

their routine activities and only the small number with severe or more generalised muscle pain come to the attention of physicians, epidemics cannot be detected without specific surveys.

SUMMARY

1. A survey covering a period of two months was made to determine the incidence of "stiff neck" among a group of one hundred and sixty-three factory workers. Twenty-nine cases were discovered, an attack rate of 17.8 per cent.

2. The attack rate was higher in women, most of whom were in their third decade, than in men, most of whom were in their fifth decade.

3. Although the disease was usually mild, some persons were incapacitated for two weeks or longer.

4. The clinical features were unlike those of Bornholm disease but resembled those of acute fibrositis.

5. The purpose of the present communication is to direct attention to the occurrence of this syndrome in epidemic form.

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THE WELTMANN COAGULATION REACTION AND THE SEDIMENTATION TEST IN ARTHRITIS*

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Two simple non-specific laboratory procedures are recognised to be of value in arthritis. One is the filament-non-filament leucocyte count (Eaton,¹ Steinberg,² Rawls³). Steinbrocker and Hartung⁴ have found the non-filament count to be increased in

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almost 100 per cent. of cases of rheumatoid arthritis. However, the significance of this finding is diminished by the fact that the percentage of non-filament granulocytes was elevated also in almost half of the cases of osteo-arthritis. Increase of the total leucocyte count or of the non-filament percentage indicates the systemic reaction to inflammation or infection. The second test is the sedimentation reaction. Since Dawson and his co-workers⁵ have stressed the importance of the sedimentation rate, it has become in the United States the most generally used test for the differential diagnosis between rheumatoid and osteo-arthritis, for prognosis and evaluation of the effect of therapy. The mechanism of the sedimentation reaction is complex. However, the quantity and intensity of protein breakdown by a pathological process and the subsequent disturbance of the equilibrium of the plasma play important rôles.

In 1930 Weltmann⁶ described a third non-specific test based on the observation that diluted serum requires different amounts of bivalent electrolytes for heat coagulation according to the pathological process involved. To sera from exudative processes, higher concentrations of calcium chloride must be added than to normal sera in order to produce coagulation. On the other hand, sera from cases where fibrotic processes and liver damage are prominent require less calcium chloride. For the last five years this test was extensively investigated in Europe, and its usefulness for diagnosis and prognosis in various conditions confirmed. In the United States only Kraemer⁷ and Levinson and his co-workers⁸ have reported their observations of the test. Their conclusions support the European workers.

The mechanism of the Weltmann coagulation reaction is not entirely understood. Since the test is carried out on serum, it is not influenced by the fibrin content of the plasma. Carriere *et al.*⁹ and Levinson *et al.*¹⁰ have demonstrated that it is not dependent on the albumin-globulin ratio or total serum protein. Kretz and Kudlac¹¹ found that the concentration of calcium and chlorides in the serum does not influence the test. They assume that the reaction depends on qualitative changes in the serum proteins brought about by local tissue changes of either exudative or fibrotic nature. The filament-non-filament count, sedimentation test and Weltmann coagulation reaction reflect different systemic and local reactions and contribute to a more comprehensive understanding of the pathological physiology.

For this reason it appeared of interest to investigate the Weltmann reaction in various types of arthritis. Rheumatoid arthritis is generally regarded as a systemic disease. In the active stages exudative processes are prevalent, manifested by frequent presence of effusions and peri-articular swellings with increased tissue fluid. Therefore, it could be assumed that rheumatoid arthritis would give coagulation reactions in the range of exudative diseases. On the other hand, osteo-arthritis is a degenerative disease and occurs in advanced age where fibrosis and cirrhotic processes are frequent, which should tend to shift the coagulation reaction within the range of the fibrotic zone.

TECHNIQUE OF WELTMANN'S REACTION

From a stock solution of 10 per cent. crystalline $\text{CaCl}_2 \cdot 6\text{H}_2\text{O}$ ten dilutions are prepared ranging from 1:1,000 to 0.1:1,000. The integral between each solution is 0.1:1,000. 4.9 ml. of solution is pipetted into each of ten test-tubes which are numbered corresponding to their concentration from one to ten and placed in a rack. Tube I contains the highest concentration of calcium chloride and is placed to the left. To each test-tube 0.1 ml. of clear non-hæmolysed serum is added. The tubes are shaken and heated in a boiling-water bath for 15 minutes. The contents of the tubes after heating may remain clear, or show various degrees of turbidity or flocculation. The number of the test-tube showing flocculation is read and gives the coagulation band. In normal sera flocculation occurs in Tubes VI or VII corresponding to 0.5 to 0.4/1,000 calcium chloride. If flocculation occurs only in the Tubes I to V it is designated as a short band, shift to the left or exudative zone. If flocculation extends to Tube VIII and further, this reaction is known as a long band, shift to the right or the fibrotic zone. This technique is cumbersome and requires a large amount of fresh solutions, glassware and labour which impedes its general use.

