Hematologi Rutin Sebagai Pemeriksaan Penunjang Dalam Praktik Klinis

Mario

Hematologi

→ “Hematologi” berasal dari Bahasa Yunani (*Haima* = darah; *Logos* = ilmu)

Fungsi pemeriksaan hematologi :

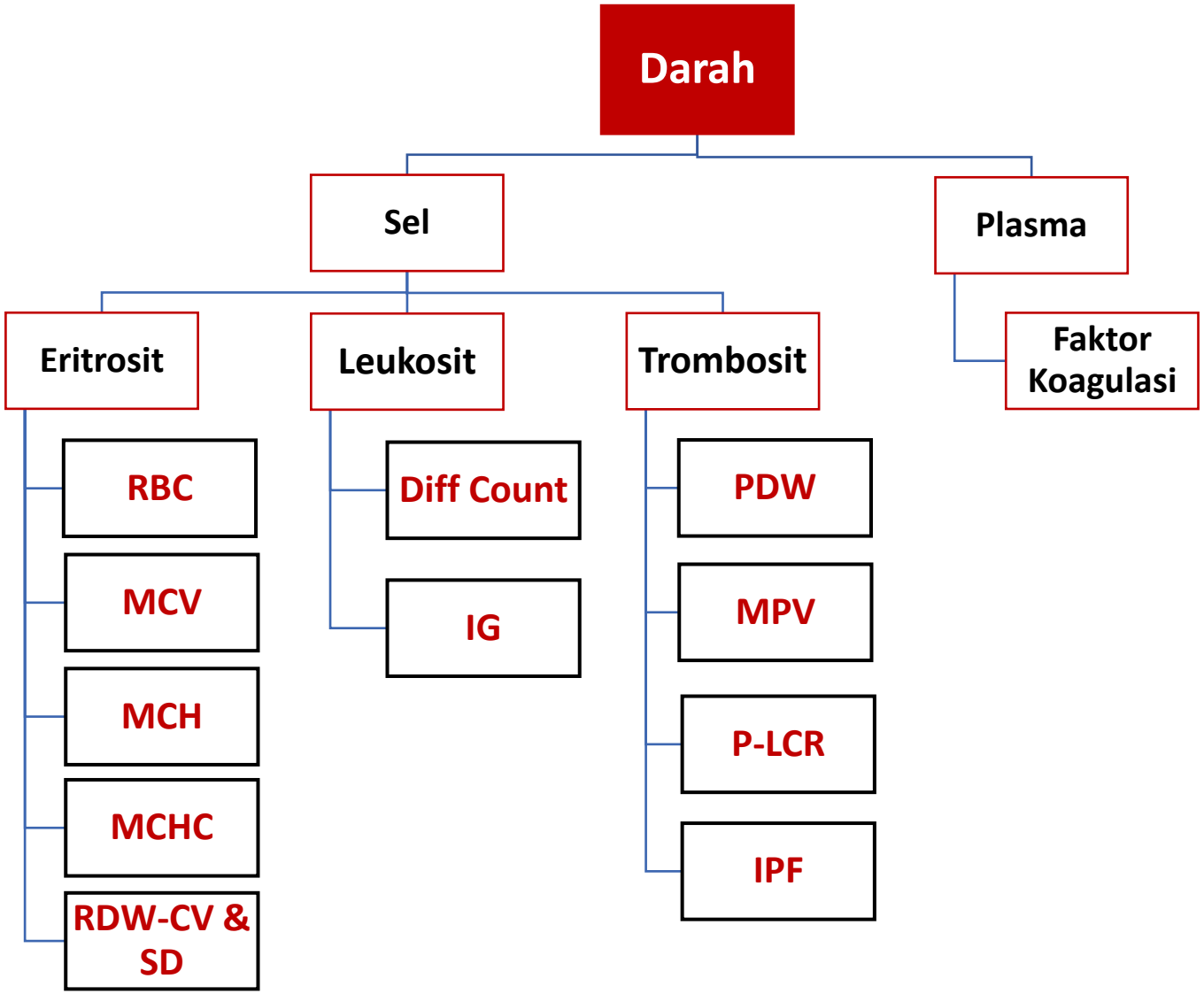
- Membantu menentukan diagnosis suatu penyakit
- Memberi informasi adanya kelainan dlm darah/tubuh
- Alat monitor respons suatu pengobatan/perjalanan penyakit

