

THE IMPORTANCE OF THE SAMPLING AND ERROR SOURCES OF THE RED CELL SEDIMENTATION RATE FOR DENTAL MEDICINE

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Abstract

Background and objectives: Erythrocyte sedimentation rate test guides dentists in the suspicion of inflammatory reactions or infections of the dental focus. In 1981, Kondi mentioned that any delay after blood sampling for the purpose of determining the ESR can lead to a false shortening of the result. The literature indicates that failure to determine within 1 hour and remixing of blood are not recommended. The objectives of our study were to verify the stability of the determinations within 4 hours after storage at room temperature and after 12 hours of refrigeration, involving also the remixing manoeuvre. **Materials and Methods:** The study was performed in the “St. Spiridon” Hospital of Iași, Romania, on 75 samples, taking also into account the rejected samples presenting source of error. **Results:** The study showed that 4 (5.33%) samples had an inadequate volume, 3 (4%) showed erythrocyte and fibrin in suspension, preventing the interpretation of the result, whereas the clot was identified in 4 (5.33%) samples. Following 4 hours after the first determination, respectively after 12 hours of refrigeration, rebalancing at room temperature and remixing, for out of the 64 (85.33%) determinations the results were comparable showing a close correlation ($r = 0.988 / 0.993 / 0.990$, $p < 0.001$) with the first determination. **Conclusions:** The study showed that performing the test 4 hours after sampling, refrigerating and remixing the sample does not influence the stability of the determination, so that, also in the case of dental patients, the moment of sampling and the time elapsed until the determination of the test, do not influence the therapeutic conduct. **Keywords:** stability, refrigeration, remixing.

1. Introduction

In dental medicine, the diagnosis is complex and is accompanied by laboratory tests that contribute to the establishment of the therapeutic conduct. The oral cavity is a gateway for agents that can cause systemic infections (1). This area of the stomatognathic system with complex roles and connections with the neighborhood and ensures a good development of digestive

function, speech and secondary respiration (2). Oral pathology represents a major public health problem, with a worldwide increase in incidence and morbidity (3).

A correct diagnosis, elimination of the causes and reduction of modifiable risk factors are paramount for successful prevention and treatment of oral diseases (4). The most important part of managing the dental patients is to offer them the

opportunity to regain lost functions: masticatory, physiognomy and fonation (5, 6). Nowadays, the best approach to avoid complications is to apply preventive strategies (7). Despite the advanced technology in modern dentistry, anxiety related to dental treatment and the fear of pain associated with it remain prevalent (8). Certainly the practical future will involve inter and multidisciplinary collaboration (9).

Biernacki described for the first time, in 1897, the ESR test, and Fahraeus and Westergren were criticized for the implications and introduction of this determination (10-13). According to recent studies, the ESR test determination is considered one of the most requested laboratory parameters, being recommended by doctors (11,14). The use of the test in different clinics has not been limited, although the erythrocyte sedimentation depends on plasma pH, the lipid and haemoglobin concentration, as well as the ratio of plasma proteins, which are considered as pathological and physiological factors (11,15).

Tudoranu and colleagues, in the national literature (1959), and later Kondi, in 1981, described the principles, material and method, reagents, blood sampling technique, as well as the Westergreen device used to determine this test (16,17). Based on the same principle of operation of the Westergreen stands, in some laboratories the ESR test determination is made on adapted stands but this time the blood is taken in vacuum tubes keeping the same ratio between the anticoagulant used (Na citrate) and the recommended amount of blood: 0,4mL/1,6mL (13,16,17). The reading of the result is made visually from the scale with millimetre divisions with which the stand is provided. The result represents the value that corresponds to the level of the supernatant formed after the erythrocyte sedimentation. The device

modernization also considered the reading evolution technique of this test, having the benefit of a faster determination for a larger number of samples, thus reducing the results reporting in a shorter time.

In the era of errors that have as a starting point the pre-analytical phase, starting with the sampling of the biological product, in the case of the ESR test determination we can also talk about errors that could negatively interfere with the determination. The errors of the test determination in the 60's was the following: incorrect blood aspiration, inadequate sampling glass maintenance or the sampling time for the determination of the ESR test in women (17).

Kondi mentioned that the test should be performed immediately after the sampling because the false decrease of the ESR could be caused by any delay, while the ratio between the collected blood and the anticoagulant used should be respected (16).

