

THE WELTMANN REACTION IN PULMONARY TUBERCULOSIS

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INTRODUCTION

In 1930, Oskar Weltmann¹ introduced a new serum coagulation reaction to distinguish exudative from fibrotic processes in the body, and since its discovery, it has been employed routinely in many European Clinics. There is a great deal of valuable literature on the subject, but singularly enough, very little is reported in the American literature. It is the purpose of this study to determine the value of the Weltmann reaction in establishing the diagnosis of active pulmonary tuberculosis and in following the progress of such cases.

TECHNIC

The test is simple to perform and requires very little apparatus. The result can be determined within 20 to 25 minutes. From a stock 10 per cent calcium chloride solution (ca $\text{Cl}_2-6\text{H}_2\text{O}$), ten dilutions are made up, varying from 0.1 per cent to 0.01 per cent. Five cc. of each dilution is pipetted into each of ten tubes. Ordinary Wassermann tubes may be used, and the tubes numbered from 1 to 10, beginning with the strongest dilution. Into each tube pipette $1/10$ of a cc. of the unhemolyzed serum to be tested. The contents are mixed thoroughly and the tubes placed in a boiling water bath for 15 minutes. They then are removed, and the test is read. The contents of the tubes may be clear, faintly opalescent, turbid, or there may be flocculation. The number of tubes in which flocculation occurs is designated by Weltmann as the coagulation band of the particular serum tested, i.e., W. C. B. = number of tubes showing flocculation. If there is very slight or doubtful flocculation in one tube, the reaction is interpreted as being intermediate. Usually, the difference between turbidity and flocculation is very sharp. The only really important precaution is to be sure that the serum is unhemolyzed. In the experience of the writers hemolysis always increases the number of tubes showing flocculation and therefore gives an inaccurate result. It has been found by other authors that irradiation, freezing, inactivation at 56°C ., and storage for two to three days has no effect on the coagulation band. Therefore, the test is relatively stable. In normal sera the first six tubes show flocculation. Occasionally, there is a slight degree of flocculation in the seventh tube. The normal coagu-

lation band then is 6 to $6\frac{1}{2}$. In his original article Weltmann stated that if the coagulation band (C. B.) was less than 6, the reaction showed a "shift to the left" and when the C. B. was 7 or more, a "shift to the right" was indicated.

MECHANISM AND INTERPRETATION

The exact nature of the chemical or physico-chemical mechanism of the Weltmann reaction has not yet been determined. Likewise, very little is known of the changes occurring in the heat coagulation of proteins. Weltmann¹ originally thought that the basis of the reaction lay in the coagulation of serum albumin by heat in the presence of electrolytes. Massobrio and de Michelis² were the first to claim that the serum proteins had an effect on the coagulation band, and that a "shift to the left" occurred when the albumin fraction was decreased and the globulin fraction was increased. This view did not coincide with the work of later investigators including Levinson and Klein,³ who found that in nephrosis, when the albumin-globulin ratio was reversed, there was an extreme "shift to the left," while in cirrhosis, when there was always a "shift to the right," there was also at times a reversal of the albumin-globulin ratio. Levinson and Klein³ showed that the hydrogen ion concentrations of the solutions used in the test played no part in the reaction. In a small number of cases they apparently found some correlation between the blood pH and the coagulation band, for as the coagulation band lengthened, the pH shifted toward the acid side, while a more alkaline pH was usually accompanied by a shorter coagulation band. Kretz and Kudlac⁴ found that the calcium and chloride content of the serum used had no effect on the C. B., while Dees⁵ claimed that calcium was essential for the reaction to take place. She found no coagulation when calcium was removed from the system by a sulfonated fatty acid, which had a marked affinity for calcium. Dees was also able to increase the coagulation band two hours after the intravenous injection of 5 cc. of 10 per cent calcium chloride solution. Levinson and Klein³ found no correlation between the level of blood cholesterol and the length of the band. In spite of our poor appreciation of its mechanism, the Weltmann reaction has been found to be of clinical value.

OBSERVATIONS OF OTHER INVESTIGATORS

Levinson and Klein,³ in 1938, studied the Weltmann reaction in cases of pulmonary tuberculosis for a period of three to five months and concluded that there was no definite correlation between the Weltmann

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reaction and the sedimentation rate, and that the former seemed to be a better index of the clinical state of the patient.

Makitra and Tyndel⁶ determined the Weltmann C. B. in 200 patients with pulmonary tuberculosis, and their results indicated that in incipient cases of exudative tuberculosis the coagulation band gave more reliable results than the sedimentation rate. These authors stated that the Weltmann reaction could be used prognostically in chronic tuberculosis. They claimed that the sedimentation rate responded readily to the slightest alterations in the body and was less stable than the coagulation band.

