 24/2/31. At previous examinations she was a carrier of acid-fast bacilli. No signs of leprosy. Nasal mucus negative. Gomes test + +.

Case 26.—F. M. S., male, 38 years, examined 26/2/31. Contact with leprous brother. No signs of leprosy. Nasal mucus negative. Gomes test + + + after taking KI.

Case 27.—M. M. S., male, 51 years, examined 26/2/31. Brother of Case 26. Hypoesthesia in cubital regions. Nasal mucus negative. Gomes test +.

Case 28.—A. R. S., boy, 13 years, examined 9/4/31. Contact with a leprous brother. Had measles at 2 years, and a virus disease during infancy. Depigmented patches, sensation normal, lymph nodes enlarged, cubital nerves painful. Nasal mucus negative. Gomes test +.

Case 29.—M. A. M. M., Portuguese woman, 44 years, examined 22/12/26. Contact with leprous husband. Disturbed sensation in the legs. Nasal mucus negative. Gomes test + +.

Case 30.—E. C., boy, 20 years, examined 12/2/27. Contact with leprous mother. Disturbed sensation in right leg. Nasal mucus and lymph nodes negative. Gomes test + +.

Case 31.—M. G. P., female, 55 years. Contact with leprous husband. Nasal mucus negative. Gomes test + +.

Case 32.—A. J. D., Brazilian man, 43 years, examined 4/3/31. Contact with leprous mother-in-law. After influenza in 1918 noticed regular patches widespread on the body; these disappeared after sometime. When examined had rheumatoid pains; skin and sensation normal. Nasal mucus negative. Gomes test + + + after taking KI. Three years later (16/6/31) showed extensive anesthetic macules on the left thigh. Received antileprosy treatment.

Case 33.—J. J. F., boy, 11 years, examined 14/6/34. Contact with leprous father. Measles at 4 years. At 10 had a generalized pruritis followed by dark patches in the gluteal regions. Enlarged lymph nodes. Smears of nasal mucus and skin negative. Gomes test + after KI.

Case 34.—I. C., boy, 20 years, examined 3/6/30. Contact with a leprous brother. No signs of leprosy. Nasal mucus negative. Gomes test + + after KI. In January, 1934, rheumatoid pains, slight enlargement of both cubitals and one radial branch. Received antileprosy treatment.

Case 35.—L. C., boy, 10 years, examined 20/2/30. Contact with leprous father. Had measles at 7 years. No signs of leprosy. Nasal mucus negative.

Gomes test +. On 10/6/34 no clinical signs of leprosy but acid-fast bacilli in nasal mucus. Received antileprosy treatment.

Case 36.—Y. C., boy, 17 years, examined 20/2/30. Contact with leprosy father. Orange-colored macule on left thigh, with normal sensation. Nasal mucus negative, but smear of skin patch showed diphtheroid acid-fast bacilli. Gomes test ++++ after KI. Received antileprosy treatment.

Case 37.—R. C., boy, 15 years, examined 3/6/30. Contact with a leprosy brother. Measles in childhood. No signs of leprosy. Nasal mucus negative. Gomes test ++ after KI. Received antileprosy treatment.

Case 38.—M. E. B., female, married, examined 14/10/31. Contact with husband suffering from cutaneous leprosy, from whom she never was separated. No signs of leprosy. Nasal mucus negative. Gomes test +.

Case 39.—F. L., boy, 16 years, examined 21/5/34. Contact with a leprosy brother. Dry skin on the inferior half of the legs. Sensation and nerves normal. Nasal mucus negative. Gomes test ++++. Five months later had lost weight and resistance was lowered. Received antileprosy treatment.

Case 40.—female, married, examined 9/11/31. Contact with leprosy husband. No signs of leprosy. Nasal mucus negative. Gomes test ++ after KI.

Case 41.—A. P. L., Brazilian woman, single, examined 12/1/31. Contact with leprosy mother. No signs of leprosy. Nasal mucus negative. Gomes test ++ after KI. In May, 1934, felt rheumatic pains. Received antileprosy treatment.