Hematologi

Pemeriksaan hematologi :

- Hemoglobin (Hb)
- Hematokrit (Ht)
- Leukosit (WBC)
- Trombosit (Plt)
- Laju Endap darah (LED)
- Evaluasi Sediaan Apus Darah Tepi (SADT)

Hematologi


Darah
Sel
Plasma
Eritrosit
Leukosit
Trombosit
Faktor Koagulasi
RBC
MCV
MCH
MCHC
RDW-CV & SD
Diff Count
IG
PDW
MPV
P-LCR
IPF

Eritrosit

Pasien usia 11 tahun, klinis : Anemia

Parameter	Hasil	Nilai Rujukan	Satuan
Hemoglobin (Hb)	**7,5**	12,0-15,0	g/dL
Hematokrit (Ht)	**25,1**	35,0-49,0	%
Eritrosit (RBC)	**3,70**	4,0-5,4	Juta/µL
Leukosit	4,56	4,50-13,5	1000/µL
Trombosit	309	150-450	1000/µL

Interpretasi :

- Anemia berat (berdasarkan WHO 2008)
- Parameter utama anemia : Hemoglobin (Hb) **bukan** Ht atau RBC
- *Rule of Three* tidak berlaku, hasil salah?

Pemeriksaan lanjutan untuk menentukan penyebab anemia :

- Indeks eritrosit (MCV, MCH, MCHC)
- *Red cell Distribution Width* (RDW)
- Retikulosit

Lanjutan

Parameter	Hasil	Nilai Rujukan	Satuan
MCV	**67,8**	80-94	fL
MCH	**20,3**	26-32	Pg
MCHC	**29,9**	32-36	%
RDW-CV	**16,5**	11,5-14,5	%
Retikulosit%	1,1	0,5-1,5	%
Ret. Absolut	0,042	0,020-0,124	$10^6/\mu L$

Interpretasi :

- Mikrositik (MCV ↓) Hipokromik (MCHC ↓)
- Hasil valid karena *Rule of Three* hanya untuk normokromik
- Anisositosis (RDW-CV ↑)
- Retikulosit normal → respon sumsum tulang terhadap anemia tidak adekuat

Pemeriksaan lanjutan :

- *Immature Reticulocyte Fraction* (IRF)
- *Reticulocyte Hemoglobin Equivalent* (Ret-He)

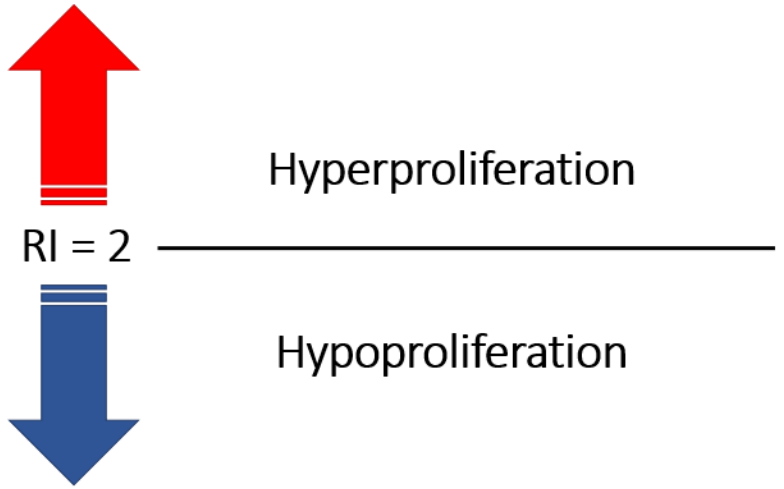
Retikulosit%

- Hasil retikulosit% pada kondisi anemia harus dikoreksi karena ada peningkatan palsu

$$\text{Absolute Reticulocyte Count} = \text{Reticulocyte \%} \times \frac{\text{Hct pasien}}{\text{Hct normal (40\%)}}$$

$$\text{Reticulocyte Index} = \frac{\text{Absolute Reticulocyte Count}}{\text{Maturation Correction}}$$