A simple modification was described elsewhere¹² which permits carrying out the entire procedure with only one test-tube, one standard solution of calcium chloride and 0.1 ml. of serum. The technique of this modification is as follows:

Into a medium-sized test-tube (about 6×0.5 inches) place 4.9 ml. of distilled water and 0.1 ml. of clear non-hæmolytic serum. Add from 0.1 ml. pipette 0.05 ml. of 1 per cent. calcium chloride (equal to 0.5 mgm.). Shake and bring to a boil over a

small flame. Cool and repeat the procedure until flocculation has taken place. Note the amount necessary to produce flocculation. Table I gives the conversion into the corresponding calcium chloride concentration and the number of the tube of Weltmann's original reaction. Violent boiling should be avoided because it may lead to foaming and loss of fluid. This is prevented conveniently by a finger cot, partially unrolled, slipped over the mouth of the test-tube. The observation for flocculation should be made after cooling.

TABLE I

Weltmann's Method:	I	II	III	IV	V	VI	VII	VIII	IX	X
Tube	I	II	III	IV	V	VI	VII	VIII	IX	X
CaCl ₂ /1,000	1.0	0.9	0.8	0.7	0.6	0.5	0.4	0.3	0.2	0.1
mgm. CaCl ₂ /5 ml.	5.0	4.5	4.0	3.5	3.0	2.5	2.0	1.5	1.0	0.5
Modification:										
ml. of 1% CaCl ₂	0.5	0.45	0.4	0.35	0.3	0.25	0.2	0.15	0.1	0.05
	Exudative Zone Shift to Left Short Band					Normal Zone		Fibrotic Zone Shift to Right Long Band		

The sedimentation tests were carried out according to the Westergren method and read after one hour. Based on thousands of cases, we agree with the authors who have demonstrated that the simple Westergren method is more significant in arthritis than the various proposed modifications which only complicate the test and often confuse the results.

ANALYSIS OF MATERIAL

In this paper a comparative study of the Weltmann reaction and the sedimentation test in 250 cases of arthritis is presented. Ninety-eight cases were rheumatoid (infectious) arthritis, 88 cases were osteo-arthritis and 64 were miscellaneous types of arthritis.

Rheumatoid (Infectious) Arthritis.—Table II gives a detailed analysis of the values of coagulation reaction and sedimentation rates. Table III classifies the material in groups according to the outcome of both tests. In this and following tables the normal coagulation band is one where flocculation takes place up to Tube VI or VII (0.5 to 0.4/1,000 CaCl₂). A slightly short coagulation band is one where flocculation occurs only up to Tube V (0.6/1,000). A markedly short coagulation band is one where flocculation occurs up to Tube IV or less (0.7 to 1.1/1,000).

TABLE II.—COAGULATION BAND AND SEDIMENTATION RATE IN NINETY-EIGHT CASES OF RHEUMATOID (INFECTIOUS) ARTHRITIS.

<i>Weltmann Reaction</i> (<i>CaCl₂ per ml.</i>).	<i>Tube.</i>	<i>Per Cent.</i>	<i>Sedimentation.</i>	<i>Per Cent.</i>
0.3	VIII	4.1	0-10	10.2
0.4	VII	6.1	11-20	8.2
0.5	VI	18.4	21-30	28.6
0.6	V	18.4	31-40	16.3
0.7	IV	27.6	41-50	16.3
0.8	III	10.2	51-60	14.3
0.9	II	9.1	61-70	2.0
1.0	I	2.0	71-80	—
1.1		4.1	81-105	6.1
Total		100.0		100.0

A normal sedimentation rate is a drop of erythrocytes of 1 to 10 mm./hour, a slightly increased rate is from 11 to 20 mm./hour, a markedly increased rate from 21 to 105 mm./hour. Normal coagulation reaction occurred in 24.5 per cent. against a normal sedimentation in only 10.2 per cent. In 18 per cent. the coagulation was only slightly short and the sedimentation rate was slightly increased in 8.2 per cent. The coagulation band was markedly short in 53 per cent. and sedimentation rate was markedly increased in 81.6 per cent. The exudative process in rheumatoid arthritis is not pronounced enough in about half the

TABLE III.—SUMMARY OF COAGULATION BAND AND SEDIMENTATION RATE IN RHEUMATOID (INFECTIOUS) ARTHRITIS.