Voigtlander,⁷ in 1934, reported 400 cases of tuberculosis, which he followed in a sanatorium. He concluded that the test was valuable in the diagnosis and prognosis of tuberculosis, and that it was a most important aid in determining whether fibrosis or exudation was present in the lung.

Dissmann,⁸ in 1934, did the Weltmann test on 274 tuberculous patients and compared the results with tests on normal individuals. He found the degree of a "shift to the left" to correlate quite closely with the severity of the exudative process present. He also found that in the presence of fibrocaceous tuberculosis and fibro-ulcerative tuberculosis the coagulation band was frequently normal. A "shift to the right" was noted in only purely productive lesions, i.e., in the closed cavity and healing stages.

In his original study Weltmann¹ made no claim that the coagulation band was specific for any disease. He committed himself only by saying that the test was of value in distinguishing between exudative and productive processes.

STUDY OF THE WELTMANN REACTION IN 85 NORMAL INDIVIDUALS AND 75 PATIENTS WITH PULMONARY TUBERCULOSIS

Before applying the Weltmann reaction to cases of pulmonary tuberculosis, it was necessary to determine the reaction of normal sera to the test. Therefore, the Weltmann reaction was determined in 85 normal individuals. This group included doctors, nurses, and medical students, all of whom were known to be normal and in whom negative chest x-rays had recently been taken. In all instances the Weltmann coagulation band was found to be 6 to 6½. This figure is in complete agreement with the normal bands reported by other investigators. A total of 75 cases of pulmonary tuberculosis was then observed. Twenty-five of these were classified as moderately advanced and far advanced,

chronic, inactive. The remaining 50 included 27 far advanced, 20 moderately advanced, and three minimal.

In the 27 far advanced cases the following results were obtained. In 14 cases the Weltmann coagulation bands reflected the clinical course of the patient, and in 13, or about 50 per cent, the test was not correlated with the clinical picture. One of these patients with a coagulation band of 8 died. In these same patients the sedimentation rate was also observed. In 23 of the 27 cases, or 84 per cent, the sedimentation rate followed the clinical course of the patient, and in four cases, or 16 per cent, it was without significance. Most of the patients in this group had both productive and exudative processes occurring simultaneously in the lung, although from observations of the temperature, pulse, and chest x-rays the predominant process could usually be determined. In this group, therefore, the Weltmann coagulation band was of value in only 50 per cent of the cases, while the sedimentation rate was a valuable guide in 84 per cent.

Twenty cases were observed in the moderately advanced group. In 16 of these, or 80 per cent, the Weltmann test mirrored the clinical activity, while in four cases, or 20 per cent, it did not. Again the sedimentation rate was determined and only in 12 cases, or 60 per cent, did it correlate with the clinical status of the patient. In 40 per cent, or in eight cases, it was of value. In this group, therefore, the coagulation band seemed of more value than the sedimentation rate.

Minimal group. There were only three cases in this group and the sedimentation rate was of no value, while the Weltmann coagulation band was a valuable guide in all. Two of these patients had minimal, soft appearing lesions in the apices without symptoms. In both the coagulation band was 5, and with clinical improvement and diminution in the size of the lesions by x-ray the band returned to normal. In the third case x-ray showed only a hard, calcific appearing lesion. The temperature and pulse were normal, and the coagulation band varied between 6 and 7. In the first two cases the sedimentation rate was rapid at the start and continued to be rapid even when x-ray and clinical signs showed healing. The sedimentation rate was rapid in the third case when all other examinations showed the lesion to be inactive and old. Of the 50 cases studied and followed over a period of months, the Weltmann coagulation band was consistent with the clinical and x-ray status of the patient in only 32 cases, or 64 per cent, while the sedimentation rate was in agreement in 40 cases, or 79 per cent. There was no definite correlation between the Weltmann coagulation band and the sedimentation rate.

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CASE REPORTS

Case 1. A 32 year old colored woman complained of a "cold" of a month's duration characterized by cough, productive of one-half cupful of mucopurulent sputum per day. She had also had low grade afternoon fever and night-sweats, although she had had no hemoptysis nor pleuritic pain.