Hct (%)	Maturation Correction
36-45	1
26-35	1,5
16-25	2
≤ 15	2,5



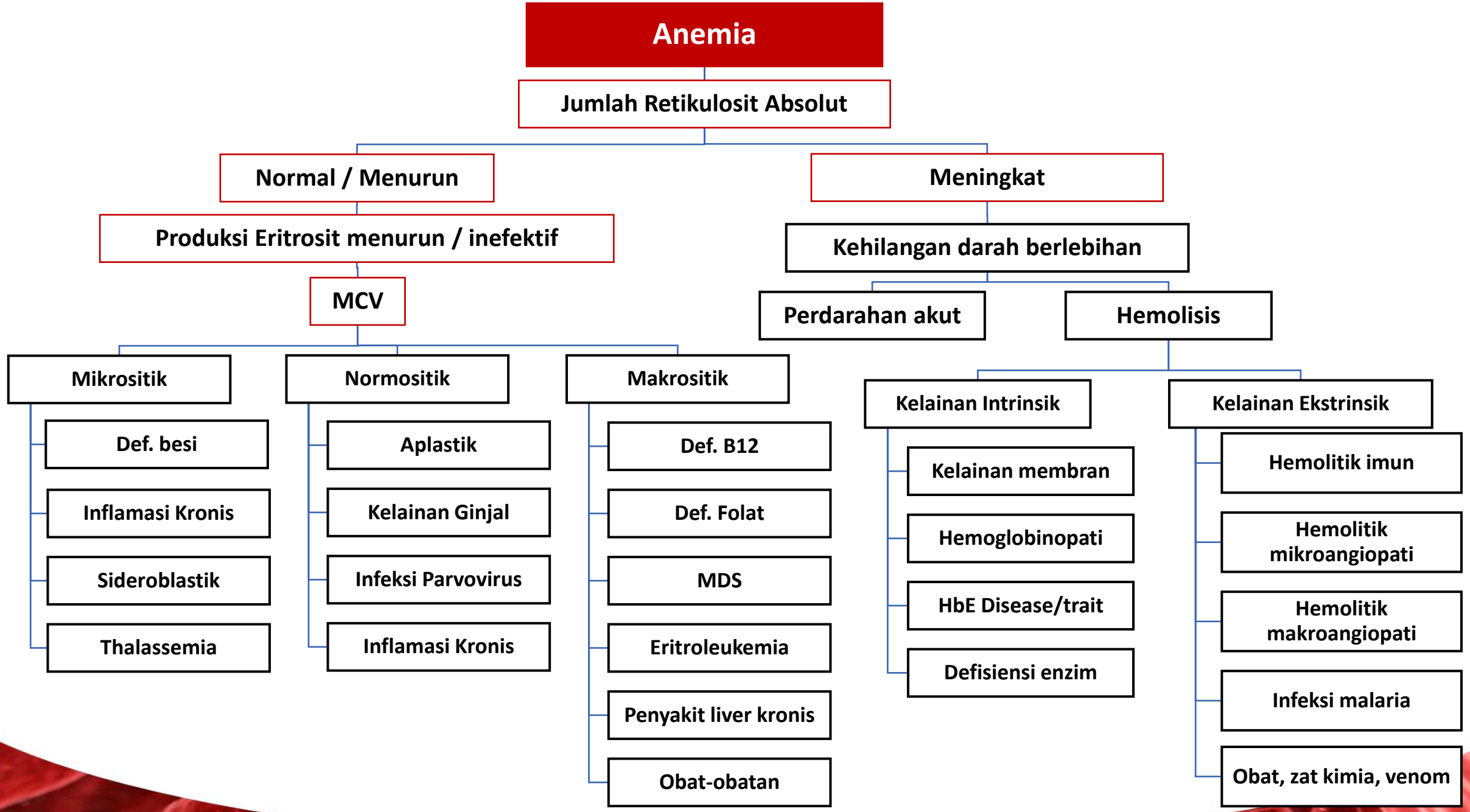
Lanjutan

Parameter	Hasil	Nilai Rujukan	Satuan
IRF	4,1	1,6-10,5	%
LFR	95,9	89,9-98,4	%
MFR	3,4	1,6-9,5	%
HFR	0,7	0,0-1,7	%
Ret-He	**13,8**	32,1-38,8	pg