Unfortunately, automatic devices for ESR test cannot identify all error sources related to the quality of the sample taken that could interfere with the determination, this aspect being also dependent on the visual appreciation of the nurse who prepares the sample for the determination.

Objectives

For this research a quantitative, experimental study was used. We considered that this methodology will provide the most appropriate guidance in establishing the methods of data collection, as well as the techniques and principles applicable when analysing the obtained results.

The purpose of this study was to verify the stability of the ESR test, starting with the first determination immediately after the sample was taken and comparing it with the repetition of the determination from the same sample, which was stored at room temperature for a period of 4 hours, then refrigerated for 12 hours and thermally

re-balanced for 1 hour This study has also as its objective the interpretation of the signals while reading the results.

2. Materials and Methods

The study was carried out in the Hematology Laboratory of "St. Spiridon" Hospital of Iasi, Romania, on a total of 75 samples. The samples were taken in the clinical sections of the hospital, respecting the sample and the recommended volume for the test determination, which corresponds to 0.4 ml of Na citrate and 1.6 ml of blood. Before each determination, the specimens were remixed 3-4 times by inversion in order to avoid false red blood cell sedimentation. The test determination was performed on the SRS 100 / II analyser of our laboratory. We took also into account the samples that presented error sources for determining the test; these were rejected by a textual explanation of the non-compliance which justified then the need for a new sampling.

For the correct interpretation of the "LEV" signals released by the analyser during the reading of the results, we proceeded with the reverification of the post-analytical sample, in order to identify the fibrin in the supernatant, which is visible only after the sedimentation of the cellular elements, as well as the suspended erythrocytes which interfere with the interpretation of the plasma column by the analyser.

Patients' informed consent was not required because the study was performed on the samples of patients who were already subjected to ESR tests and the repetition of the determinations was dictated through the identified nonconformities.

Inclusion criteria

In order to carry out this research we included all samples taken during a day's work from the clinical sections of „St. Spiridon" Hospital.

Rejection criteria

No determinations were made from the samples that presented a clot in the erythrocyte sediment or were completely coagulated. These were identified before the introduction of the samples into the analyser.

The informed consent was not necessary because the repetition of the determinations did not require a new sample to be taken, the repeatability of the determinations being made after the release of the results on the clinical sections, respecting thus the working conditions pre-established by us for the purpose of the research.

3. Results

The study showed that 4 (5.33%) samples had an inadequate volume, 3 (4%) had showed erythrocyte and fibrin in suspension, preventing the interpretation of the result, whereas the clot was identified in 4 (5.33%) samples.

Within 4 hours after the first determination, respectively after 12 hours of refrigeration, rebalancing at room temperature and remixing, in the case of 64 (85.33%) determinations the results were identical ($\pm 1-2\text{mm}$) with the first determination, both in the case of the results within the normal range, as well as the pathological reference range.

The results were processed in SPSS Statistics 17.0. It can be seen from the first table (Table 1) that the average of the 3 determinations is very close:

- at the first determination: 7.59;
- at the second determination: 8.06;
- at the third determination: 6.59.

Table 1. Paired Samples Statistics

		Mean	N	Std. Deviation	Std. Error Mean
Pair 1	Det_1	7.59	64	9.670	1.209
	Det_2	8.06	64	11.739	1.467
Pair 2	Det_2	8.06	64	11.739	1.467
	Det_3	6.59	64	8.548	1.069
Pair 3	Det_1	7.59	64	9.670	1.209
	Det_3	6.59	64	8.548	1.069

In the case of the 3 determinations, the standard deviation from the mean has a higher value, due to the presence of the pathological cases in the study, which have a value > 20 (**Error! Reference source not found.**).

Table 1. Paired Samples Correlations

	N	Correlation	p
Pair 1 Det_1 & Det_2	64	0.988	0.000
Pair 2 Det_2 & Det_3	64	0.993	0.000
Pair 3 Det_1 & Det_3	64	0.990	0.000

It can be seen from (Table 1) that all pairs of determinations are strongly and positively correlated ($r = 0.988 / 0.993 / 0.990$, $p < 0.001$). Therefore, it can be confirmed that the same sample was used for all determinations, as graphically shown in **Error! Reference source not found.**.