Physical Examination. The patient was thin and appeared to be chronically ill. Examination of the lungs revealed dulness in both apices anteriorly and posteriorly and many fine dry râles over the same areas. X-ray showed a dense infiltration involving the left apex and subapical region. There was a questionable cavity on the left below the clavicle. The diagnosis was moderately advanced pulmonary tuberculosis with probable cavitation on the left. The sputum was positive for acid-fast bacilli, and successive counts showed Gaffky III, IV and IV. The temperature varied between 38° C. (100.4° F.) and 39° C. (102.2° F.); the pulse was 90-100. At the time of admission the sedimentation rate was 1.30 mm. per minute and W. C. B. 6. Later coagulation bands failed to change from the original figure. Obviously, this was an active, moderately advanced case of pulmonary tuberculosis, and the sedimentation rate was a far better guide than the Weltmann coagulation band.

Case 2. A 21 year old white woman was admitted because an x-ray of the chest made two weeks previously showed a "spot" on the right lung. A brother, during an army examination, had been found to have tuberculosis. For one month the patient had had a cough productive of a small amount of white sputum. Also, for this period she had had a "stitching" pain in the right chest, which was worse upon taking a deep breath. There was no history of fever, hemoptysis, night-sweats, or weight loss. The physical examination was completely negative, and x-ray of the chest showed a "soft infiltration" in both apices and right subapical area. There was no evidence of cavitation. The diagnosis was moderately advanced pulmonary tuberculosis. Sputum was negative for acid-fast bacilli on five occasions. Temperature remained steady at 37° C. (98.6° F.) and pulse 80 with several rises to 100. The sedimentation rate on admission was 0.24 mm. per minute and coagulation band was 4. Here, we believe, the Weltmann coagulation band showed correctly a "shift to the left" indicating an exudative type of process in the lungs. Here again, there was no correlation between the sedimentation rate and the coagulation band.

Case 3. A 23 year old white woman complained of having lost 30 pounds during the eight months before admission. Four months before admission, she had developed a cough productive of small amounts of mucopurulent sputum daily, weakness, and afternoon fever. Physical examination showed a chronically ill, emaciated woman in no particular distress. Examination of the lungs showed dulness and post-tussive râles over the left apex anteriorly and over both apices posteriorly. X-ray was interpreted as showing moderately dense mottling and linear shadows in the upper half of both lung fields. On both sides there was one or more thin-walled cavities in the range of 2-4 cm. in diameter. The shadows indicated a mixture of exudative and proliferative disease. The diagnosis was far advanced pulmonary tuberculosis. Sputum-Gaffky II—temperature ranged between 37.5° C. (99.5° F.) and 38.5° C. (101.3° F.), and pulse 90-100. The sedimentation rate was 1.54 mm. per minute and Weltmann coagulation band 5. Here is an instance of agreement between the two tests, in which both reflected the clinical picture.

Case 4. A 27 year old white woman was diagnosed as having pulmonary tuberculosis in 1933. She had spent 20 months in a sanatorium, and while there, pneumothorax had begun on the left and was continued with 300 to 500 cc. every two weeks thereafter.

She had been referred to the hospital because x-ray had shown an area suspected of being tuberculous on the right. There had been no complaints. The patient was well developed and well nourished and did not appear ill. Examination of the lungs showed fine dry râles, decreased tactile fremitus, and breath sounds over the left anterior chest. There were some post-tussive râles over the right anterior chest. X-ray showed a 50 per cent pneumothorax on the left with an adherent apex. There was a small amount of calcified infiltration in the apex of the left lung and upper one-third on the right. No cavities were seen. The diagnosis was pulmonary tuberculosis, moderately advanced with an artificial pneumothorax (left). Sputum was negative for acid-fast organisms on three examinations. Temperature ranged between 37° C. (98.6° F.) and 37.5° C. (99.5° F.), pulse 80-90. The sedimentation rate was 0.67 mm. per minute and coagulation band 7. The clinical picture was that of chronic inactive tuberculosis, and the Weltmann showed a slight "shift to the right" indicating a predominance of fibrosis. The sedimentation rate here agreed neither with the Weltmann reaction nor with the clinical picture.

