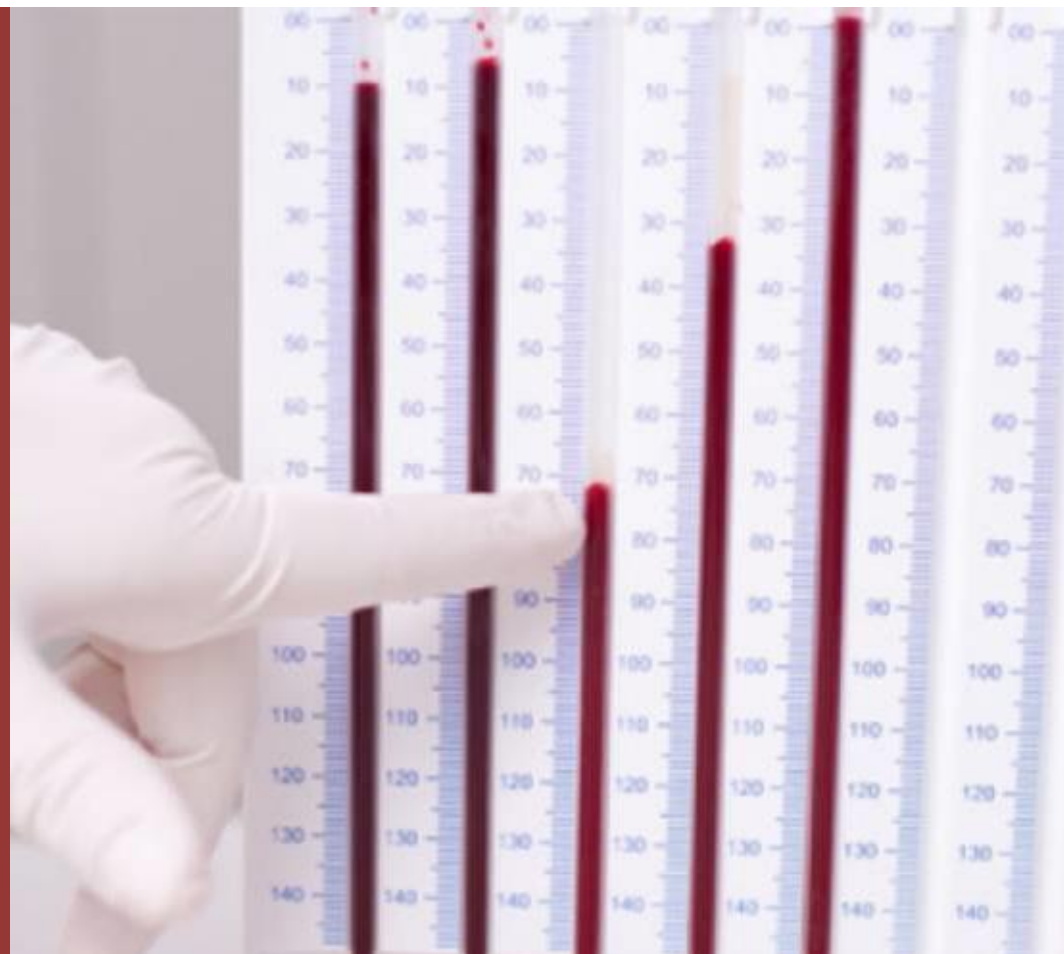Hrvatska komora medicinskih biokemičara

# *Brzina sedimentacije eritrocita*
## *– gdje smo danas?*

**Ivana Lapić**
Klinički zavod za laboratorijsku dijagnostiku, KBC Zagreb

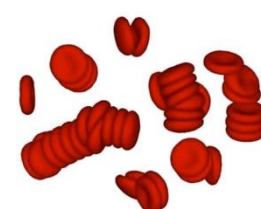| Does your laboratory perform ESR? | a) | Yes | 128/129 (99) |
| | b) | No | 1/129 (1) |
| Which method is used for ESR? (multiple answers possible) | a) | Automated method | 35/128 (27) |
| | b) | Manual method | 85/128 (66) |
| | c) | Both | 8/128 (7) |

Biljak VR, Lapić I, Vidranski V, Herceg I, Tomić F, Šimac B, Horvat M, Čičak H, Vuljanić D, Dorotić A, Nikler A. Policies and practices in the field of laboratory hematology in Croatia - a current overview and call for improvement. Clin Chem Lab Med. 2021;60:271-282.

**Top 25 Tests by Volume at Five Referral Hospitals**

| Rank | AKUH, Nairobi | CA, Bangalore | UCH, Ibadan | UMMC, Kuala Lumpur | Denver Health |
|---|---|---|---|---|---|
| 1 | CBC | CBC[a] | CBC | CBC | CBC |
| 2 | Urinalysis | Glucose | Electrolytes, urea, and creatinine | Renal function | Basic metabolic panel[b] |
| 3 | Urea, electrolytes | Creatinine | Glucose | Liver function | Glucose |
| 4 | Stool microscopy | TSH | Urinalysis | Blood glucose | Urinalysis |
| 5 | Glucose | Thyroid function | Blood group and crossmatch | Magnesium serum | Chlamydia detection |
| 6 | C-reactive protein | Renal function | Liver function | Lipid profile | HbA$_{1C}$ |
| 7 | Malarial parasites | Urinalysis | Lipid profile | PT/INR | Phosphorus |
| 8 | Stool Helicobacter pylori antigen | Potassium | Blood film for malaria parasite | APTT | Magnesium |
| 9 | Liver function | Liver function | Urine microscopy | Urinalysis | PT/INR |
| 10 | Urine microscopy | Platelet count | AFB studies | HbA$_{1C}$ | Comprehensive metabolic panel[c] |
| 11 | Surgicals[d] | Urine culture | PT/INR | Blood group | TSH |
| 12 | Crossmatch | Lipid profile | Other microscopy | Calcium, phosphorus | Liver function |
| 13 | Malaria antigen | PCV | Surgicals | Blood culture[e] | Lipid panel[f] |
| 14 | HbA$_{1C}$ | HbA$_{1C}$ | Hb electrophoresis | HBsAg | PTT |
| 15 | Lipid profile | Vitamin B$_{12}$ | Cytology | HIV combo | Troponin-I |
| 16 | HIV | Hemoglobin | Syphilis | HCV | Urine culture |
| 17 | Thyroid function | Sodium | Blood culture | C-reactive protein | Blood group |
| 18 | ESR | Vitamin D | ESR | CKMB | Lactate |
| 19 | TSH | Blood group | HIV | ESR | Antibody screen |
| 20 | Unit packed RBCs | Calcium | Blood group | Thyroid function | Drugs of abuse screen, urine |
| 21 | Pregnancy | Coagulation profile | HCV | Syphilis | Cytology |
| 22 | Cytology | CBC with ESR | Stool microscopy | Troponin | Syphilis |
| 23 | Calcium | Blood culture | HBsAg | Uric acid serum | Surgicals |
| 24 | Blood culture | Electrolytes | HbA$_{1C}$ | Lactate | Blood culture |
| 25 | Syphilis | ALT | Phosphorus | Urine culture | Pregnancy |

Horton S, Fleming KA, Kuti M, Looi LM, Pai SA, Sayed S, Wilson ML. The Top 25 Laboratory Tests by Volume and Revenue in Five Different Countries. Am J Clin Pathol. 2019 Apr 2;151(5):446-451.

# Otkriće fenomena brzine sedimentacije eritrocita (SE)



Edmund Faustinus Biernacki
(1866-1911)

A cylinder designed by Biernacki for measurement of the ESR (from Deutsche Medizinische Wochenschrift 1897).

Biernacki's paper on the ESR from 1894 in German [8].

- razlikuje se ovisno od osobe
- krv s manjim udjelom stanica brže sedimentira
- ovisi o razini fibrinogena u krvi
- u febrilnim stanjima s povećanom koncentracijom fibrinogena u krvi brzina sedimentacije eritrocita je povišena
- u krvi bez fibrinogena proces sedimentacije eritrocita se usporava

Grzybowski A, Sak J. A short history of the discovery of the erythrocyte sedimentation rate. Int J Lab Hematol. 2012;34:442-4.
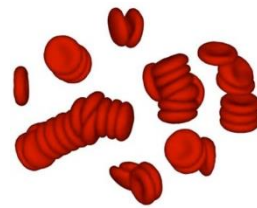
From the Stockholm Hospital for Tuberculosis at Söderby.

Acta Med Scand 54: 247-282. 1921

## Studies of the Suspension Stability of the Blood in Pulmonary Tuberculosis [1]
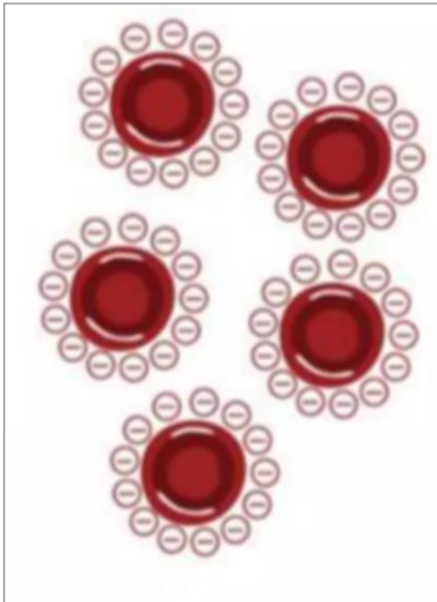
by

ALF WESTERGREN.