<i>Coagulation Band.</i>	<i>Per Cent.</i>	<i>Sedimentation.</i>	<i>Per Cent.</i>
Longer	4.1	—	—
Normal	24.5	Normal	10.2
Slightly short	18.4	Slightly increased	8.2
Markedly short	53.0	Markedly increased	81.6

cases to give a marked shift to the left. The coagulation band is therefore inferior as an indicator of rheumatoid arthritis to the sedimentation rate. On the other hand, we found in 4.1 per cent. a longer coagulation band than normal. It is possible that fibrotic changes had taken place either due to some phase of rheumatoid arthritis or to intercurrent diseases such as parenchymatous degeneration of liver or fibrotic tuberculosis. In 43 cases the reliability of both tests was gauged by the clinical course during long observation. The sedimentation gave a correct expression in 41 cases or 95 per cent., while the coagulation band did so only in 34 cases or 79 per cent.

While the sedimentation test is superior as a general indicator of the severity, course and therapeutic effect, yet in some cases the coagulation reaction may uncover important complications, and reflect more accurately the progress of the arthritis. The following case histories are given as illustrations.

CASE 1.—S. B., white, female, aged fifty-two. Suffered from pain, swelling, stiffness and limitation of motion in numerous joints. When first seen, the left knee especially was involved and effusion and flexion contracture were present. There were periarticular swellings of the first phalangeal joints, and of the wrists and elbow joints. Rheumatoid arthritis was diagnosed. The sedimentation rate was 100 and the coagulation band was long—0.3/1,000 CaCl_2 —indicating a fibrotic process. A check-up of the history revealed recurrent pleurisy fifteen and twenty years previously, and the examination showed old fibrotic tuberculosis with pleural adhesions. The influence of the fibrotic changes on the electrolytic threshold is evidently greater than of the exudative changes of rheumatoid arthritis.

CASE 2.—H. B., white, male, aged forty-five. Suffered four years from pain and swelling of ankles, feet, knees, wrists, elbows and spine. Examination showed periarticular swelling of these joints and effusion in the right knee. X rays showed narrowing of the joint spaces and erosions of the articular surfaces of the wrists, elbows and knee joints. A diagnosis of rheumatoid arthritis was made. The sedimentation was 110 mm./hour. The coagulation band, however, was normal—0.4:1,000 CaCl_2 . Further examination showed an old scar over the left ankle from a healed-up sinus during youth (probably tuberculous), scars in the cornea and an old fibrotic tuberculosis of the lungs. He also had a cholecystectomy two years before because of cholecystitis and stones. These fibrotic and cirrhotic changes explain the normal coagulation band in the face of an active rheumatoid arthritis. This case reacted poorly to treatment, and was still at the same level of activity after four years' observation.

Osteo-Arthritis.—Tables IV and V show a detailed analysis and summary of the results in 88 cases. Contrary to expectation,

TABLE IV.—COAGULATION BAND AND SEDIMENTATION RATE IN EIGHTY-EIGHT CASES OF OSTEO-ARTHRITIS.

<i>Weltmann Reaction</i> (CaCl_2 per ml.).				<i>Tube.</i>	<i>Per Cent.</i>	<i>Sedimentation.</i>	<i>Per Cent.</i>
0.3	VIII	4.5	0-10	69.8
0.4	VII	28.5	11-20	15.2
0.5	VI	27.3	21-30	5.6
0.6	V	30.7	31-40	5.6
0.7	IV	4.5	41-50	—
0.8	III	1.2	51-60	1.9
0.9	II	3.4	61-70	1.9
1.0	I	—	—	—
1.1	—	—	—	—
Total		100.0		100.0

TABLE V.—SUMMARY OF COAGULATION BAND AND SEDIMENTATION RATE IN OSTEO-ARTHRITIS.

