

at the return of Columbus in 1493, and knew Columbus and members of his crew. In his "Historia general y natural de las Indias," and in a report drawn up at the command of Charles V of Spain, he recites: That the disease was contracted from Indian women by the Spaniards with Columbus; that it was brought by them to Spain and thus transmitted to the army of Charles VIII by Spanish soldiers; and that syphilis should be called the West Indian disease, rather than the French or Neapolitan disease. He also mentions in independent corroboration of Dias de Isla, that one of the brothers, Pinzon, contracted the disease, and that it "is common among the Indians, but in those regions is not so dangerous as with us."

Oviedo was an advocate for Spain, and it has been urged that the theory of the Indian origin of syphilis may have been readily adopted by him in his attempts to palliate the cruelty of the Spaniards toward the Indians. No such charge, however, will stand against Las Casas, whose efforts were all in behalf of the Indians, but who, nevertheless, did not hesitate to give in detail the facts of syphilis among them.

The father of Las Casas accompanied Columbus on his second voyage, and Las Casas himself was in Haiti in 1498, where he lived many years and wrote his "Historia general de las Indias." He records: "There were, and still are, two things which at the beginning were very dangerous to the Spaniards. One is the disease syphilis, which in Italy is known as the French evil. . . ."

"It is, however, known for certain that it came from this island, either when, with the return of the Admiral Don Christóbal Colón with the news of the discovery of the West Indies, the first Indians arrived, whom I saw myself in Seville, or it may be that certain Spaniards were already tainted with this disease at the time of their first return to Castile. . . ."

"I took the trouble on several occasions to interrogate the Indians of this island as to whether this disease was of great antiquity, and they answered, 'Yes.' . . ."

"It is also an undoubted fact that all Spaniards addicted to sexual excess, who did not in this island observe the virtue of continence, were attacked by the disease, not one in a hundred escaping, unless the woman was healthy." He too emphasizes the greater severity of the disease among the Spaniards than among the natives.

In addition to Oviedo and Las Casas, numerous others of the early chroniclers of Spanish America (Pancé, Sahagún, Hernández), testify as shown by the researches of Montejo, to the pre-Columbian existence of syphilis in America. They show not only that the disease was known to the Indians, but that the Indians had numerous names for it; that they were fairly familiar with its symptoms and course, and had well-worked-out methods of treatment for it; and that the disease was much milder in its course among the Indians than among the Spaniards, who contracted it from them.

This brief summary of the discoveries of Montejo y Robledo from his researches among original Spanish authorities, furnishes the final link connecting the origin of syphilis with America, and, it would seem, compels us to conclude that syphilis was introduced into Europe from Haiti by the sailors of Columbus on their return in 1493 from his first voyage to America.

THE LANDAU IODIN SERUM TEST FOR SYPHILIS*

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A good deal of interest has been aroused lately in the new serum test for syphilis proposed by Landau.¹ It is declared that this test is more sensitive than the Wassermann reaction and that its simplicity makes it available for every one. Among the many tests said to have these qualities, the Landau demands attention because of the popular interest shown in it and the possibility that it may come into more or less general use. Any new test for deciding so important a diagnosis as that of syphilis must be subjected to the sharpest scrutiny, and tried in many thousand cases.

Landau at first used as a reagent a 0.05 per cent. solution of iodine in liquid petrolatum. The composition of various samples of this solvent varied enough, however, to make it difficult to obtain a reliable reagent, so that he later adopted carbon tetrachloride (CCl₄) as a solvent. In this he dissolves 1 per cent. of iodine (a saturated solution which requires trituration to complete it); and uses 0.1 c.c. of this reagent to 0.2 c.c. of the serum to be tested. These are shaken together in a test tube 12 mm. in diameter, and allowed to stand at room temperature for four hours. If, at the end of this time, the serum above the decolorized reagent is a clear yellow, the reaction is recorded as positive. If the serum is an opaque grayish-white, it is recorded as negative. Only fresh serum, obtained not more than six hours before, and free from any cloudiness or hemoglobin stain, can be used. If the result is not easy to determine, 0.2 c.c. of ammonia solution may be added to clear up the doubt.

Landau, with his first technic, reported that he obtained, in a series of 122 cases, only one result that did not agree with the clinical diagnosis. This was a positive test in a case of a leg ulcer, clinically and serologically nonsyphilitic. He reported also that the reaction gave fifty-five positive readings in a series of ninety syphilitics, in whom only forty-nine positive Wassermann reactions were obtained.