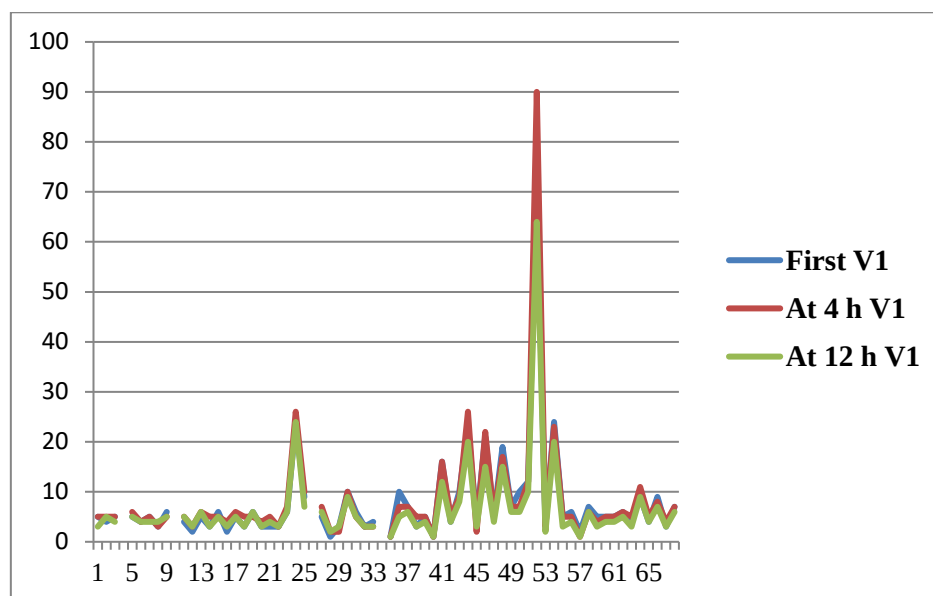


Figure 1. Graphical representation of the ESR test results, in the three moments of the determination

4. Discussion

Generally, the blood or the resulting compounds must be preserved, transported and stored under conditions that meet quality criteria and follow the standardized procedures (18).

The errors that appear with the sampling of the biological product, the analytical and post-analytical phase corresponding to the release of the results have registered a significant improvement as a consequence of the automation, standardization and technological progress registered so far (19,20). The patient is involved in the total testing process, starting with the medical decision regarding the recommended determinations and until receiving the results (20,21).

The "key role" of the laboratory is represented by the "conventional" pre-analytical step which involves all the sample preparation processes for the introduction into the automatic analyzers and the actual analysis (20, 22, 23).

Hashemi et al. noted in their study that in order to indicate the dynamics and gravity of a disease the determination of the ESR test it is still often used, this test being considered, for example, as an important

part in the rheumatic diseases' diagnosis, as well as in the giant cell arteritis diagnosis (11,24). The role of the test in establishing the clinical decisions of the non-emergency conditions has been restored in haematology, rheumatology and orthopaedics specialties (11, 25-31).

As in the case of any other test laboratory, the quality of the sample taken for determining the ESR test, as well as the interpretation of the signals released instead of the results are equally important for clinicians in order to complete the patient's clinical picture which is established in the context of the clinical findings and is correlated with all recommended biological analyses. This test should be of equal importance, as a false increase or decrease in ESR determination may lead to repeated examinations or even more expensive procedures like any other determination recommended by clinicians (20,32). In the national literature the following are mentioned as causes of rejecting the sample taken for the determination of this test: haemolysis plasma, insufficient volume taken, as well as the whole coagulated sample, as described in