Case 42.—E. M., boy, 14 years, examined 1/7/31. Contact with leprosy mother. Had measles at 6 years. Presents brown patches on the body and arms; sensation normal. Nasal mucus negative. Gomes test ++.

Case 43.—A. C. M., male, 33 years, examined 6/2/31. Contact with leprosy wife. Skin and sensations normal; felt vague pains. Nasal mucus negative. Gomes test ++++. Received antileprosy treatment.

Case 44.—O. S., female, single, 26 years examined 12/3/30. Contact with leprosy father who died 7 months ago, and a brother. No signs of leprosy. Nasal mucus negative. Gomes test negative even after KI. Re-examined on 19/5/34; lymph nodes enlarged, dry skin on limbs, sensation normal; nasal mucus negative. Gomes test ++ after taking KI. Given treatment.

Case 45.—M. L. C. S., female 28 years, examined 12/11/26. Contact with leprosy husband. Feeling "picadas" in the hands. Nasal mucus negative. Re-examined on 31/8/29; hypoesthesia and sensation of heat on the inferior part of legs. Nasal mucus negative. Gomes test ++ after taking KI.

Case 46.—M. S., female, single, 28 years, sister of Case 44, examined 3/2/30. Contact with leprosy father and brother. Hypoesthesia on the legs. Nasal mucus negative. Gomes test ++ after KI.

Case 47.—L. A., girl, 18 years, examined 11/1/29. Skin and nerves normal, lymph nodes enlarged. Nasal mucus negative. Gomes test ++ after KI. On previous examination, 41 months before, when she had contact with leprosy father, she presented enlarged lymph nodes and both cubitals and median nerves were painful.

Case 48.—A. M., girl, 16 years, examined December, 1929. No signs of leprosy. Nasal mucus negative. Gomes test negative, becoming positive (++++) after KI. On 6/10/26 (34 months before), when in contact with leprosy mother, had positive nasal mucus, and a smear from lymph node showed a group of acid-fast bacilli.

Case 49.—H. R., 26 years, examined 18/12/26. Skin and nerves normal. Nasal mucus negative. Gomes test +. Smear from lymph node positive.

Case 50.—A. M., girl, 16 years, examined January, 1927. No signs of leprosy. Nasal mucus negative. Gomes test +++. Three months before she had had contact with a leprosy brother; nasal mucus was positive then.

Case 51.—A. D. C., 24 years, examined 24/6/30. No signs of leprosy. Nasal mucus negative. Gomes test ++; after KI it became +. Fifty-three months before, when in contact with leprosy sister, she had pain in the cubital and median nerves. The nasal mucus was negative.

Case 52.—A. C., female, 41 years, examined 20/2/30. Pain in knees, hypoesthesia in the inferior part of the legs. Nasal mucus negative. Gomes test ++ after KI. Examined 39 months before, when in contact with leprosy husband, the Gomes test was positive (+), without signs of leprosy and with negative nasal mucus.

Case 53.—I. C., 23 years, examined 18/6/30. Contact with leprosy mother. Discrete rubor of face, sensation normal. Nasal mucus negative. Gomes test ++. Forty-nine months previously smears of nasal mucus and from submaxillary lymph node were positive.

Case 54.—A. C., 6 years, examined 24/5/30. No signs of leprosy. Nasal mucus negative. Gomes test ++. Forty-four months before, when in contact with leprosy uncle and grandfather, had positive nasal mucus, just after measles.

Case 55.—H. R., 14 years, examined 9/4/29. No signs of leprosy. Gomes test +. Fifty-two months before, when in contact with two leprosy brothers, had positive smear from lymph nodes, without signs of leprosy. Same result twice on other occasions.

Case 56.—M. R. B., female, 24 years, examined 29/3/30. Sensitiveness of left cubital nerve. Nasal mucus negative. Gomes test +. Forty-six months previously, when in contact with leprosy husband (they were married only six months before), she presented enlarged lymph nodes and painful cubital and median nerves.

