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Original Article

Orthopaedic Section

# "Leukergy": The Simple Albeit Forgotten Test for Bone Infections

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## ABSTRACT

**Background:** Acute infections of the bone and joints with overt signs of inflammation, sinus formation and systemic illness are relatively easy to diagnose, but the low grade infections are the more difficult ones.In the presence of normal clinical parameters like ESR, total WBC count, C-reactive protein and blood culture but with a clinical possibility of an infection, a positive leukergy plays an important role in the diagnosis and the management of bone and joint and soft tissue infections.

**Aim of the Study:** To know the validity of leukergy in diagnosing of bone and joint infections, to compare and correlate leukergy with other clinical parameters, and also, to use leukergy for the premature diagnosis of low grade infections without any obvious clinical signs.

**Materials and Methods:** Sixty patients with bone or joint infections underwent evaluation for the Total White Blood Cell Count (TWBCC), ESR, C-reactive protein (CRP), blood culture, X-rays of the affected parts, wound culture and for the leukargy agglomerate test of the peripheral blood. The percentage of the aggregated leukocytes on the slide was determined and clinical and laboratory grading was done.

**Results:** The leukergy test was found to be positive in all the 60 patients who were studied, thus reflecting one hundred percent positivity, with ESR being the second (68%) other than clinical parameter which was studied.

**Conclusion:** We conclude that leukergy is more specific in detecting infections as compared to other laboratory tests like ESR, total white cell count, blood culture or the C-reactive protein.


**Key Words:** Bone infection, Leukergy, Agglomerate test

## INTRODUCTION

Bone joint, and soft tissue infections are the commonest problems which are encountered in our day to day orthopaedic practice. A prompt diagnosis of the bone and joint infections is important, in order for the appropriate treatment to be started as soon as possible, so that the most severe complications like osteomyelitis and septic arthritis can be prevented. The acute infections with overt signs of inflammation, sinus formation and systemic illness are relatively easy to diagnose, but the low grade infections are the more difficult ones. In the presence of normal clinical parameters like the Erythrocyte Sedimentation Rate (ESR), Total White Blood Cell Count (TWBCC), C-reactive protein (CRP) and blood culture but with a clinical possibility of an infection, a positive leukergy plays an important role in the diagnosis and the management of bone and joint and soft tissue infections. The persistent elevation of the ESR suggests an infection, but it is neither very sensitive nor specific [1,2]. The results are better if the ESR is considered in conjunction with the measurement of the C-reactive protein level, but even then it is generally unreliable. A low level of lactic acid in the fluid which is aspirated from a joint reliably rules out an infection, but an elevated level is not diagnostic [3]. The radiographs may be difficult to interpret. Especially in the presence of an implant, isotope scanning is sensitive but not specific, and labeled white cell scanning gives a high incidence of false-positive results. Leukergy is one of the relatively newer techniques which are available for an easy and a prompt diagnosis of bone and joint infections and it is also cost effective. We undertook this study as an attempt to correlate the various clinical parameters with the phenomenon of leukergy in the diagnosis of bone and joint infections.

## AIM AND HYPOTHESIS OF THE STUDY

We hypothesized that leukergy was a sensitive and an as reliable marker which was best correlated with other laboratory investigations and a cost effective and a rapid diagnostic tool in bone and joint infections. Also, leukergy can be used for an early diagnosis of low grade infections without any obvious clinical signs. Thus, our aim was to know the validity of leukergy in diagnosing of bone and joint infections, to compare and to correlate leukergy with other clinical parameters, and also, to use leukergy for an early diagnosis of low grade infections without any obvious clinical signs. The validity and the cost effectiveness of the same were also evaluated along with other variables.

## MATERIALS AND METHODS

60 patients with bone and joint infections, who attended our hospital for the past 2 years as in-patients and outpatients, who were diagnosed to have bone and joint infections, were included in our prospective study. The patients with clinical criteria which were suggestive of bone and joint infections, those with asymptomatic bone and joint infections and symptomatic patients with normal clinical parameters were included in our study. After taking a detailed history and after an examination, hematological investigations which included TWBCC, ESR, CRP and blood culture were done. The X-rays of the affected parts and the wound culture too were obtained in all the patients and special investigations were carried out whenever they were necessary.