- objašnjen mehanizam sedimentacije eritrocita

- definirana metoda određivanja
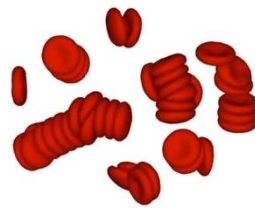
# Definicija

*mjera učinka različitih fizioloških i patofizioloških čimbenika na brzinu taloženja eritrocita u* **vertikalno** *postavljenoj graduiranoj pipeti tijekom* **sat vremena***, pri čemu u uzorku krvi dolazi do* **razdvajanja staničnog od plazmatskog dijela**



**MAKROMOLEKULE PLAZME (+)**

**Fibrinogen**
Plazminogen
C-reaktivni protein
alfa-1-antitripsin
Haptoglobin
Komponente komplementa
Imunoglobulini
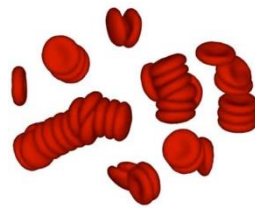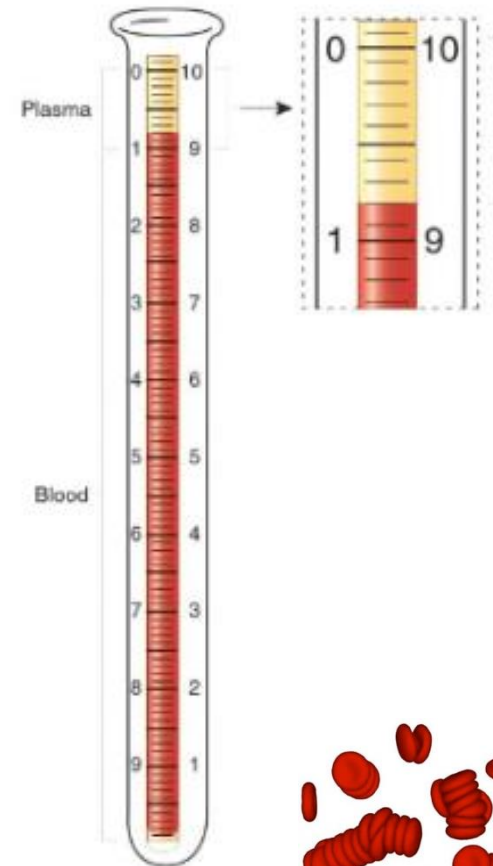
# Metoda po Westergrenu

- **Puna krv** razrijeđena u omjeru **4:1** s antikoagulansom **trinatrijevim-citratom dihidratom (3,8 %)**

- Westergrenova pipeta: duljina 30 cm, graduirani dio 20 cm, promjer 2,55 mm

- Okomito postavljanje

- Očitavanje stupca eritrocita **nakon sat vremena**



*a) Westergren tube   b) Westergren tube on the rack*
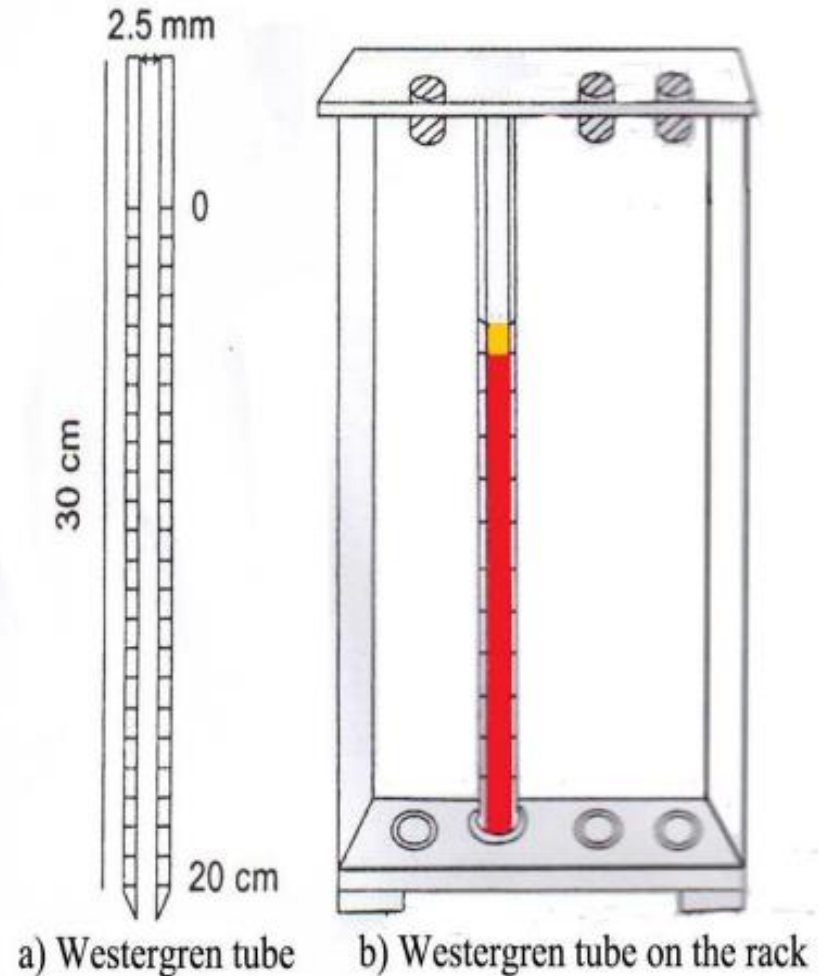
*Referentna metoda*
*za određivanje brzine sedimentacije eritrocita (1973., ICSH)*
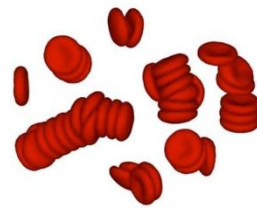
# Mehanizam sedimentacije eritrocita



**1**
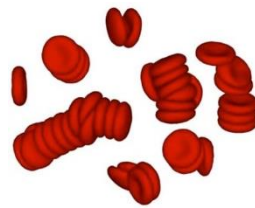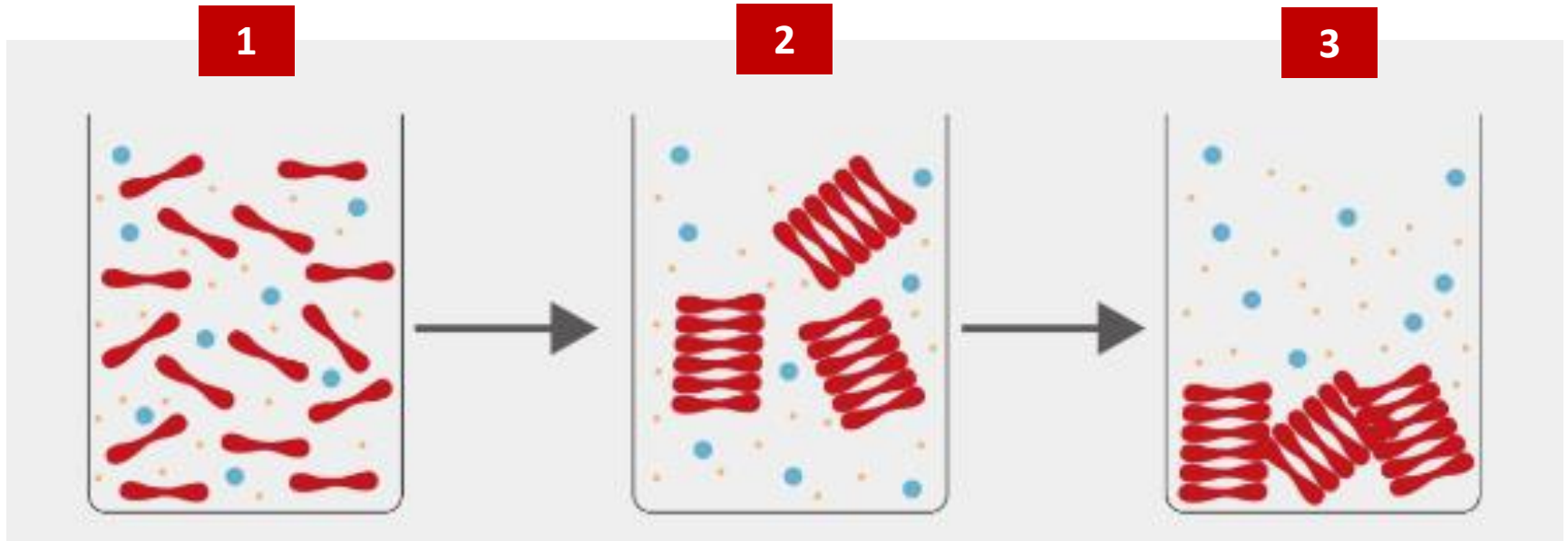
**Agregacijska (lag) faza**

*nakupljanje eritrocita u rouleaux formacije*

**2**

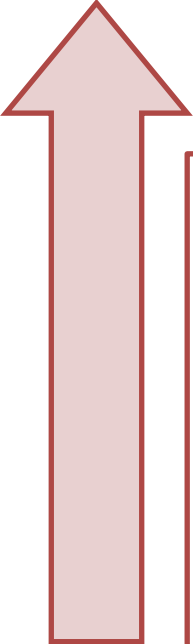**Dekantacijska faza**

*taloženje konstantnom brzinom*

**3**

**Faza nakupljanja**

*sedimentacija agregata usporenom brzinom*

**1 sat**

# Čimbenici koji utječu na SE

- Upalni parametri

- Karakteristike eritrocita (oblik, volumen i broj)