These results have not been substantiated by others. Golay,² using the carbon tetrachloride reagent, obtained forty-one positive, eleven doubtful, and eleven negative reactions in a series of sixty-three syphilitics, in which only thirty-seven positive Wassermann reactions were obtained. But he also reports in seventeen nonsyphilitics, all of whom had negative Wassermann reactions, a positive Landau test in eight cases. One of these was a case of gonorrhea, three cases of soft ulcer, two of tuberculosis and two of malignant tumor: 47 per cent. positive in nonsyphilitics! He concludes that the test is positive in a large percentage of cases of systemic disease, but reports negative reactions in all of three cases of "skin disease of external origin" and three healthy persons.

Villaret and Pierret³ report agreement with the Wassermann reaction in thirty-two cases of thirty-nine

* From the Dermatological Department of Cook County Hospital.

1. Landau, Wilhelm: Untersuchungen über eine Reaktion luetischer Sera mit einem Jodöl-Reagens, Wien. klin. Wchnschr., 1913, xxvi, 1702.

2. Golay, J.: La réaction de Landau, Rev. méd. de la Suisse romande, 1914, xxxiv, 571.

3. Villaret and Pierret, R.: Tr. Soc. biol. de Paris, Presse méd., July 29, 1914, p. 582.

examined, and agreement with the clinical diagnosis in twenty-seven of thirty-three cases.

Capello⁴ reports that in forty-one cases, the Landau reaction agreed with the Wassermann in only twenty-seven, leaving fourteen, or 34 per cent., in which it differed. In three cases of late syphilis under mercury treatment, the Wassermann reaction was negative, while the Landau gave a strong positive in two and a doubtful positive in one. In two cases clinically and serologically nonsyphilitic, the Landau test gave a strong positive. Of four cases in which the Wassermann reaction was a strong positive, the Landau gave a doubtful result in one and a frank negative in three.

My technic is the same as that prescribed, except that for the first of my series I used very small test tubes, in order to make the small column of serum longer and more easily seen. Later I adopted the regulation size, 12 mm. diameter, running a series of parallel reactions in both kinds of tubes, until I was satisfied that my results were practically the same with both, and that my early tests could be admitted as reliable. I also used from the beginning twice the prescribed quantities of serum and reagent, 0.4 c.c. of serum and 0.2 c.c. of reagent. But in order to check this with the original technic, and to check my results on each serum, I made each time two tests, one with the original quantities and a parallel test with the double quantities. The measurement of the reagent is a difficult matter in the ordinary pipets. My work was made much easier by the use of a Wright pipet, graduated in 0.1 c.c. In this, several doses of reagent can be taken up, separated by columns of air, and the movement of the thin liquid much more easily controlled.

On shaking the mixture of serum and reagent, an emulsion is formed which soon becomes a light yellow and then white. All serums decolorize the carbon tetrachlorid, so that it separates out and remains as a white layer under the serum.

The reading of the final result is by no means always easy. All degrees of opalescence occur, and even the addition of ammonia does not always clear up the doubt. Golay makes the same observation, and this accounts for the large number of doubtful reactions recorded by him and Capello. I have tried to avoid as far as possible recording doubtful reactions, and I believe that my use of two tests for each serum has been helpful in that direction. Where any doubt existed, I have tried to give the new test the benefit of it.

My results with fifty tests in forty-six cases of syphilis are shown in the accompanying table.

COMPARATIVE RESULTS WITH THE LANDAU AND WASSERMANN REACTIONS

	No. Cases	Landau Reaction			Wassermann Reaction	
		+	+	-	+	-
Primary syphilis.....	5	4		1	5	
Active secondary.....	16	7		9	16	
Latent.....	11	1	1	9	5	6
Tertiary.....	17	13		4	13	4
Tabs.....	1			1	1	
Totals.....	50	25	1	24	40	10

One latent case under treatment gave a positive Landau and a negative Wassermann. This is greatly outweighed by the five latent cases which gave negative Landau reactions and positive Wassermans. In

the tertiary cases the honors are even. Nine cases gave positive reactions with both tests. Four gave positive Landau reactions and negative Wassermans. Two of these were on the same patient. Four gave negative Landau reactions and positive Wassermans.