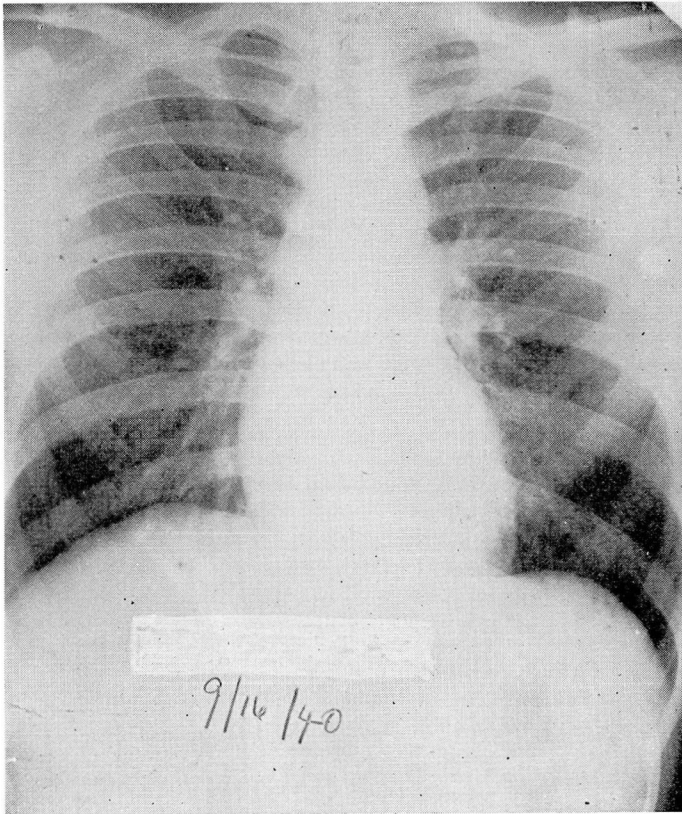


FIGURE 1. X-ray of the chest taken on admission on 9/16/40. This was interpreted as being essentially normal save for rather heavy hilar shadows. The sedimentation rate was rapid, and the Weltmann coagulation band = 4.

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Case 5. A 17 year old colored girl had had a "bad cold" for the five weeks preceding admission. There had been no hemoptysis, weight loss, nor pleuritic pain. Physical examination revealed post-tussive râles over the left apex anteriorly and posteriorly. On the right there were post-tussive fine dry râles and distant breath sounds over the apex anteriorly and posteriorly. X-ray showed a conglomerate patch of infiltration filling the second anterior interspace and extending over adjacent ribs on the right. On the left a patch of infiltration overlying the first interspace and adjacent ribs and a smaller area along the course of the eighth posterior rib. There were no definite cavities. The diagnosis was pulmonary tuberculosis, moderately advanced. A bilateral pneumothorax was contemplated, and this was started on the left side one week following admission (2/14/42). Sputum examination showed the following: 2/2/42, negative—2/7/42, Gaffky III—2/9/42, Gaffky II—2/11/42, Gaffky II—3/2/42, negative. The temperature remained at 37° C. (98.6° F.) with an occasional rise to 37.5° C. (99.5° F.), pulse 80-100, and remained steady at 80 following the pneumothorax. The sedimentation rate on admission was 1.36 mm. per minute and coagulation band 8.

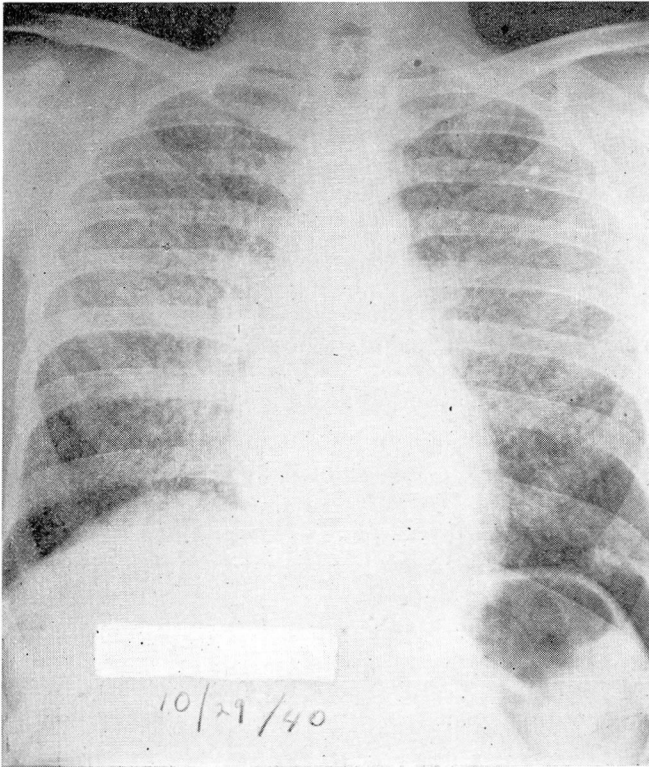


FIGURE 2. X-ray of the chest taken one week before death interpreted as showing miliary tuberculosis, later proved at autopsy. The sedimentation rate was very much elevated, and the Weltmann coagulation band = 0.

This case illustrates again the lack of correlation between the two tests, and in this particular instance the value of the sedimentation rate over the coagulation band.