- Akutna upala

- Kronična upala

- Maligne bolesti

- Autoimune bolesti

- Anemije

- Trudnoća

- Starija dob

- Izrazita leukocitoza

- Policitemija

- Srpasta anemija, sferocitoza, akantocitoza

- Hipofibrinogenemija

- Hipogamaglobulinemija

- Povećana viskoznost plazme
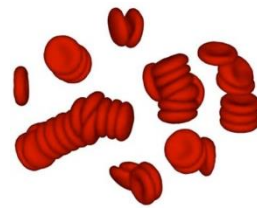
# Treba li koristiti SE u upali?
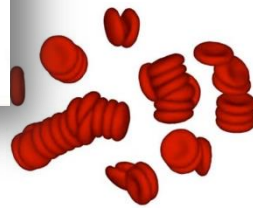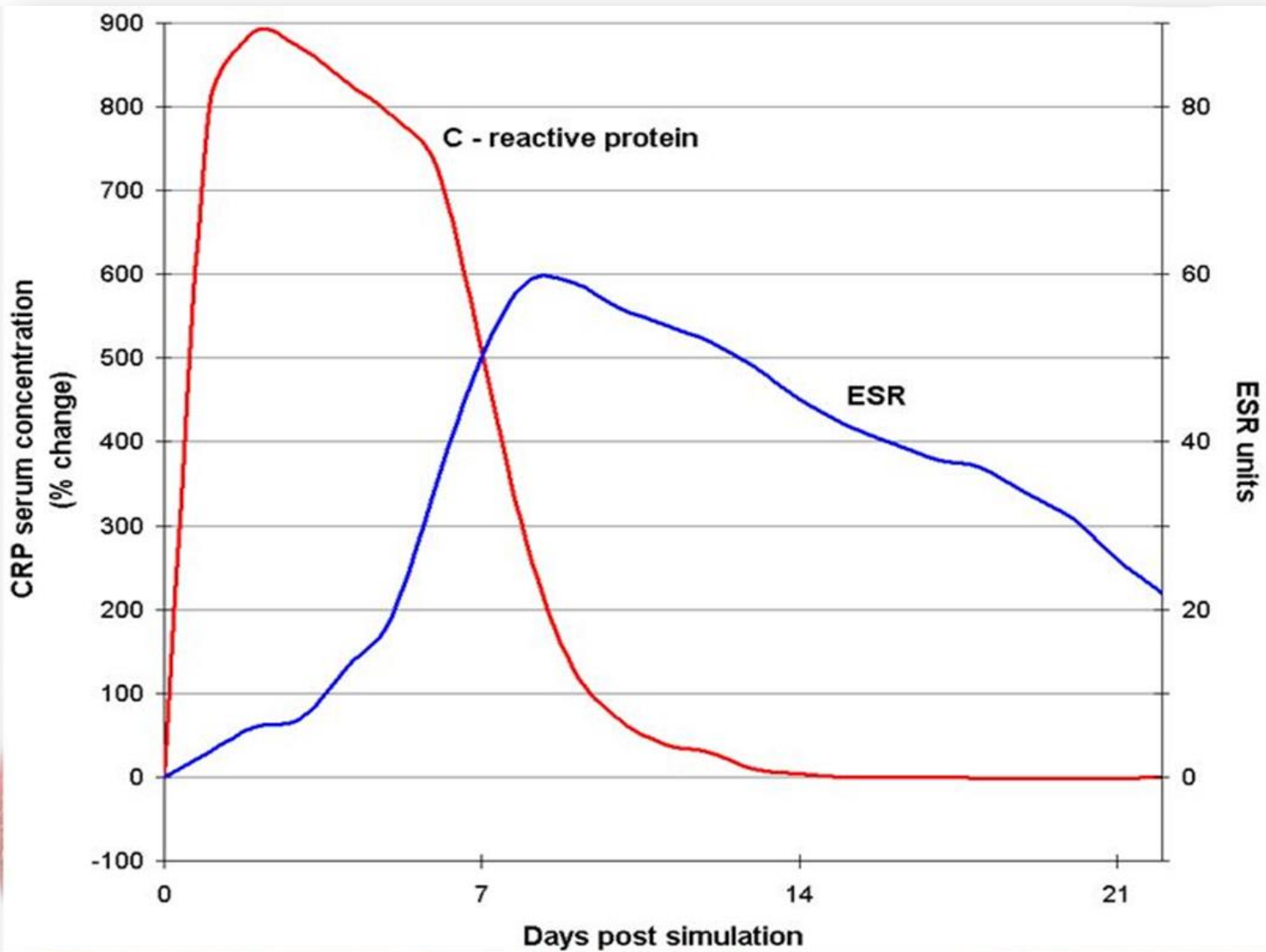
# Klinički i laboratorijski značaj



**REUMATSKE BOLESTI**
- reumatoidni artritis
- reumatska polimialgija
- arteritis divovskih stanica



**ORTOPEDSKE INFEKCIJE**
- Periprotetične zglobne infekcije



**HODGKINOV LIMFOM**

---

- postavljanje dijagnoze,
- praćenje tijeka bolesti
- praćenje uspješnosti liječenja

- SE > 30 mm govori u prilog dijagnozi infekcije

- stupnjevanje bolesti i stratifikacija rizika

1. Dasgupta B,, et al. 2012 Provisional classification criteria for polymyalgia rheumatica: a European League Against Rheumatism/American College of Rheumatology collaborative initiative. Ann Rheum Dis. 2012;71:484-92.
2. Ness T, et al. The diagnosis and treatment of giant cell arteritis. Dtsch Arztebl Int. 2013;110:376-86.
3. Barrack R, et al. General assembly, diagnosis, laboratory test: proceedings of international consensus on orthopedic infections. J Arthroplasty. 2019;34:S187-95.
4. Eichenauer DA. ESMO Guidelines Committee, et al. Hodgkin lymphoma: ESMO clinical practice guidelines for diagnosis, treatment and follow-up. Ann Oncol 2018;29:iv19–9.
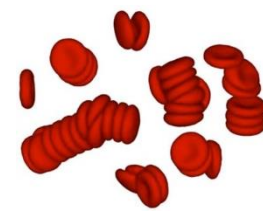
# National minimum retesting intervals in pathology

## March 2021

**Authors:** Dr Tim Lang, County Durham and Darlington NHS Foundation Trust
Dr Bernie Croal, Aberdeen Royal Infirmary, NHS Grampian

| ESR | | | |
|---|---|---|---|
| H-ESR1 | Temporal arteritis/polymyalgia rheumatica | Every three months following first month of treatment | Dasgupta B *et al. Rheumatology* 2010;49:186–190.[91] *[Level of evidence – B.]* |
| H-ESR2 | Rheumatoid arthritis | Every month until treatment has controlled the disease (NICE CG79 recommends use of CRP) | NICE. CG79, 2009.[92] *[Level of evidence – A.]* |
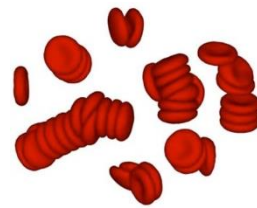
# Sistematski pregledi



| | Rezultat | Jedinica | Referentni interval |
|---|---|---|---|
| (K) Eritrociti | **3.24** | x10$^{12}$/L | 4.34 - 5.72 |
| (K) Hemoglobin | **111** | g/L | 138 - 175 |
| (K) Hematokrit | **0.316** | L/L | 0.415 - 0.530 |
| (K) MCV | **97.5** | fL | 83.0 - 97.2 |
| (K) MCH | **34.3** | pg | 27.4 - 33.9 |
| (K) MCHC | 351 | g/L | 320 - 345 |
| (K) RDW | 13.2 | % | 9.0 - 15.0 |
| (K) Retikulociti | 15.7 | /1000 Erc | 5.0 - 21.6 |
| (K) Retikulociti | 51 | x10$^9$/L | 22 - 97 |
| (K) Indeks zrelosti retikulocita | 0.16 | | 0.02 - 0.18 |
| (K) Eritroblasti | 0.0 | x10$^9$/L | < 0.6 |
| (K) Eritroblasti | 0 | /100 Lkc | < 3 |
| | Rezultat | Jedinica | Referentni interval |
| (K) Leukociti | 5.4 | x10$^9$/L | 3.4 - 9.7 |