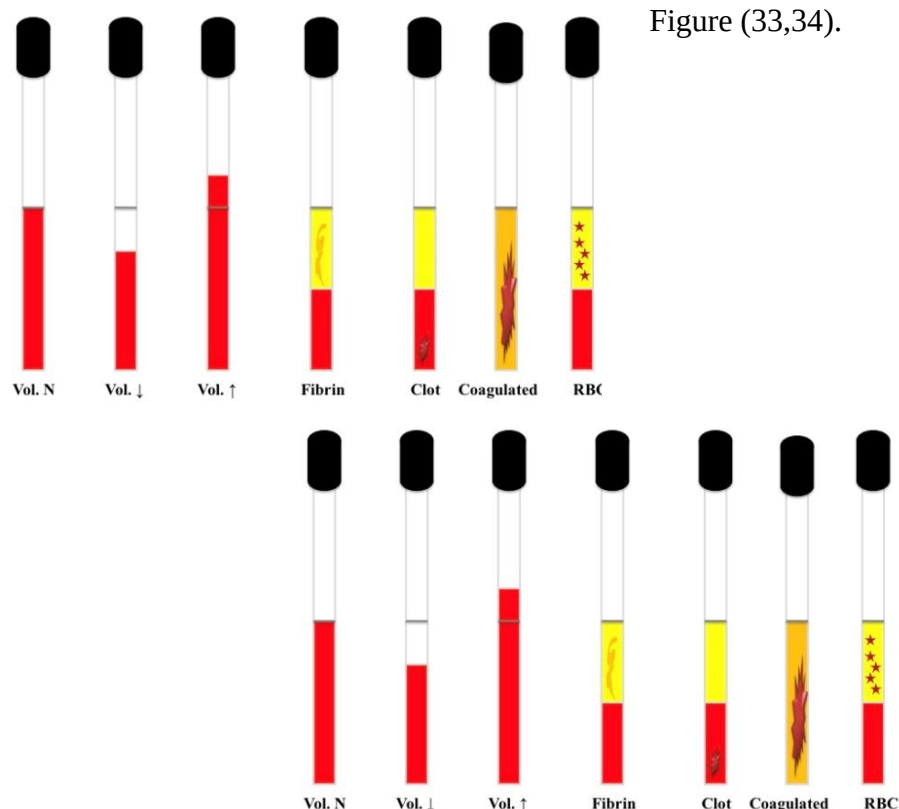
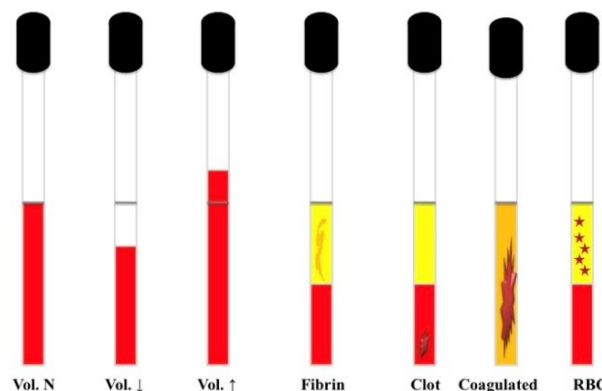


Figure (33,34).

Figure 2. Representation of the sources of error that interfere with the determination and interpretation of the result, for determining the ESR test (personal collection)

The verification of the samples to exclude the accidental presence of the clot in the erythrocyte sediment is done by a gentle inversion manoeuvre before their



Figure, 3) following the consumption of cellular elements: leukocytes, red blood cells, platelets, as well as coagulation factors involved in clot formation.

If the accidental presence of the clot or the total coagulation of the blood is confirmed, the non-compliance is explained textually and the repetition of the sampling is

introduction into the analyzer's working area. The accidental presence of the clot in the erythrocyte sediment generates false low results (

recommended: "Sample with clot/coagulated. Repeat the sampling." Although the recommended blood volume to be used for the determination is visually assessed by the nurse, by examining the sample as insufficient or more collected, as described in Figure 2, these samples are, however, inserted into the analyser, so that the result released by the analyser of the "LEV" volume (low erythrocyte volume) may be transmitted to the laboratory information system (SIL). Once the result is released, the non-conformity of the volume is textually explained by the analysis manager: „LEV-Sample with insufficient / larger volume. Repeat the sampling. "

Another situation in which the analyser interprets the result as "LEV" is

where the optical reading is blocked by the presence of fibrin in the supernatant (