DISCUSSION

We have demonstrated before that the Gomes test is not absolutely specific. Instances of fixation were observed with cases of tuberculosis, ozena, deep mycosis, tropical ulcer and leishmaniosis. However, exclusive of tuberculosis all of these other diseases present characteristic symptoms which do not allow of confusion with leprosy.

Leprosy being a home infection, new cases should be sought among the contacts of a leprosy person, and it is for such cases and conditions that our serological evidence is of great importance. The

search for the leprosy bacillus in the lymph nodes is difficult for both physician and patient, and patients seldom allow a repetition of the examination. The finding of the organism is occasional, and when the result is negative the patient generally does not allow a second attempt to find it.

TABLE 1.—Cases showing clinical and/or bacteriological signs of infection.

A. CASES WITH PREVIOUS SIGNS

- Case 5. Nasal mucus positive, 11 months before.
- Case 6. Nasal mucus positive, 1 month before.
- Case 12. Nasal mucus positive, 5 years before.
- Case 18. Nasal mucus positive, several years before.
- Case 45. Rheumatoid pains and "picadas", forty-four months before.
- Case 47. Cubitals and medians painful, forty-one months before.
- Case 48. Nasal mucus and lymph node positive, thirty-four months before.
- Case 50. Nasal mucus positive, three months before.
- Case 51. Cubitals and medians painful, fifty-three months before.
- Case 53. Nasal mucus and lymph node positive, forty-nine months before.
- Case 54. Nasal mucus positive, forty-four months before.
- Case 55. Lymph node positive, fifty-two months before.
- Case 56. Enlarged nodes and nerve pain, forty-six months before.

B. CASES WITH ACTUAL SIGNS

- Case 8. Hypoesthesia of right leg.
- Case 10. Hypoesthesia.
- Case 11. Small atypical lesion.
- Case 14. Rhinitis.
- Case 15. Epistaxis.
- Case 20. Lymph node positive.
- Case 21. Atypical lesions.
- Case 27. Hypoesthesia of forearms.
- Case 28. Atypical lesions.
- Case 29. Heat sensation retarded.
- Case 30. Heat sensation retarded.
- Case 33. Discrete signs.
- Case 35. Nasal mucus positive.
- Case 36. Atypic patch with acid-fast bacilli.
- Case 39. Dry skin on inferior part of legs.
- Case 43. Vague pains.
- Case 46. Hypoesthesia on inferior part of legs.
- Case 49. Lymph nodes positive.

C. CASES BECOMING POSITIVE LATER

- Case 9. Became leprous 8 months after childbirth.
- Case 19. Became leprous later.
- Case 32. Became leprous 3 years later.
- Case 34. Became leprous 4 years later.
- Case 52. Became leprous 39 months later.

It is now to be asked, if positive complement-fixation indicates actual infection, whether the *Myco. leprae* is latent in the tissues. Evidence is afforded by an analysis of the cases that have been summarized. In the foregoing tabulation are listed (a) cases that had previously shown clinical and/or bacteriological evidence of infection, (b) cases showing such signs at the time of examination, and (c) cases that became leprous later.

The number of cases shown by this analysis to have had slight clinical signs, actual or pre-symptomatic, or positive lymphatic or nasal smears, is so large that we are led to believe that a positive Gomes test does correspond to a latent microbism. Nevertheless, it is not easy to predict the destiny of such cases, compared with the other group, in which deviation of the complement does not occur. Leprosy being a product of various factors, it must be remembered that the mere presence of the causative agent does not permit generalization as to what will follow. Thus, some patients suffer from anergic states, while others do not, or they suffer at another time and under different conditions. These facts are important not only in connection with leprosy, but also in general pathology. Only a calamity such as a pandemic of influenza is capable of revealing the truth in this matter.

The problem of leprosy is so complex and so great that we cannot overlook any opportunity, however small, to interfere with its progress. In the cases in which the complement-fixation test is positive, especially when activated by potassium iodide, we advise starting antileprotic treatment. We cannot be certain that such treatment will prevent the outbreak of the disease in an individual, notwithstanding the fact that none of those treated by us developed the disease, but in any case such treatment puts the patient under closer observation, which facilitates detection of subsequent phenomena.