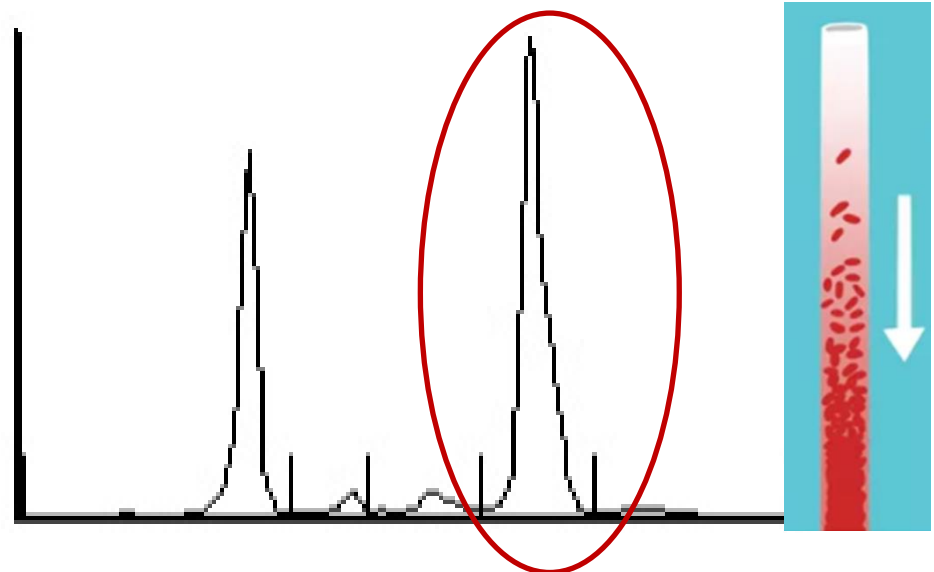| (K) Sedimentacija eritrocita | **130** | mm/h | 3 - 23 |
|---|---|---|---|



(S) Ukupni proteini = **87** g/L (RI: 66 – 80)

# ICSH preporuke kroz vrijeme

- **plastične** umjesto staklenih pipeta

- uzorkovanje krvi uz **EDTA** koji je za analizu potrebno razrijediti s trinatrijevim-citratom dihidratom pripremljenim otapanjem (3,2 %)

  **1977**

- definirana **standardizirana metoda za usporedivost** s rutinski korištenom metodom, izvodi se u nerazrijeđenom uzorku krvi hematokrita 0,33 ± 0,03 koristeći originalnu Westergrenovu pipetu

- Povezanost prema formuli:

  metoda po Westergrenu (razrijeđeni uzorak)

  = metoda po Westergrenu (nerazrijeđeni uzorak) x 0,86 - 12

  **1988**

- Izvještavanje rezultata u milimetrima (**mm**)

  **1993**
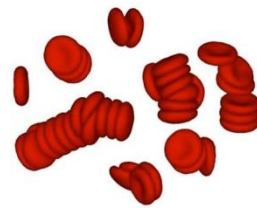
ORIGINAL ARTICLE                                    WILEY | ISLH International Journal of Laboratory Hematology

## ICSH recommendations for modified and alternate methods measuring the erythrocyte sedimentation rate

**2017**

A. Kratz[1] | M. Plebani[2] | M. Peng[3] | Y.K. Lee[4] | R. McCafferty[5] | S.J. Machin[6] |
on behalf of the International Council for Standardization in Haematology (ICSH)
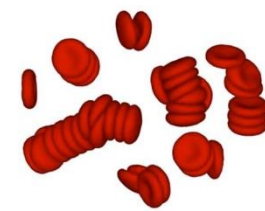
# *Automatizirane metode*

## *Modificirana Westergrenova metoda*



- automatizirano (optičko) očitavanje stupca eritrocita nakon sedimentiranja

- epruvete sa citratom

- epruvete različitih dimenzija i promjera od preporučenih

# Analiza iz nerazrijeđenog EDTA uzorka
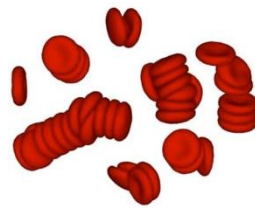
Analiza iz epruvete
za kompletnu krvnu sliku

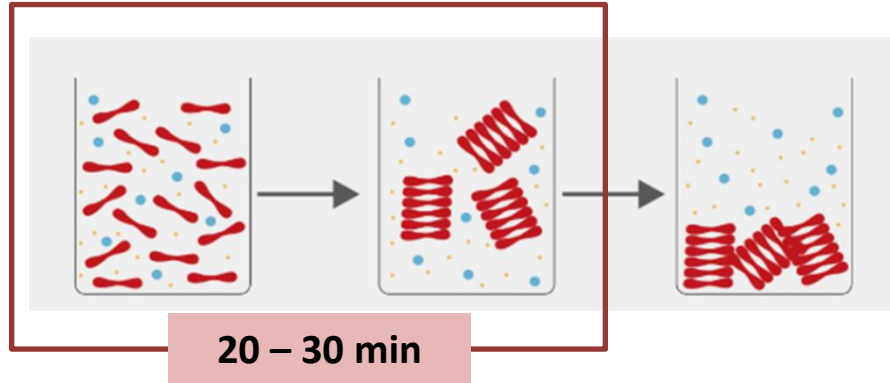Povećana sigurnost pacijenta

Povećana stabilnost eritrocita

Smanjena količina medicinskog otpada

Epruvete različitih proizvođača

Analiza u mikroepruvetama
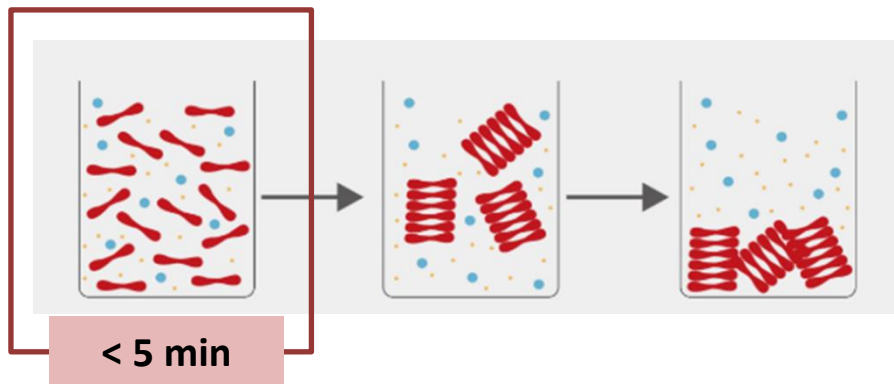
# Automatizirane metode

## Modificirane Westergrenove metode

**20 – 30 min**

- optičko mjerenje razlike visine stupca eritrocita neposredno nakon automatiziranog miješanja uzorka i nakon određenog vremena sedimentiranja
- rezultat se matematički se preračunava u vrijednost SE nakon sat vremena

## Alternativne metode

**< 5 min**

- kinetičke metode
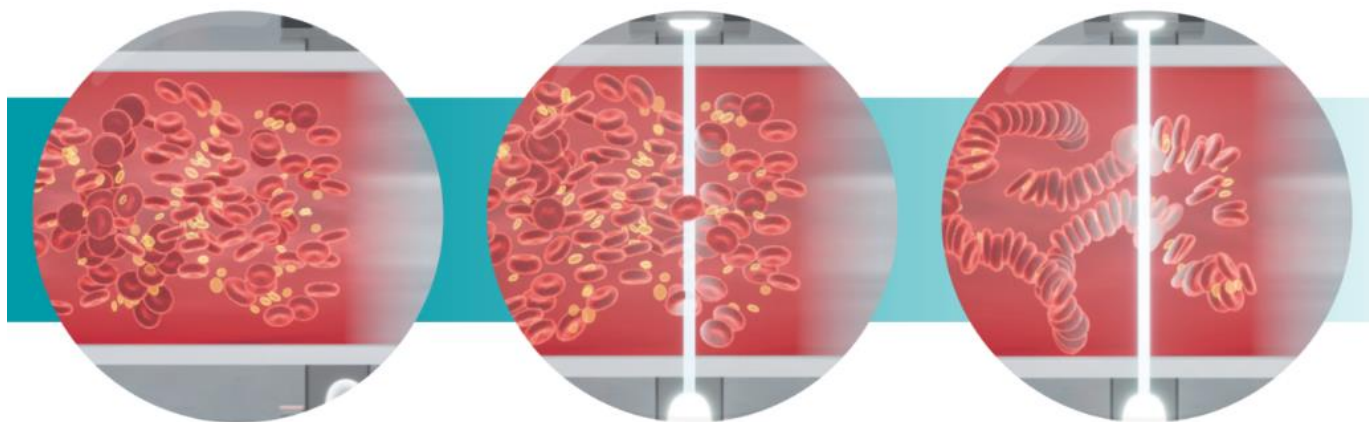- mjere nastajanje *rouleaux* formacija
- načela mjerenja: fotometrijska reologija, centrifugiranje
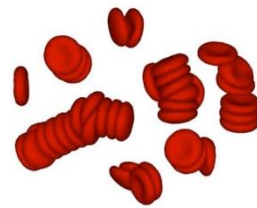
# Automatizirane metode

## Alternativne metode

### Fotometrijska reologija

Ubrzani protok krvi kroz kapilaru...

...uzrokuje agregaciju eritrocita...
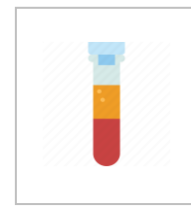
...što dovodi do promjene intenziteta svjetlosti.
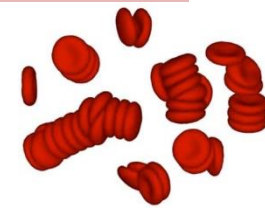
### Centrifugiranje

1500 – 2000 rpm

Infracrveni laser

Detekcija granice između eritrocita i plazme

# *Validacija automatiziranih metoda*

Kratz A, Plebani M, Peng M, Lee YK, McCafferty R, Machin SJ; International Council for Standardization in Haematology (ICSH).