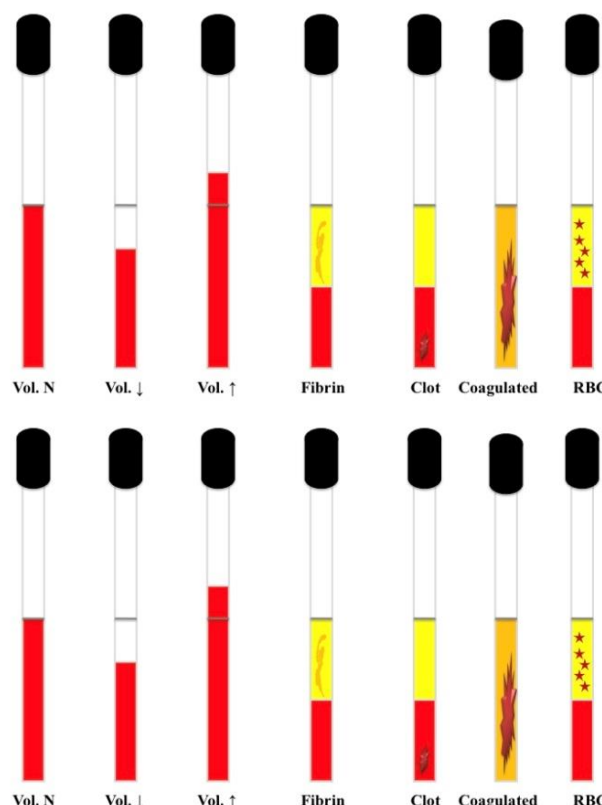
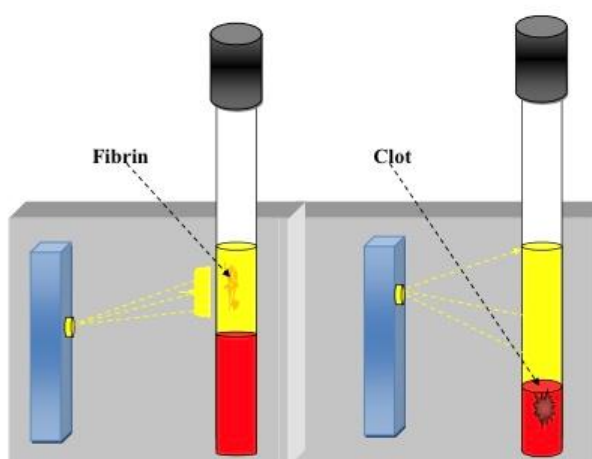


Figure3). Informing the clinician about the non-compliance will be textually explained:



Figure, 3), this being an aspect that could not be identified before the determination from the total blood and without a previous sedimentation of the cellular elements, which would have allowed a visualization of the plasma representing the supernatant. In this context, it is recommended to repeat the sampling as a result of the accidental presence of fibrin in the sample supernatant, which favours the interpretation of the final result (

“The presence of fibrin in the supernatant identified post-analytically after the sedimentation of the cellular elements has optimized the interpretation of the result by the analyser. Repeat the sampling.” There are situations in which the analyser releases the same result as “LEV”, but in this context a re-examination of the sample is recommended, post-analytically, in order to exclude, as the case may be, the accidental presence of red blood cells in the sample suspension, as depicted in

Figure , which also interferes with the determination, by obstructing the passage of the light beam, with a view to measuring the plasma column formed following the sedimentation of the cellular elements: red blood cells, platelets, and leukocytes.

This aspect must be textually explained in order to inform the clinician, by using the following comment: “The analyser cannot interpret the result due to the presence of red blood cells in the supernatant, this being the result of slow sedimentation. The situation experienced in anaemia.”

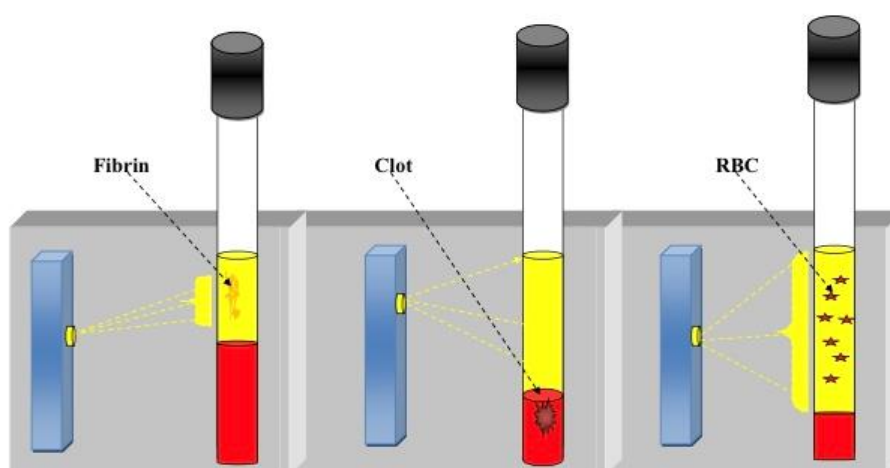


Figure 3. Interpretation of “LEV” signalling in situations where the sample presents quality defects: fibrin in the supernatant, the clot in the sediment and suspension in the hematoma (personal collection)