<i>Coagulation.</i>	<i>Per Cent.</i>	<i>Sedimentation.</i>	<i>Per Cent.</i>
Longer	4·5	—	—
Normal	55·7	Normal	69·8
Slightly short	30·7	Slightly increased	15·1
Markedly short	9·1	Markedly increased	15·1

long coagulation bands were found only in 4·5 per cent., a fraction of one per cent. higher than in rheumatoid arthritis. Normal coagulation bands were found in 55·7 per cent., while the sedimentation rate was normal in almost 70 per cent. The percentage of slightly short coagulation bands was 30·7 and of markedly short bands 9·1 per cent. The sedimentation rate was slightly increased in 15 per cent. and markedly in 15 per cent. A group of 14 cases was followed clinically for a long period to check on the relative correctness of both tests. It was found that sedimentation was correct in 9 cases (92·7 per cent.), while the coagulation band was correct in 5 cases (63·5 per cent.). Therefore, also in osteo-arthritis the sedimentation rate is more significant than the coagulation band. Only in a small percentage is the degenerative character of osteo-arthritis reflected by the shift of the coagulation band into the fibrotic zone. As in rheumatoid arthritis, the test is useful in discovering intercurrent complications as illustrated by the following case history:

CASE 3.—C. C., white, female, aged fifty-six. For two years she had pain and swelling of the phalangeal joints and a trigger finger of the fourth right finger following a sprain. The examination revealed changes in the fingers characteristic of Heberden's nodes. There was also peri-articular swelling of the first phalangeal joint of the left fourth finger. The clinical diagnosis was a mixed type of arthritis. Sedimentation rate was 15 mm. and the coagulation band was considerably shortened (0·7/1,000 CaCl₂). After a period of observation of four months and following an attack of influenza, fever, cough, night sweats, and loss of weight appeared. A check-up showed an exudative tuberculosis with infiltration of both apices. Intradermal tuberculin test was positive in a dilution of 1 : 1,000,000. On check-up sedimentation rate was 35 mm. In this case the coagulation band indicated the presence of an exudative condition sooner and more definitely than the sedimentation rate.

MISCELLANEOUS CASES

1. *Gout.*—Of 9 cases, examined during attacks, the sedimentation rate was slightly increased in 3 and markedly increased in 6. The coagulation band was longer in 1, normal in 5 cases, slightly

shorter in 2 and markedly shorter in 1. Gout, although regarded generally as a metabolic disease, shows usually during acute attacks an increase in sedimentation rate. This is perhaps explained by marked inflammatory changes in the joints characteristic of the acute phase. The coagulation band was shorter only in one-third of the cases. It returned to normal when the sedimentation was still elevated. In gout degenerative changes of liver, kidney, myocardium and blood vessels are frequent. This may counteract the tendency toward shortening of the coagulation reaction by inflammatory joint changes. While in rheumatoid arthritis the coagulation reaction was markedly shorter in 53 per cent., in gout it was so only in 11.1 per cent. Therefore, in atypical cases, which resemble rheumatoid arthritis and have a normal or long coagulation band in the presence of a high sedimentation rate, the possibility of gout should be investigated.

2. *Gonorrhœal Arthritis*.—Out of 9 cases, 3 gave a normal sedimentation, 2 gave a slightly increased and 3 a markedly increased sedimentation. Two gave a normal Weltmann reaction, 2 a slightly shorter and 3 cases a markedly shortened Weltmann band (0.7 to 1.0/1,000 CaCl_2). Two cases gave a longer coagulation band (0.3 and 0.4/1,000 CaCl_2). Both the sedimentation test and the Weltmann reaction showed characteristic changes in the acute exudative stage and tendency to become normal when the response to treatment was favourable. The transition from a shorter to a longer band after the subsidence of the symptoms led to the discovery of an incipient liver cirrhosis in the following case:

CASE 4.—J. G., white, male, aged forty-seven. The patient contracted gonorrhœa three months before examination, followed by pains and swelling of knees and hands. Examination revealed periarticular swelling and tenosynovitis of the metacarpo-phalangeal joint of the right index finger, swelling and effusion of the right knee joint and tenderness over both hips. Sedimentation was 50 mm. and the coagulation reaction was 0.6/1,000 CaCl_2 . The gonococcus complement-fixation test was strongly positive. Under fever therapy there was a gradual recession of symptoms, the sedimentation dropped to 32, and the coagulation reaction became normal (0.5/1,000 CaCl_2). One month later, the symptoms having subsided almost completely, sedimentation was normal (10 mm.) and coagulation band short (0.2/1,000 CaCl_2). Examination revealed cirrhosis of the liver, chronic myocarditis and arterio-sclerosis.

3. *Tuberculous Arthritis*.—Of 4 cases sedimentation was normal in 1 case, slightly increased in 1, markedly increased in

2 (up to 105 mm.). The Weltmann band was normal in 2, markedly short in 1 and long in 1.