**ICSH recommendations for modified and alternate methods measuring the erythrocyte sedimentation rate.**

Int J Lab Hematol. 2017;39:448-57.

**PRECIZNOST**
- u seriji
- iz dana u dan

**USPOREDBA S WESTERGRENOVOM METODOM**
- najmanje 60 uzoraka
- zasebna analiza u niskom (do 40 mm), srednjem (40 – 80 mm) i visokom području (> 80 mm)
- uredan hematokrit

**PROVJERA REFERENTNIH INTERVALA (RI)**
- za svaku skupinu po dobi i spolu analizom najmanje 20 uzoraka zdravih ispitanika
- prihvaćaju se ako je ≥ 90% rezultata unutar RI
- izrada vlastitih RI, prema CLSI EP28-A3c

- ispitivanje stabilnosti uzorka, prijenos uzorka (engl. *carryover*), utjecaj interferencija...
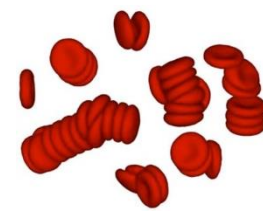
# Što zahtijeva ISO 15189:2022?

**HRVATSKA NORMA**

**HRN EN ISO 15189**

ICS: 03.120.10;
11.100.01

Četvrto izdanje,
prosinac 2022.

Zamjenjuje HRN EN ISO 15189:2012;
HRN EN ISO 22870:2016

## 7.3.5 Biological reference intervals and clinical decision limits

c) When changes are made to an examination or pre-examination method, the laboratory shall review the impact on associated biological reference intervals and clinical decision limits and communicate to the users when applicable.
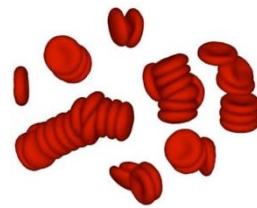
# Ispitivanje preciznosti



**CUBE 30 touch**

| | Declared mean (range), mm | Mean ± SD, mm | Within-run CV, % | Between-run CV, % | Manufacturer acceptance CV, % |
|---|---|---|---|---|---|
| ESR control cube normal level I (lot 621) | 9 (1–15) | 9 ± 1 | 5.2 | 9.4 | ≤15 |
| ESR control cube abnormal level II (lot 621) | 72 (47–97) | 66 ± 3 | 2.6 | 2.2 | |

ESR, erythrocyte sedimentation rate; SD, standard deviation; CV, coefficient of variation.

Lapić I, Rade A, Kraljević A, Miloš M, Coen Herak D, Daskijević L, Cerovac P, Rogić D. Analytical validation of the modified Westergren method on the automated erythrocyte sedimentation rate analyzer CUBE 30 touch. Clin Chem Lab Med. 2023;61:1463-9.

**Table 1** Intrarun precision obtained by analysing 11 patient samples in five replicates

| | ESR (mm) (n=5) | SD (±) | CV (%) |
|---|---|---|---|
| S1 | 4.6 | 0.5 | 10.7 |
| S2 | 10.2 | 1.3 | 13.0 |
| S3 | 15.2 | 0.8 | 4.9 |
| S4 | 23 | 5.1 | 22.2 |
| S5 | 33.2 | 1.6 | 4.8 |
| S6 | 41 | 1.9 | 4.6 |
| S7 | 56.4 | 1.5 | 2.7 |
| S8 | 68.2 | 4.8 | 7.0 |
| S9 | 75.4 | 2.6 | 3.4 |
| S10 | 85.6 | 2.1 | 2.4 |
| S11 | 107.8 | 2.4 | 2.2 |

CV, coefficient of variation; ESR, erythrocyte sedimentation rate.



**Ves-Matic Cube 200**

| | Intrarun precision | | Inter-run precision | | |
|---|---|---|---|---|---|
| | Mean ± SD | CV (%) | Mean ± SD | CV (%) | Bias (%) |
| Seditrol® Level 1 lot C128 (10 ± 7 mm) | 13 ± 1 | 4.0 | 13 ± 1 | 7.5 | 30 |
| Seditrol® Level 2 lot C228 (64 ± 26 mm) | 64 ± 1 | 1.8 | 64 ± 1 | 0.7 | 0 |

Abbreviations: CV, coefficient of variation; SD, standard deviation.



**iSED**
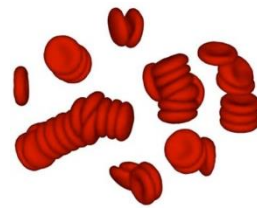
1. Lapić I, Piva E, Spolaore F, Musso G, Tosato F, Pelloso M, Plebani M. Ves-Matic CUBE 200: is modified Westergren method for erythrocyte sedimentation rate a valid alternative to the gold standard? J Clin Pathol. 2019;72:716-719.
2. Lapić I, Miloš M, Tosato F, Piva E, Zadro R, Rogić D, Plebani M. Analytical validation of the iSED automated analyzer for erythrocyte sedimentation rate. Int J Lab Hematol. 2020;42:109-115.

# Iz dana u dan
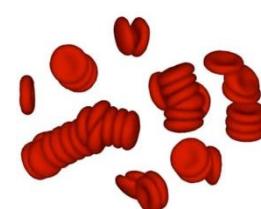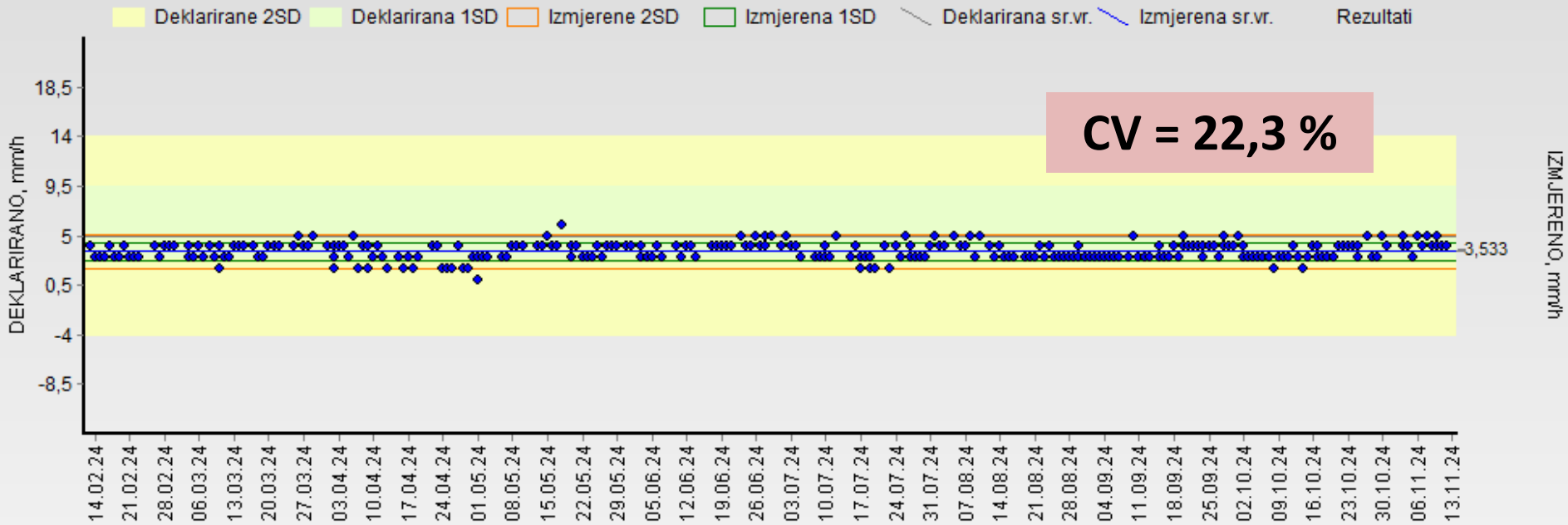
# Usporedba s Westergrenovom metodom
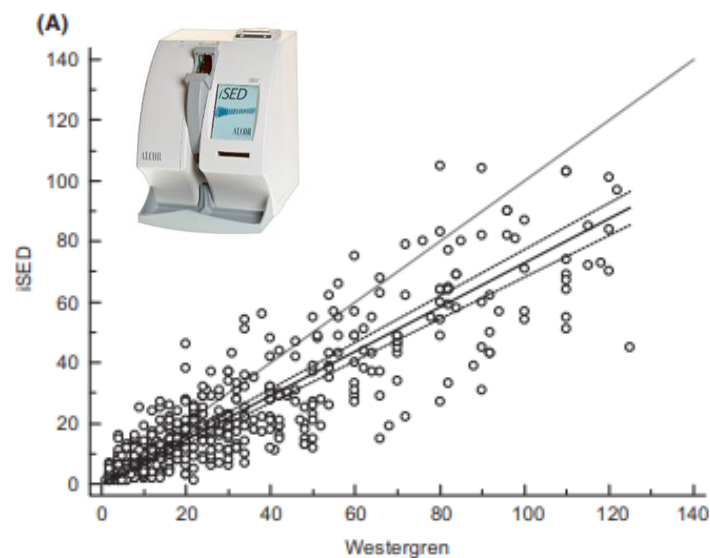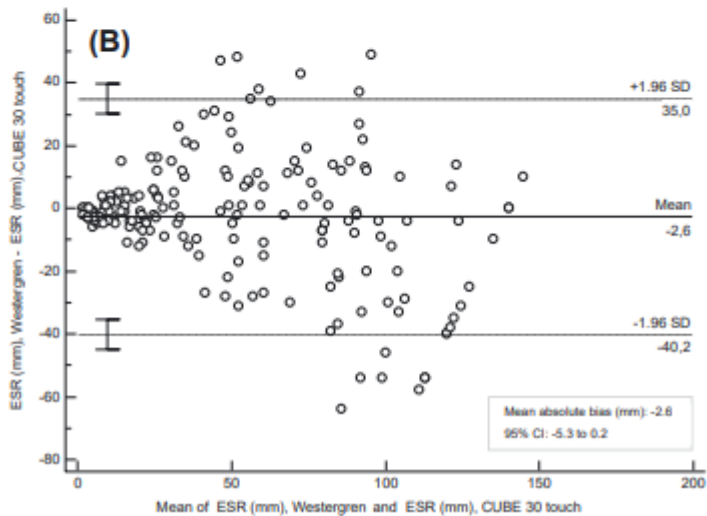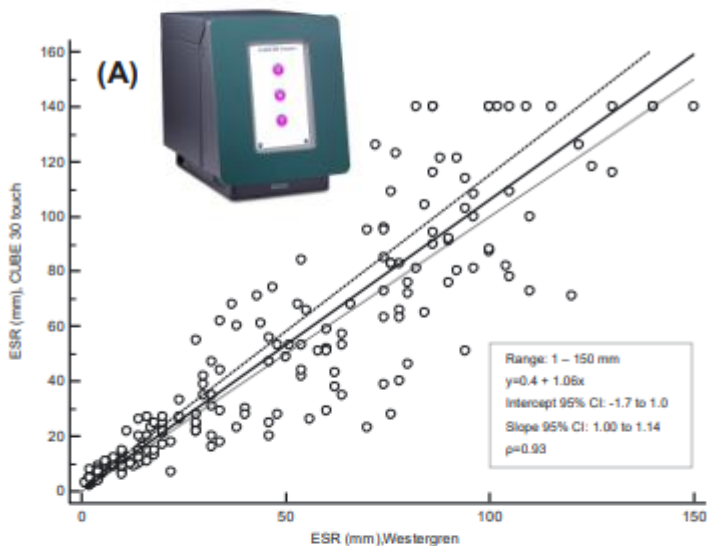