Studies mentioned that in the iron-deficiency anaemia, due to the microcytosis which slows the erythrocyte sedimentation, the increase of the ESR does not correspond to the number of erythrocytes (34). In 1986, Sox and Liang mentioned that macrocytes sediment faster than normal microcytes and normal cells; this information is recalled in a recent study by Hashemi and co-workers (11,34). In their research, they mentioned that the rejection between erythrocytes is the result of the negative charge on their surface, and the neutralization of this burden is due to the plasma proteins that have a positive charge, thus promoting aggregation (11,33,36). Consequently, increased ESR will be associated with increased plasma proteins, contributing on a scale of 10: 1 for albumin, 2 for alpha- and gamma-globulin, 5 for beta-globulin, and 10 for fibrinogen (11). In 1981, Kondi drew the attention to the fact that in interpreting the results, the plasma factors and the erythrocytes influence the sedimentation rate of the red blood cells (16). In anaemia, erythrocytes play a role in accelerating the sedimentation, and the globulin and fibrinogen favour the formation of red blood cells (16). Low values of ESR are found in allergic states and epidemic

hepatitis; and the increase in value is found in multiple myeloma, hemopathy, nephrosis, acute polyarticular rheumatism, reticulosis, heart attack, septicemia, acute tuberculosis, Hodgkin's disease, as well as in infectious and inflammatory diseases (16).

And at that time, Kondi drew the attention to the sources of error that may interfere with the test's determination, which relate to the following aspects:

- reading immediately after sampling, or at the latest within the first 2-3 hours after sampling, as any delay may falsely lower the ESR;
- polycythaemia that decreases the value of ESR;
- anaemia pathology in which the value is increased, and in this context the test is of minor importance(16). The determination of ESR at room temperature can also cause large errors in patients with cryoglobulinemia because plasma gelling prevents erythrocyte sedimentation, simulating slightly increased or normal velocities (16).

If the recommended temperature at which the test determination is to be performed was kept during this period, the Synevo Guide draws attention to the fact

that the remixing of the taken blood is not recommended for a reuse of the sample in order to determine the ESR, if the reading failed within one hour after sampling, and without explaining the possible interferences with respect to the erythrocyte sedimentation mechanism in this context (34,35).

In order to verify the stability of the determination and based on these considerations, by considering the blood remix, we repeated the determination of the ESR test from the same sample immediately after sampling, the sample being stored at room temperature within 4 hours after the first determination and, implicitly, within 12 hours after refrigeration, thermally rebalancing it before determining, for 1 hour, at room temperature.

As shown in figure 1 and in accordance with the biostatistical data represented in Table 1, 2, it is shown that the test determination at the 3 set times was performed from the same sample, and the results obtained were positively and strongly correlated ($r = 0.988 / 0.993 / 0.990$, $p < 0.001$). We can support that, according to the storage temperatures, the results have an acceptable and significant correlation and were not influenced by the blood remix before each reading.

In dental medicine, it is very important to know the error sources from taking the samples, because the sedimentation speed of the red blood cells also has clinical significance:

- in the case of control of dental outbreak infection,
- of oral lesions of chronic paracoccidioidomycosis,
- evaluation of the relationship between periodontitis and anemia,
- in situations of lack of vertical facial development with functional prognosis caused by the opening of the gonial angle and the overclosing of the mandible (36-39).

5. Conclusions

Based on the information from the literature, we can conclude that there is the possibility to meet situations in which the clinician makes decisions based on the ESR test determination, which is being considered as one of the most fundamental tests performed in the laboratories diagnosis.

Considering that it is an important marker in making clinical decisions for a wide range of pathologies, helping to treat and manage patients, we draw the attention of laboratory specialists and not only to the sources of error related to the quality of the sample taken, and the interferences of fibrin and erythrocytes in the sample supernatant that results in the analyser's interpretation of a false "LEV" result, which could be correlated with the higher or insufficiently taken volume, without performing a macroscopic post-determination reverification.

Laboratory medicine bears the stamp of responsibility, quality and the promotion of results in relation to the real biological state and of the dental patient; being in permanent collaboration with the dentist.

Depending on how we interpret a result in the case of this test, we can draw the attention to the fact that the importance of a result is not the result itself but the serious consequences that the result can have on subsequent investigations, as well as in the treatment and patient monitoring.

Abbreviations

ESR - sedimentation rate of red blood cells

LEV - low erythrocyte volume

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Conflict of interest

The authors declare no conflicts of interest.

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