In our study, the phenomenon of leukergy was based on the white cells which agglomerated in the peripheral blood of the patients with inflammatory diseases, and this detection was used for the

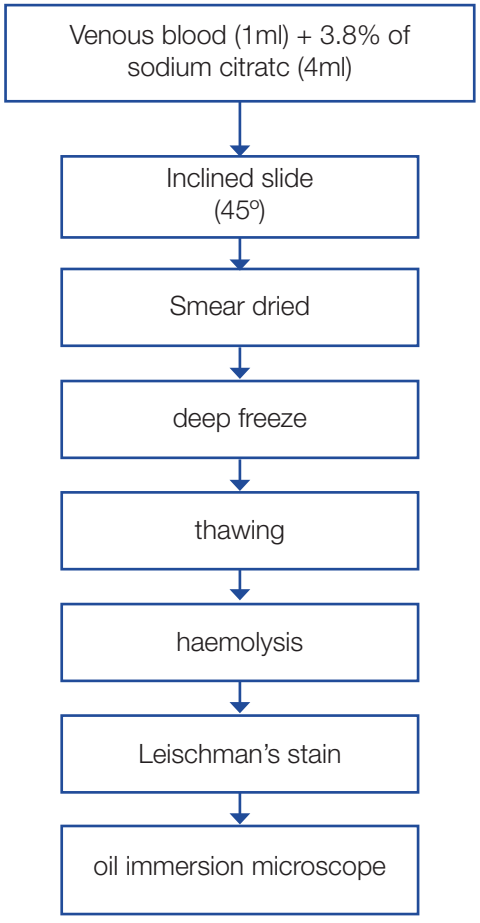
diagnosis of the bone and joint infections. If the phenomenon of leukergy was observed, then it was considered as a positive test. The procedure of the leukergy test has been shown in the [Table/Fig-1]. The calculation of leukergy was based on the formula, which is as follows: Leukergy % = [(number of cells in clumps)/300]*100. Thus, the percentage of the aggregated leukocytes on the slide was determined by counting 300 cells and this was calculated according to the above formula. The cells were considered as aggregated when 3 or more were at a distance of less than 1 cell diameter. A clinical and a laboratory grading were done, which are shown in [Table/Fig-2(A) & (B)].

## RESULTS

The demographic data has been shown in [Table/Fig-3]. The patients, who were included, were in the age range from 1 to 80 years. The type of presentation with respect to the surgery and the type of infection has been highlighted in [Table/Fig-3]. A non-surgical cause of the infection (78.3%) was the most common type of presentation, with osteomyelitis being the most common infection (20%), [Table/Fig-3].

Different parameters like ESR, total WBC count, CRP, blood culture and the organisms which were isolated were categorized accordingly and the details have been shown in [Table/Fig-4]. A majority (68.3%) had ESR of more than 30, though the alterations in the TWBCC were equally distributed from the normal upper limit range. CRP was positive in a significant majority of the patients, which was in contrast to what was seen in the blood culture. 48% patients had Staphylococcus aureus in the wounds, as was evidenced from the culture. However, with no growth was observed in 43% of the patients [Table/Fig-4].

The clinical and the leukergy grading are shown in [Table/Fig-5]. [Table/Fig-6] presents a correlation between the various tests. The leukergy test was found to be positive in all the 60 patients who were studied, thus reflecting one hundred percent positivity, with ESR being the second (68%) other than clinical parameter which was studied [Table/Fig-6].




**[Table/Fig-1]:** Steps for procedure for the leukargy test. Step 4 and 5 are repeated 4 to 5 times while performing the test.

| Grading | Observation |
|---|---|
| **A. Laboratory grading:** | **Laeukocyte aggregation** |
| Grade 0 | <10% |
| Grade 1 | 11% - 19% |
| Grade 2 | 20-34% |
| Grade 3 | More than 35% |
| **B. Clinical Grading:** | **Clinical signs** |
| Grade 0 : | No local or systemic signs of disease. |
| Grade 1 : | Mild local pain without pus formation and no systemic signs. |
| Grade 2: | Moderate local pain without pus formation and no systemic signs. |
| Grade 3 : | Severe local pain, pus. fever and other systemic signs of sepsis. |