Razlike su posljedica mjerenja različitih faza procesa sedimentacije eritrocita.

# Usporedba s Westergrenovom metodom

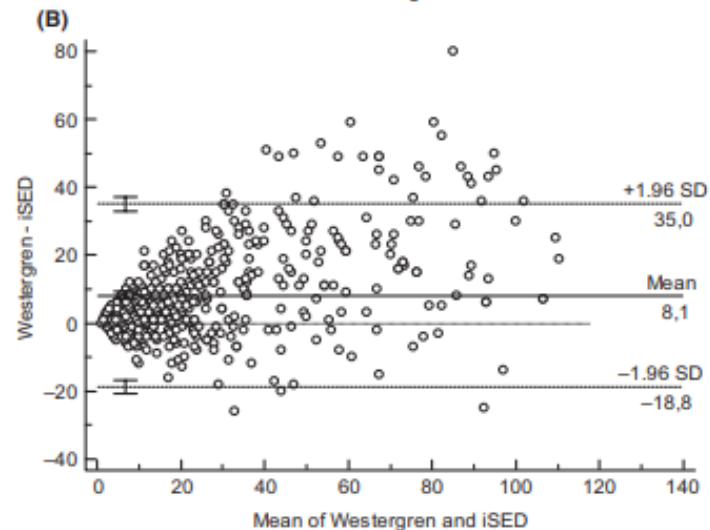| | Ves-Matic Cube 200 | | | | TEST1 | | | |
|---|---|---|---|---|---|---|---|---|
| | Intercept (95% CI) | Slope (95% CI) | p | Mean bias (95% CI) | Intercept (95% CI) | Slope (95% CI) | p | Mean bias (95% CI) |
| Low (n = 169) | −1.5 (−3.7 to −0.3) | 1.5 (1.3–1.9) | 0.65 | −5.6 (−7.7 to −3.4) | −0.7 (−1.1 to 0) | 1.1 (1.0–1.1) | 0.97 | 0 (−0.3 to 0.3) |
| Medium (n = 35) | −157.1 (−365 to −83) | 9.2 (−18 to 18) | 0.48 | 2.1 (−6.3 to 10.5) | 1.0 (−8.6 to 4.7) | 1.0 (0.9–1.2) | 0.94 | −0.8 (−1.9 to 0.3) |
| High (n = 41) | −170.8 (−416 to −58) | 2.5 (1.4–5.0) | 0.39 | 23.3 (16.5–30.1) | 15 (−13.6 to 30.7) | 0.8 (0.7–1.1) | 0.56 | −5.7 (−9.3 to −2.0) |

**Ves-Matic Cube 200**

**TEST1**

Lapić I, Piva E, Spolaore F, Tosato F, Pelloso M, Plebani M. Automated measurement of the erythrocyte sedimentation rate: method validation and comparison. Clin Chem Lab Med. 2019;57:1364-73.

| ESR range, mm | n | ρ | Intercept (95% CI) | Slope (95% CI) | Mean absolute bias (95% CI), mm | Mean relative bias (95% CI), % |
|---|---|---|---|---|---|---|
| <40 | 93 | 0.90 | 0.6 (0–2.0) | 1.1 (1.0–1.3) | −2.2 (−3.8 to −0.6) | −16.7 (−24.9 to −8.6) |
| 40–80 | 53 | 0.40 | −134.3 (−278.0 to −75.8) | 3.2 (2.2–5.5) | −1.5 (−8.6 to 5.7) | 5.8 (−5.7 to 17.4) |
| >80 | 45 | 0.39 | −110.0 (−259.0 to −31.1) | 2.2 (1.3–3.8) | −4.8 (−12.5 to 3.0) | −2.1 (−10.0 to 5.8) |

ESR, erythrocyte sedimentation rate; ρ, Spearman's rank correlation coefficient; CI, confidence interval.

**CUBE 30 touch**

Lapić I, Rade A, Kraljević A, Miloš M, Coen Herak D, Daskijević L, Cerovac P, Rogić D. Analytical validation of the modified Westergren method on the automated erythrocyte sedimentation rate analyzer CUBE 30 touch. Clin Chem Lab Med. 2023;61:1463-9.

| | N | ρ | Intercept (95% CI) | Slope (95% CI) | Mean bias (95% CI) |
|---|---|---|---|---|---|
| Low third (<40 mm) | 383 | 0.720 | −0.7 (−2.0 to −0.1) | 0.9 (0.8 to 1.0) | 3.0 (2.3 to 3.8) |
| Medium third (40-80 mm) | 91 | 0.528 | −53.1 (−81.6 to −36.0) | 1.7 (1.4 to 2.2) | 17.7 (14.8 to 20.5) |
| Upper third (>80 mm) | 53 | 0.297 | −89.8 (−193.0 to −43.3) | 1.7 (1.2 to 2.8) | 28.4 (22.8 to 34.0) |

Abbreviations: CI, confidence interval; ρ, Spearman's rank correlation coefficient.

**iSED**
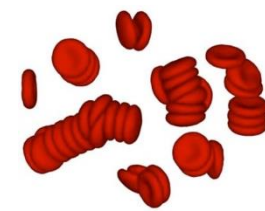
Lapić I, Miloš M, Tosato F, Piva E, Zadro R, Rogić D, Plebani M. Analytical validation of the iSED automated analyzer for erythrocyte sedimentation rate. Int J Lab Hematol. 2020;42:109-115.

# Utjecaj hematokrita...

## ...je značajniji kod modificiranih Westergrenovih metoda

| | n | ρ | Intercept (95% CI) | Slope (95% CI) | Mean absolute bias (95% CI), mm | Mean relative bias (95% CI), % |
|---|---|---|---|---|---|---|
| Normal hematocrit[a] | 104 | 0.94 | 1.6 (1.1–2.9) | 0.84 (0.76–0.93) | 2.5 (−0.1 to 5.1) | −3.1 (−11.7 to 5.6) |
| Low hematocrit | 87 | 0.77 | 0.3 (−8.8 to 6.8) | 1.11 (0.98–1.29) | −8.9 (−13.7 to −4.2) | −11.5 (−18.0 to −5.0) |

ρ, Spearman's rank correlation coefficient; CI, confidence interval. [a]Normal hematocrit for males is from 0.415 to 0.530 L/L, while for females from 0.356 to 0.470 L/L.

Lapić I, Rade A, Kraljević A, Miloš M, Coen Herak D, Daskijević L, Cerovac P, Rogić D. Analytical validation of the modified Westergren method on the automated erythrocyte sedimentation rate analyzer CUBE 30 touch. Clin Chem Lab Med. 2023;61:1463-9.