Of forty tests in nonsyphilitics, all of whom had negative Wassermans, twenty-nine gave negative Landaus, eleven positives. In these eleven cases, no history of syphilis could be obtained, although one, an old hemiplegic, may be suspected because of a history of cerebral hemorrhage at the age of 21. The positive Landau tests in this series were as follows:

One case of ulcer of the cheek from caustic applied by a dentist.

One of five cases of ulcer molle.

Two of five cases of gonorrhea.

One case of gonorrheal epididymitis.

One case of salpingitis and abortion.

One case of pulmonary tuberculosis with lupus of the palate.

One case of hemiplegia with ulcer of the leg.

One case of seborrheic dermatitis.

Two cases of dermatitis venenata, both from rhus toxicodendron.

My results differ from those of the other investigators of this subject in the low percentage of positive results in known syphilitics, 52 per cent. of positives in the forty-six cases, while the Wassermann reaction gave 84.8 per cent. of positives. It might be thought, from the large percentage of positives in tertiary cases, that the administration of iodids had something to do with the production of a positive Landau test. But all our secondary cases received iodids, and the Landau was especially weak in them, differing markedly from all the European writers on the subject, and agreeing most nearly with Kolmer,⁵ who reports 71.6 per cent. of positive Landau reactions in Wassermann-positive serums. Mine gave 62.5 per cent. of positive Landaus in Wassermann-positive serums. Kolmer obtained 70 per cent. of positive tests in Wassermann-negative serums, which may be due to the fact that he used only 0.01 c.c. of the reagent, instead of 0.1 c.c., or with the fivefold amounts, 0.05 c.c. of reagent to 1.0 c.c. of serum. If the test depended on the same constituent of the serum that binds complement in the Wassermann test, it might be expected to give with a smaller amount of reagent a larger proportion of positives in syphilitics at the same time that a number of positives in nonsyphilitics would appear. But the corresponding increased percentage of positives in syphilis does not appear in Kolmer's series.

Leaving out the case of old hemiplegia as a suspect syphilis, my series of nonsyphilitics gave 27.8 per cent. of positive reactions. Golay, in seventeen nonsyphilitics, obtained 47 per cent. positive Landau reactions. Capello, in forty-one cases of both classes, obtained a positive Landau reaction in two which are probably nonsyphilitic, one a subacute polyarthritis and the other listed as clinically nonsyphilitic, both giving negative Wassermans. A test giving so large a percentage of positive results in nonsyphilitic cases can certainly be of no value in the diagnosis of syphilis, and the idea that it is a test for syphilis can do incalculable harm.

The hope with which I undertook this work, that a negative Landau test might prove of value in eliminating syphilis from the diagnostic possibilities of a case, has been destroyed by the failure of the test to equal

4. Capello, G.: Contributo allo studio della reazione di Landau nella sifilide, *Gazz. d. osp.*, 1915, xxxvi, 423.

5. Kolmer, J. A.: Concerning Landau's Color Test for Serodiagnosis of Syphilis, *THE JOURNAL A. M. A.*, May 1, 1915, p. 1461.

the Wassermann reaction in my series of known syphilitics. My statistics do not bear out the idea of Golay and Capello, who think that under treatment the test remains positive longer than the Wassermann reaction.

The Landau reaction is, as Golay says, an interesting phenomenon, which may some day be made use of in research. As a means of diagnosis, however, it deserves no consideration, but should be relegated to the same shelf as its predecessor and possible relative, the iodine reaction of the leukocytic granules.

SUMMARY

1. No reliance can be placed on a positive Landau, for it occurs in a large percentage of nonsyphilitics.
2. A negative Landau is of no value in proving the absence of syphilis, for a large proportion of syphilitics have negative Landaus.
3. So far as this series of cases can show, no definite relation exists between syphilis and the Landau serum reaction.

A FURTHER NOTE ON LANDAU'S COLOR TEST FOR SERODIAGNOSIS OF SYPHILIS*

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Shortly after the publication of my paper concerning Landau's color test for the serodiagnosis of syphilis¹ I learned that 0.1 c.c. instead of 0.01 c.c. of the 1 per cent. iodine in carbon tetrachloride reagent should have been used with 0.2 c.c. of serum. THE JOURNAL,² from which I obtained this technic, had quoted from an Italian medical journal³ which was responsible for the error. Additional foreign literature⁴ states that the correct quantity of the iodine reagent is 0.1 c.c. and since my work had been done with 0.01 c.c. reagent or ten times less the amount given by Landau I have continued the work with this correction, the results being summarized in this paper.