4. *Traumatic Arthritis*.—Of 7 cases sedimentation was normal in 5 cases, slightly increased in 1, markedly increased in 1. Coagulation bands were normal in 5 cases, slightly short in 2 cases in which signs of secondary inflammation were present clinically.

5. *Sacro-Iliac Arthritis*.—Of 11 cases, not definitely classified, the sedimentation was normal in 4, slightly increased in 4, and markedly increased in 3 cases. The coagulation band was normal in 7 cases and slightly short in 4. In this group the sedimentation rate indicated more frequently inflammatory changes than the coagulation reaction.

6. *Myositis*.—Of 8 cases sedimentation was normal in 5, markedly increased in 2 cases, slightly increased in 1 case. Coagulation bands were normal in 5 cases, slightly short in 1 and long in 2 cases.

7. *Neuritis*.—Of 3 cases sedimentation rate was normal in 2 and slightly increased in 1. The coagulation band was normal in all 3 cases.

8. *Tenosynovitis*.—Of 6 cases sedimentation was normal in 3 cases, slightly increased in 2 and markedly increased in 1. Coagulation was normal in 3 cases, short in 2 and long in 1.

9. *Arthralgia*.—In 2 cases of subjective pain in the joints with no objective symptoms sedimentation rates and coagulation bands were normal. Such cases present a difficult problem because of the possibility of an incipient rheumatoid arthritis which did not as yet advance to objective symptoms. Corroborative laboratory evidence is therefore important.

10. *Ankylosing Spondylitis (Strumpell-Marie Type)*.—Of 3 cases 1 showed high sedimentation rate of 110 mm. and a short coagulation band (0.8/1,000 CaCl₂). One case which still showed some activity had a sedimentation of 4 mm., but a short coagulation band (0.7/1,000 CaCl₂). In the third case, which had been quiescent for a long period, sedimentation was 40 mm. and coagulation was normal.

11. *Recurrent Rheumatic Fever*.—In 2 cases of recurrent attacks of rheumatic fever and arthritis in adults the first case showed sedimentation of 38 and short coagulation band (0.7/1,000 CaCl₂); the other case came under observation at the beginning of a recurrence and is reported below:

CASE 5.—The patient was white, male, aged thirty-six. He had pain in joints in childhood for only one day. At the age of seventeen numerous joints were involved, but chiefly ankles, the right knee and the fingers. This attack lasted six to seven months. At twenty-eight years of age he had acute swelling of the left knee joint and was in bed for one month. At the time of examination he had indefinite pain in the knees and the toes, but no objective swelling or limitation of motion. The heart showed a compensated mitral stenosis and insufficiency. Sedimentation was 5 mm., but coagulation was short (0.6/1,000 CaCl₂). Within the next three weeks effusions developed in both knees, left ankle and wrists, and tenderness in the spine. Sedimentation increased to 30 mm. In this case the coagulation indicated a recurrence of rheumatic fever before the clinical symptoms and while the sedimentation rate was still normal.

SUMMARY AND CONCLUSIONS

The analysis of 250 cases leads to the conclusion that the Weltmann coagulation reaction in arthritis does not possess the general utility of the sedimentation test. In rheumatoid arthritis the coagulation reaction was in the exudative range in 71 per cent., but in only 53 per cent. the coagulation band was markedly shorter. In osteo-arthritis only 5 per cent. of the cases fall in the fibrotic range. Neither exudation nor fibrosis is pronounced enough in these groups of arthritis to give a clear-cut line of cleavage. Also as a check on the clinical course and effect of treatment the sedimentation test is superior to the coagulation reaction. On the other hand, in both groups there were cases where the coagulation band was more accurate or led to the discovery of concurrent exudative or fibrotic processes not revealed by the sedimentation test. In the group of miscellaneous types of arthritis these general conclusions are borne out. A high sedimentation rate and normal or longer coagulation band may be valuable for detection of atypical gout. This observation, however, requires confirmation in a larger material.

The coagulation band in arthritis cannot and should not substitute the sedimentation test as a diagnostic or prognostic procedure. It may, however, be carried out together with the sedimentation test and the filament-non-filament count as the third important non-specific test. Each of these tests reflects a different segment of systemic or local manifestations of disease which supplement each other. The combination of the three tests permits a more balanced estimation of the underlying pathological physiology. The described modification renders the technique of the coagulation reaction just as simple as of the other two tests.