## ...u odnosu na alternativne metode

**TABLE 3** Results of ESR comparison between iSED and the Westergren method for samples with normal and low hematocrit values

| | | N | ρ | Intercept (95% CI) | Slope (95% CI) | Mean bias (95% CI) |
|---|---|---|---|---|---|---|
| Normal hematocrit | Site-1 | 320 | 0.817 | 0.3 (−0.5 to 0.9) | 0.8 (0.7 to 0.9) | 4.6 (3.4 to 5.7) |
| | Site-2 | 37 | 0.804 | 2.6 (−0.1 to 6.0) | 1.4 (1.0 to 1.9) | −8.3 (−11.6 to −4.9) |
| Low hematocrit | Site-1 | 207 | 0.889 | −2.4 (−3.6 to −0.6) | 0.7 (0.7 to 0.8) | 13.3 (11.1 to 15.5) |
| | Site-2 | 83 | 0.879 | 6.7 (3.5 to 10.7) | 0.8 (0.7 to 0.9) | 2.7 (−1.4 to 6.8) |

Abbreviations: CI, confidence interval; ρ, Spearman's rank correlation coefficient.
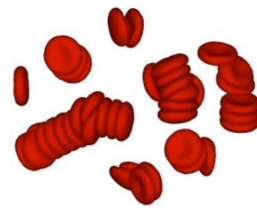
Lapić I, Miloš M, Tosato F, Piva E, Zadro R, Rogić D, Plebani M. Analytical validation of the iSED automated analyzer for erythrocyte sedimentation rate. Int J Lab Hematol. 2020;42:109-115.

# *Stabilnost*


**Ves-Matic Cube 200**

| Samples (n = 20) | Ves-Matic Cube 200 | | | TEST1 | | |
|---|---|---|---|---|---|---|
| | Mean, mm | Mean difference, mm (95% CI) | p-Value | Mean, mm | Mean difference, mm (95% CI) | p-Value |
| Fresh | 26 | | | 32.2 | | |
| Stored at RT | | | | | | |
| 4 h | 25 | −1.0 (−5.8 to 3.9) | 0.685 | 32.1 | −0.1 (−2.6 to 2.5) | 0.967 |
| 8 h | 20.6 | −5.4 (−13.3 to 2.5) | 0.166 | 30.5 | −1.7 (−5.5 to 2.2) | 0.384 |
| 24 h | 10.2 | −15.8 (−25.5 to −6.1) | 0.003 | 27.5 | −4.7 (−10.5 to 1.1) | 0.106 |
| Stored at 4 °C | | | | | | |
| 4 h | 25.4 | −0.6 (−4.7 to 3.5) | 0.764 | 37.1 | 5.0 (−0.7 to 10.6) | 0.082 |
| 8 h | 24.7 | −1.4 (−4.9 to 2.2) | 0.436 | 34.5 | 2.3 (−2.8 to 7.4) | 0.359 |
| 24 h | 18.8 | −7.1 (−11.8 to −2.4) | 0.005 | 31.7 | −0.5 (−6.1 to 5.1) | 0.855 |

RT, room temperature.


**TEST1**

Lapić I, Piva E, Spolaore F, Tosato F, Pelloso M, Plebani M. Automated measurement of the erythrocyte sedimentation rate: method validation and comparison. Clin Chem Lab Med. 2019;57:1364-73.


**CUBE 30 touch**

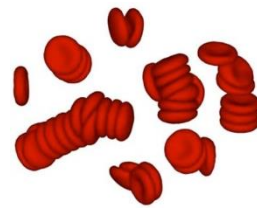| Samples | Mean, mm | Mean difference (95% CI), mm | p-Value |
|---|---|---|---|
| Fresh samples | 12 | N/A | N/A |
| **Samples stored at room temperature** | | | |
| 4 h | 11 | −1 (−3 to 0) | 0.063 |
| 8 h | 10 | −2 (−4 to 0) | 0.054 |
| 24 h | 3 | −9 (−14 to −5) | <0.001 |
| **Samples stored at 4 °C** | | | |
| 4 h | 12 | 0 (−1 to 1) | 0.772 |
| 8 h | 12 | 0 (−1 to 1) | 0.421 |
| 24 h | 9 | −3 (−4 to −1) | 0.002 |

CI, confidence interval; N/A, not applicable. p<0.05 was considered statistically significant.
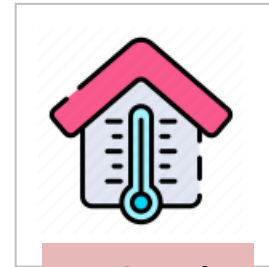

**≤ 8 sati**


**≤ 24 sata**

Lapić I, Rade A, Kraljević A, Miloš M, Coen Herak D, Daskijević L, Cerovac P, Rogić D. Analytical validation of the modified Westergren method on the automated erythrocyte sedimentation rate analyzer CUBE 30 touch. Clin Chem Lab Med. 2023;61:1463-9.

# Utjecaj interferencija - hemoliza

**Table 3** Results of haemolysis interference (HI) on ESR results

| HI range (g/L)* | n | Median (g/L) | Mean bias, % (95% CI) |
|---|---|---|---|
| 1.0–1.5 | 11 | 1.2 | −18 (−44 to 7) |
| 1.5–2.5 | 12 | 1.9 | −14 (−39 to 12) |
| 2.5–5.0 | 10 | 3.2 | −41 (−60 to −23) |

*HI range was reported as g/L of haemoglobin.
ESR, erythrocyte sedimentation rate; HI, haemolysis index.

**Ves-Matic Cube 200**

Lapić I, Piva E, Spolaore F, Musso G, Tosato F, Pelloso M, Plebani M. Ves-Matic CUBE 200: is modified Westergren method for erythrocyte sedimentation rate a valid alternative to the gold standard? J Clin Pathol. 2019;72:716-719.

| Hemolysis index, g/L | n | Samples | Median (IQR), mm | p-Value | Mean bias, % |
|---|---|---|---|---|---|
| 0–0.49 | 43 | Native | 22 (12–55) | 0.668 | −4.5 |
| | | Hemolyzed | 21 (13–64) | | |
| 0.5–1.0 | 20 | Native | 18 (7–32) | 0.089 | −5.6 |
| | | Hemolyzed | 17 (9–32) | | |
| >1.0 | 10 | Native | 6 (2–18) | 0.156 | 16.7 |
| | | Hemolyzed | 7 (2–15) | | |

IQR, interquartile range. p<0.05 was considered statistically significant.

| | Median (min–max) | p-Value | Mean bias, % |
|---|---|---|---|
| **Ves-Matic Cube 200** | | | |
| Non-hemolyzed | 10.5 (4–110) | 0.032 | −13.4 |
| Hemolyzed | 8.5 (2–102) | | |
| **TEST1** | | | |
| Non-hemolyzed | 20.5 (4–120) | 0.562 | −18.9 |
| Hemolyzed | 21 (2–120) | | |
| **Westergren** | | | |
| Non-hemolyzed | 10 (3–105) | 0.008 | −24.5 |
| Hemolyzed | 6.5 (2–82) | | |

1. Lapić I, Rade A, Kraljević A, Miloš M, Coen Herak D, Daskijević L, Cerovac P, Rogić D. Analytical validation of the modified Westergren method on the automated erythrocyte sedimentation rate analyzer CUBE 30 touch. Clin Chem Lab Med. 2023;61:1463-9.
2. Lapić I, Miloš M, Tosato F, Piva E, Zadro R, Rogić D, Plebani M. Analytical validation of the iSED automated analyzer for erythrocyte sedimentation rate. Int J Lab Hematol. 2020;42:109-115.

**CUBE 30 touch**

**iSED**
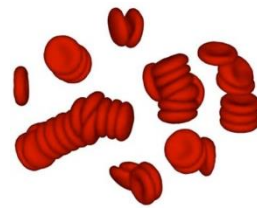
# Utjecaj interferencija - lipemija



**Table 6:** Results of assessment of the effect of artificially induced lipemia on erythrocyte sedimentation rate measured on the CUBE 30 touch analyzer.

| Lipemia index, g/L | n | Samples | Median (IQR), mm | p-Value | Mean bias, % |
|---|---|---|---|---|---|
| 0–1.99 | 11 | Native | 40 (9–82) | 0.770 | −7.5 |
| | | Lipemic | 37 (9–95) | | |
| 2.0–5.0 | 13 | Native | 13 (2–21) | 0.175 | 30.8 |
| | | Lipemic | 17 (9–27) | | |
| >5.0 | 10 | Native | 22 (13–53) | 0.004 | −50.0 |
| | | Lipemic | 11 (8–51) | | |

IQR, interquartile range. p<0.05 was considered statistically significant.



**CUBE 30 touch**

Lapić I, Rade A, Kraljević A, Miloš M, Coen Herak D, Daskijević L, Cerovac P, Rogić D. Analytical validation of the modified Westergren method on the automated erythrocyte sedimentation rate analyzer CUBE 30 touch. Clin Chem Lab Med. 2023;61:1463-9.