A 1 per cent. solution of iodine was prepared according to weight by dissolving 1 gram of iodine crystals in 62.7 c.c. pure carbon tetrachloride (specific gravity 1.59 at laboratory temperature) and the container was tightly stoppered to prevent evaporation. The regular and routine test was conducted by placing 0.2 c.c. of serum in a small test tube, adding 0.1 c.c. of the reagent and gently shaking until all color had been removed from the reagent.

The reagent has a deep purple blue color and owing to its high specific gravity settles in the test tube below the serum. After thorough agitation the mixture assumes a brownish color and the carbon tetrachloride quickly settles to the bottom of the tube in a layer resembling chloroform.

Each serum was also tested routinely with five times the quantity of serum and reagent, namely, 1 c.c. of serum and 0.5 c.c. of reagent. This mixture results in the formation of a heavy brownish sediment overlaid with serum.

Immediately after serum and reagent are mixed the whole is distinctly cloudy; after standing for four hours at room temperature a syphilitic serum, according to Landau, becomes clear transparent yellow, whereas with a nonsyphilitic serum the fluid becomes a whitish gray and is opaque.

When 1 c.c. of serum and 0.5 c.c. of reagent are used the readings cannot usually be made at the end of four hours because of insufficient time for clearing. With this technic the mixtures must be centrifuged or the readings delayed for twenty-four hours.

I have experienced considerable difficulty in reading the reactions. With those reactions in which the supernatant serum is perfectly clear or quite cloudy no difficulties arise in recording the result, but in many instances the serum is neither clear nor distinctly cloudy, but is faintly opalescent, so that different observers will vary considerably in reading the same reactions. For this reason a portion of the unused serum should be on hand for comparison; but under any conditions the reading and interpretation of the tests are difficult and unsatisfactory.

I have again tested each serum with Landau's original reagent of iodized petrolatum, prepared by the addition of 5 drops of 10 per cent. tincture of iodine to each 10 c.c. of white paraffin oil, followed by thorough mixing. As the color of this mixture tends to fade spontaneously I have prepared fresh mixtures twice a week. The test with this reagent was conducted by placing 0.2 c.c. serum in a small test tube and adding 2.5 c.c. of the reagent followed by thorough mixing and standing aside at room temperature for from fifteen to twenty-four hours. A control without serum was included with each set of tests.

Immediately after mixing the serum and reagent the mixture is of a light pinkish color; the serum, however, quickly settles to the bottom of the tube and is of a deeper yellow color, while the deep pink tint returns to the supernatant oil. I have usually shaken the tubes once or twice more during the following six hours.

According to Landau a syphilitic serum decolorizes the mixture after fifteen hours, while the color persists a reddish yellow with normal and nonsyphilitic serum.

MATERIALS AND METHOD OF STUDY

In all 172 serums and fourteen cerebrospinal fluids⁵ have been tested. The majority of these were collected within twenty-four to forty-eight hours of the time when these tests were made and were centrifuged if necessary to render them clear and free of corpuscles. Markedly opalescent serums as those collected soon after a meal were discarded; the majority were clear while a few were faintly tinged with hemoglobin. The latter were more likely to become cloudy and opaque with the iodine reagent than were perfectly clear serums.

I found no differences, however, in the results of the tests, whether a serum was secured within three hours or three days of the time when the tests were made, and likewise practically the same results were observed with fresh active serums and the same serums after heating at 55 C. (131 F.) for thirty minutes (inactivation). The plan of study was the following:

TECHNIC

- (a) Two-tenths c.c. fresh active serum + 0.1 c.c. iodine tetrachloride of carbon reagent; the results were

* From the Laboratories of the Philadelphia Polyclinic and College for Graduates in Medicine.

1. Kolmer, J. A.: Concerning Landau's Color Test for Serodiagnosis of Syphilis, THE JOURNAL A. M. A., May 1, 1915, p. 1461.

2. Color Test for Syphilis, Misc. Abstr., THE JOURNAL A. M. A., Oct. 10, 1914, p. 1317.

3. Un nuovo metodo diagnostico della sifilide, abstr., Riv. Osp., July 15, 1914, p. 641.

4. Réaction des sérums syphilitiques avec le réactif de W. Landau, abstr., Presse méd., May 2, 1914, p. 335.

5. I am indebted to Miss A. McNitt of the laboratory of the Philadelphia General Hospital for a number of these serums.