Case 6. A 27 year old colored handy-man had been well until three weeks before admission, when he complained of general malaise and mild frontal headache. The last week before admission, he had also complained of fatigue and anorexia. On admission the temperature was 37.5° C. (99.5° F.), pulse 70, and respiration 20. General appearance was that of a well developed, well nourished colored man who did not appear acutely ill. There were no positive physical findings. A diagnosis of miliary tuberculosis was suggested. Laboratory findings were within normal limits except for a white blood count of 3,600. During the first week of admission, he ran a low grade afternoon fever together with a relatively slow pulse. Examination of the lungs showed a few coarse moist bilateral basilar râles. X-ray taken in the first week of hospitalization is shown in Figure 1. During the following month his temperature ranged around 39° C. (102.2° F.), and pulse 70-80. He lost 20 pounds in weight, and his appetite was poor. There was no cough, but he had drenching night-sweats. A film taken one week before death and four weeks following the first x-ray is shown in Figure 2. During the week before death occurred, the lungs were full of coarse moist râles, and he was dyspneic and orthopneic. A miliary tubercle was seen in the fundus of the right eye. At autopsy miliary tubercles were found in the lungs, liver, spleen, kidneys, and right eye.

The sedimentation rate remained elevated throughout, and the coagulation band showed a consistent "shift to the left," finally falling to 0.

SUMMARY

The Weltmann coagulation band was determined in 85 normal individuals and a remarkably constant result obtained, i.e., 6-6½.

In 75 cases of pulmonary tuberculosis, followed for a period of three to four months, an attempt was made to define how closely the coagulation band reflected the clinical picture and whether there was any correlation between the band and the sedimentation rate. In this group of 75 cases, 25 were chronic, arrested, inactive cases, and here the Weltmann reaction consistently showed a "shift to the right" and was a better indication of the clinical status than the sedimentation rate. In the remaining 50 cases the Weltmann coagulation band followed the clinical picture in 32 cases, or only 64 per cent, while the sedimentation rate was a good index in 40 cases, or 79 per cent. When the cases were divided into far advanced, moderately advanced, and minimal, it was shown that in the 27 far advanced cases, the Weltmann reaction was reliable in only 50 per cent as against 84 per cent with the sedimentation test. In the moderately advanced group of 20 cases, the sedimentation rate showed 60 per cent reliability and the coagulation band 80 per cent. There were only three minimal cases studied, and the sedimentation rate was of no value in any while the Weltmann test was reliable in all.

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CONCLUSION

1. Neither the Weltmann reaction nor the sedimentation rate is completely reliable or infallible in the diagnosis and prognosis of pulmonary tuberculosis. In these cases the sedimentation rate has been a somewhat better index of the clinical status of the patient. In doubtful cases it may be of value to do both tests.

2. In the chronic, arrested, inactive cases the Weltmann reaction consistently showed a "shift to the right" and was a better indication of the clinical status than the sedimentation rate.

3. There is no definite correlation between the Weltmann coagulation band and the sedimentation rate.

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BIBLIOGRAPHY

1. Weltmann, Oskar: The significance of the exudative and fibrotic processes in the blood serum, *Medizinische Klinik* 26:240, 1930.
2. Massobrio, E., and de Michelis, U.: La siero-coagulazione di Weltmann nelle epatopatie in rapporto al quando proteico del siero, *Minerva med.*, 2:729-734, November 24, 1933.
3. Levinson, S. A., and Klein, R. I.: The Weltmann serum coagulation reaction and a comparison with the sedimentation rate and clinical findings in pulmonary tuberculosis, *Am. Rev. Tbc.* 37:200-237, February, 1938.
4. Kretz, J., and Kudlac, O.: Untersuchungen über das Verhalten der Serumeiweisskörper mittels der Weltmannschen Reaktion, *Ztschr. f. klin. Med.* 127:590-608, 1934.
5. Dees, C. Susan: A clinical study of the Weltmann serum coagulation reaction, *J. Pediatrics* 17:44-72, July, 1940.
6. Makitra, A., and Tyndel, M.: Der praktische Wert des Weltmannschen Koagulationsbandes für Diagnose und Prognose der Tuberkulose, *Beitr. z. Klin. d. Tuberk.* 84:265-269, 1934.
7. Voigtlander, W.: Untersuchungen über die Serumkoagulationsreaktion von Weltmann bei Lungentuberkulose, *Klin. Wchnschr.* 13:1718-1721, December 1, 1934.
8. Dissmann, E.: Über den Wert der Weltmannschen Reaktion bei der Beurteilung der Lungentuberkulose, *Beitr. z. Klin. d. Tuberk.* 84:270-277, 1934.