# Zašto ispitati utjecaj interferencija?

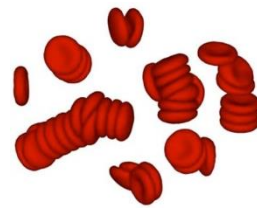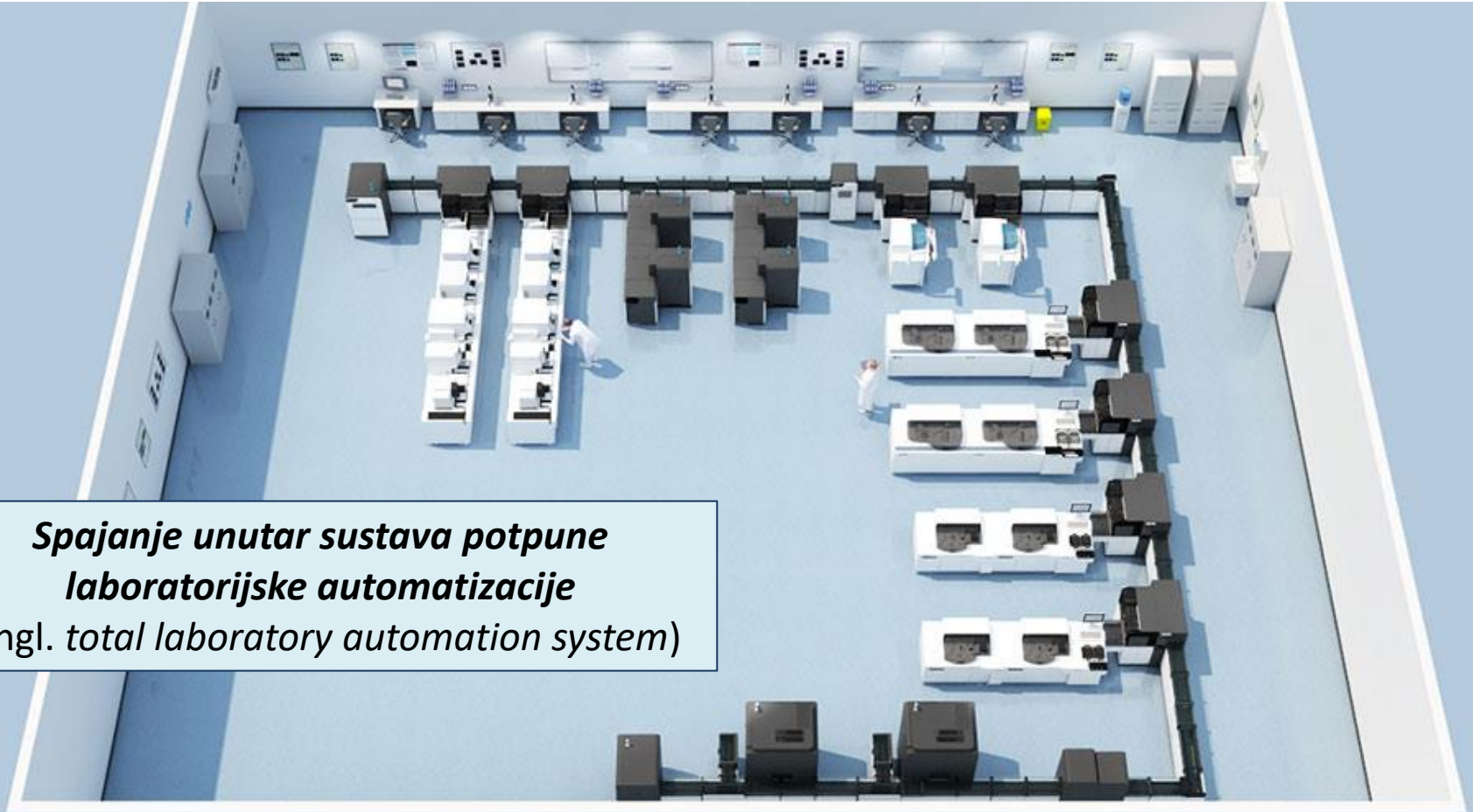| Pretraga | | | Rezultat | |
|---|---|---|---|---|
| **Grupa** | **Naziv** | **S...** | | |
| Hematologija | (K) Sedimentacija eritrocit | SE | 25 | H |
| LIH indeksi | L-SE | L | 12 | |
| | H-SE | H | 517 | |
| | I-SE | I | 2 | |

HIL indeksi izmjereni u uzorku seruma/plazme iz istog vađenja

**AUTOVALIDACIJA**

- HIL indeksi (H = 500, L = 500)
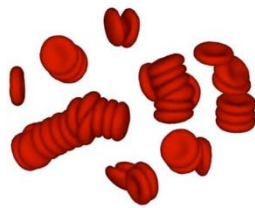- Autovalidacijski raspon (1 – 100 mm)
- Delta check (90%, 5 dana)

90 % autovalidiranih nalaza SE

# Budućnost



Spajanje unutar sustava potpune laboratorijske automatizacije
(engl. *total laboratory automation system*)

# *Budućnost*

# Optimizacija radnog procesa



1. PRILAGODBA IZGLEDA CRTIČNOG KODA



2. RASPODJELA NA PRIJEMU UZORAKA



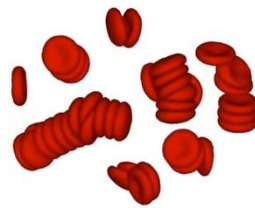3. PRILAGOĐENI REKOVI
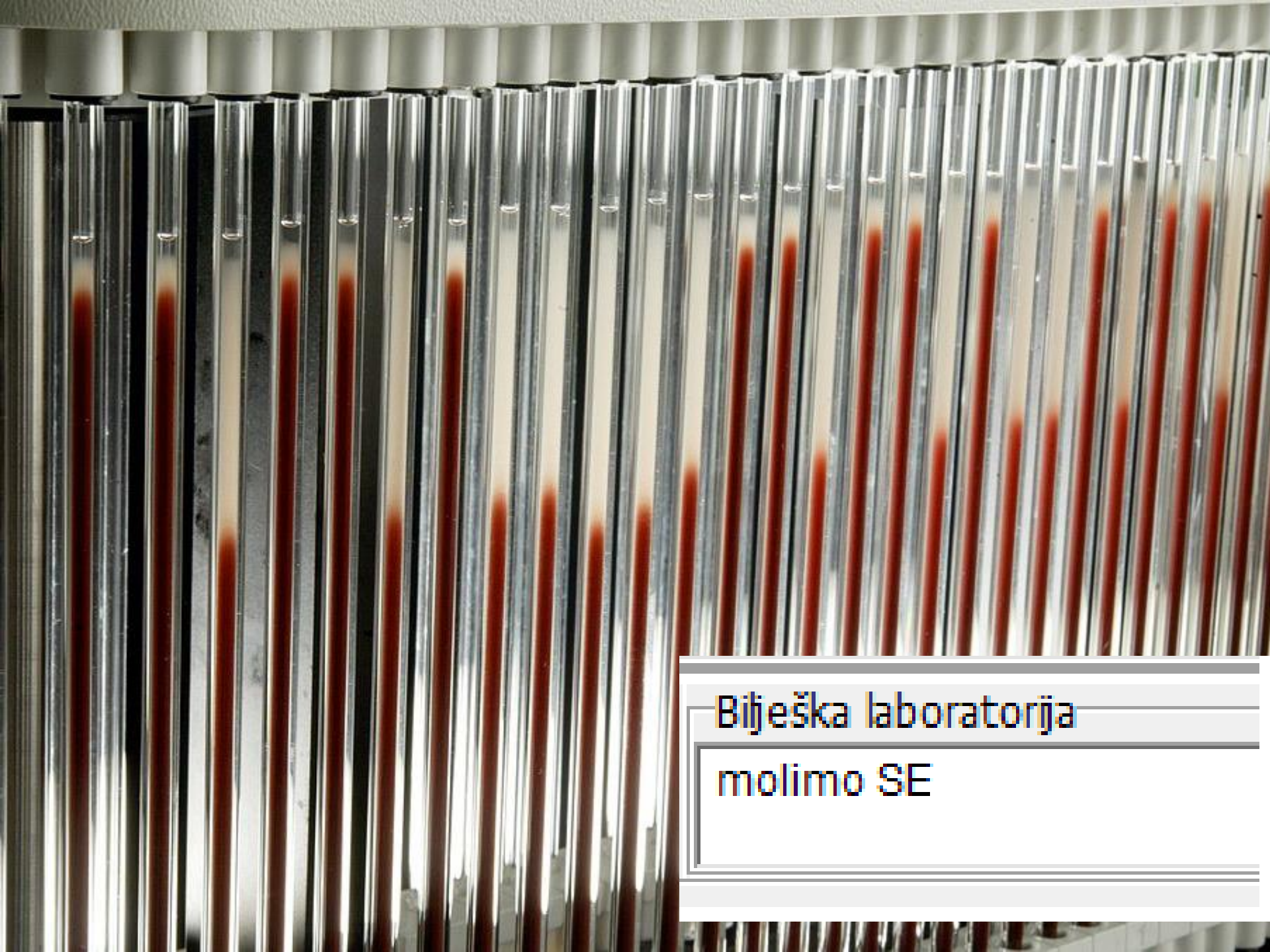


4. IZDVAJANJE UZORAKA ZA SE

# Prednosti uvođenja automatiziranih metoda

- analiza iz nerazrijeđenog EDTA uzorka

- automatizirano očitavanje rezultata

- skraćeno vrijeme analize

- provedba unutarnje kontrole kvalitete

- povezanost s laboratorijskim informacijskim sustavom

- uvođenje autovalidacije

- smanjena mogućnost ljudske pogreške

- optimizacija radnog procesa u hematološkom laboratoriju

- smanjenje opterećenja laboratorijskog osoblja

Kratz A, Plebani M, Peng M, Lee YK, McCafferty R, Machin SJ; International Council for Standardization in Haematology (ICSH). ICSH recommendations for modified and alternate methods measuring the erythrocyte sedimentation rate. Int J Lab Hematol. 2017;39:448-57.

# Automatizirane metode – koja je bolja?

Bilješka laboratorija

molimo SE