**[Table/Fig-2]:** Grading of infection

| Age (years)* | n | % |
|---|---|---|
| 1 to 10 | 11 | 18.4 |
| 11 to 20 | 11 | 18.3 |
| 21-30 | 7 | 11.7 |
| 31-40 | 8 | 13.3 |
| 41-50 | 8 | 13.3 |
| 51-60 | 10 | 16.7 |
| 61-70 | 4 | 6.7 |
| 71-80 | 1 | 1.7 |
| **Sex [m]:[f]:** | **[41]:[19]** | **[68]:[32]** |
| **Timing of presentation:** | **n** | **%** |
| Non surgical infection: | 47 | 78.3 |
| Post surgical infection: | 13 | 21.7 |
| Type of Infection: | n | % |
| Osteomyelitis | 12 | 20 |
| Septic arthritis | 9 | 15 |
| Implant failure | 3 | 5 |
| Discitis | 3 | 5 |
| Tuberculosis | 3 | 5 |
| Rheumatoid arthritis | 1 | 1.6 |
| Rheumatic fever | 2 | 3.4 |
| Synovitis | 5 | 8.4 |
| Bursitis | 2 | 3.4 |
| Foreign body | 1 | 1.6 |
| Tumours | 3 | 5 |
| Others(ulcers/cellulitis/abscess/ hematoma) | 16 | 26.6 |

**[Table/Fig-3]:** Demographic data
*Chi-square test, P = .119.

| ESR (mm/1st hr) | n | % |
|---|---|---|
| 3 to 30 | 19 | 31.7 |
| >30 | 41 | 68.3 |
| **WBC count (cu.mm)** | **n** | **%** |
| < 10,000 | 28 | 46.7 |
| > 10,000 | 32 | 53.3 |
| **C-Reactive Protien** | **n** | **%** |
| Positive | 14 | 63.6 |
| Negative | 8 | 36.4 |
| **Blood Culture** | **n** | **%** |
| Positive | 2 | 3.3 |
| Negative | 28 | 96.7 |
| **Type of organism:** | **n** | **%** |
| Staph. Aureus | 29 | 48.3 |
| Strept. Pyogens | 5 | 8.3 |
| Sterile | 26 | 43.4 |

**[Table/Fig-4]:** Parameters studied

| | clinical | | leukergic | |
|---|---|---|---|---|
| Grading of infection | n | % | n | % |
| grade 0 | 4 | 6.7 | 0 | 0 |
| grade 1 | 11 | 18.3 | 7 | 11.7 |
| grade 2 | 24 | 40 | 37 | 61.7 |
| grade 3 | 21 | 35 | 16 | 26.6 |

**[Table/Fig-5]:** Clinical and leukergy gradings

| Test | Total number of cases/ tests conducted | number of positive cases | % | Cost per test (Rs.) |
|---|---|---|---|---|
| ESR | 60 | 11 | 68.3 | 50 |
| WBC | 60 | 32 | 53.3 | 40 |
| Blood Culture | 30 | 2 | 6.7 | 200 |
| CRP | 22 | 14 | 63.6 | 200 |
| Clinical Grading | 60 | 56 | 93.3 | Nil |
| Leukergy | 60 | 60 | 100 | 50 |

**[Table/Fig-6]:** Comparision and correlation of various tests

## DISCUSSION

Fleck [4] described "Leukergy" as a phenomenon which was found in citrated blood, which manifested itself as an agglomeration of the clumping of leukocytes. They explained that in this phenomenon, the clumps could contain up to 20 to more cells with a marked tendency of cellular homogenecity. They also suggested that this phenomenon could appear in infectious diseases in man and animals, and that it could be experimentally elicited by an intravenous injection of live or killed gram negative bacteria [e.g. Bacterium Coli, Salmonella Typhi, Bacterium Proteus] or by an intra-pleural injection of turpentine [4]. The high occurrence of leukergy in infectious diseases and the regular appearance of leukergy in the experiments seem to allow us to look on it as a phenomenon with a distinct role in the pathogenesis of the disease [4].

In 1983, Karivand Medalia et al., applied this phenomenon to diagnose real bacterial infections in mice [5]. The procedure was based on the observation that bacterial infections were associated with the clumping of leukocytes. Their study demonstrated that the infection of mice with either *E. coli* or *P. mirabilis* which were limited strictly to the urinary tract, resulted in elevated leukergy values. The difference between these two bacteria in increasing the leukergy values may be due to the greater severity of the *P. mirabilis* infection. *E.coli* mainly affects the bladder (cystitis) whereas in the *P. mirabilis* infection, the bacteriuria indicates a kidney involvement [6].

Though a number of previous investigators had demonstrated the effectiveness of this tool in different scenarios, it was Fleck et al.,[7] who simplified it further and conducted investigations both in adults and in laboratory animals [8], which indicated that the leukergy test had the potential of a diagnostic tool. The methodology which was followed in our study for calculating the percentage of leukergy was very similar to that which was used their studies.

Otremski et al., [9] claimed the diagnostic importance of the leukergy test in bone and joint infections when they observed more than 98% positivity in their group of patients. It was more accurate than ESR, TWBCC, or a blood culture. Also, the effectiveness of the treatment was correlated with the leukergic test values.

Our study has shown that the quantitative assessment of leukergy in the peripheral venous blood was a useful test for the diagnosis of bone sepsis and for monitoring the infective process during the therapy. Our study also demonstrated that leukergy was found to be more sensitive than the TWBCC or ESR. In the 60 patients who were studied, leukergy was found to be positive in all the cases with infections, whereas the white cell count was found to be positive in only 32 patients and the ESR was identified only in 41 patients. A study with 100% effectiveness requires no statistical analysis to prove the same. Occasionally, leukergy was found to forewarn us of an impending deterioration before the appearance of the clinical signs and to indicate the necessity for a continued antibiotic treatment. It proved to be a reliable indicator of the disease activity even when the other laboratory tests were normal.

Previous attempts [9] which were made to develop a serological technique for the reliable diagnosis of bone infections resulted in complicated tests which required special equipment. At the same time, these proved to be expensive and unreliable. The measurement of leukergy has been shown to be a simple, rapid and an inexpensive technique which required no special equipment.

In our study, we did not explore the mechanism of leukergy but only documented its relationship to bone sepsis. This phenomenon probably results from a cellular rather than a humeral activity. During bacteraemia, the circulating mediators are released, which lead to an increased sensitivity of the neutophil adhesive receptors, as was claimed previously.

One needs to consider the important relevant application of this test in other conditions too. More recently, the widespread use of a simple urine-drop test for the antigen detection, which was feasible even in a peripheral community environment, which was developed by Fleck, was considered to be related to the above test [9]. The differentiation of the bacterial from the viral infections by using a simple single test slide: the role of the leukergy test could not be neglected [10]. The transient myocardial ischaemia which was seen during the exercise testing was related to the leukergy test, as was reported by Kowalki et al., recently [11]. The evaluation of the leukergy test as an indicator of infections in the hip joints in children was considered to be relevant in 2000 by Sharma

et al. [12]. The microvascular response in patients with cardiogenic shock was also linked to the leukergy phenominon in 2000 by Kirschenbaum et al,. [13]

The leukergy test may be valuable in distinguishing the septic from the mechanical loosening of prostheses, as was claimed previously [14]. A more precise bone scan may be performed alternate to the above detailed test; however, the facilities and the cost may limit the investigation.Though its sensitivity is far higher than that of the leukergy test in bone infections, not at all the time is it specific eg. in malignancy. It should be noted, however, that the leukergy result must be interpreted with caution, since its level may be raised in some non infectious conditions such as polycythaemia rubra vara, Ischemic heart disease and in some rheumatic diseases. The leukergy test is simple and rapid and it can be done in any laboratory facility after a brief training. The time which is taken for testing the leukergy is few minutes, whereas the other tests take few hours to days.

## CONCLUSION

Leukergy was positive in all the patients and it was detected the presence of an infection in all the cases. Leukergy was proved to be more specific than other laboratory tests. But the role of the leukergy test has been found to be extensive and infinite [15, 16]. The leukergy test is simple, short and inexpensive and it helps in the early diagnosis of an impending infection. It can serve as a routine test in any clinical setting for detecting the presence of an infection. We conclude that leukergy was more specific in detecting an infection when it was compared to other laboratory tests like ESR, total white cell count, blood culture or the C-reactive protein.

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