Interpretasi :

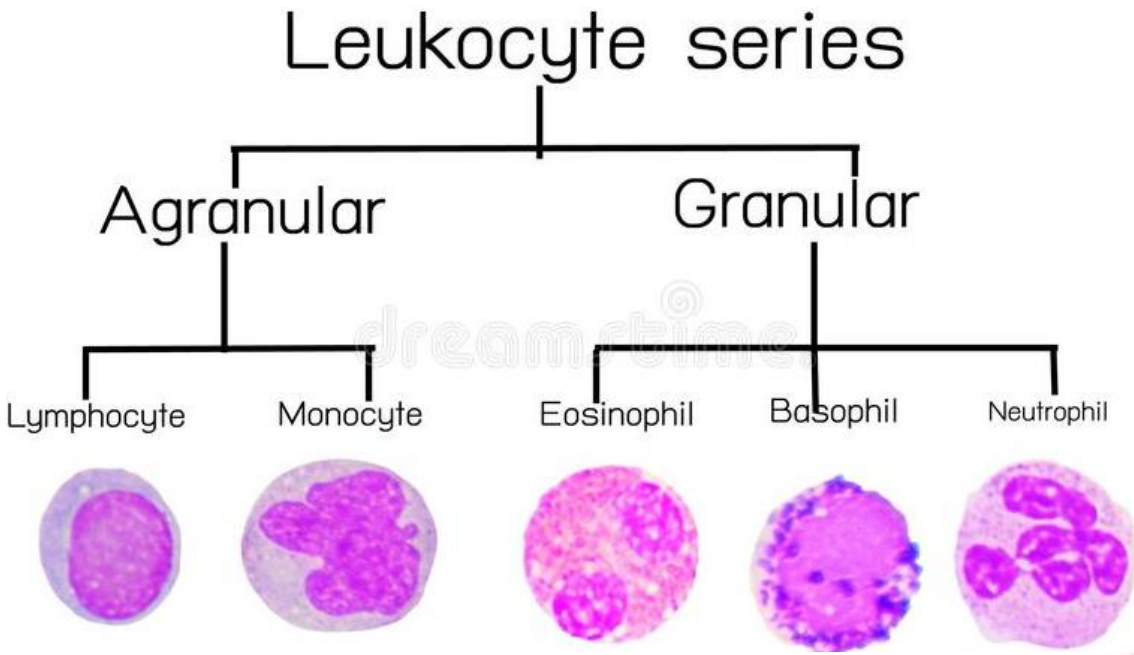
- IRF (N) → sumsum tulang tidak menunjukkan regenerasi eritropoiesis yang sesuai dengan tingkat anemia
- Ret-He (↓) → kurang tersedia Fe untuk eritropoiesis

- Diagnosis : Anemia hipokromik mikrositik susp. e.c Defisiensi besi


Anemia
Jumlah Retikulosit Absolut
Normal / Menurun
Produksi Eritrosit menurun / inefektif
MCV
Mikrositik
Def. besi
Inflamasi Kronis
Sideroblastik
Thalassemia
Normositik
Aplastik
Kelainan Ginjal
Infeksi Parvovirus
Inflamasi Kronis
Makrositik
Def. B12
Def. Folat
MDS
Eritroleukemia
Penyakit liver kronis
Obat-obatan
Meningkat
Kehilangan darah berlebihan
Perdarahan akut
Hemolisis
Kelainan Intrinsik
Kelainan membran
Hemoglobinopati
HbE Disease/trait
Defisiensi enzim
Kelainan Ekstrinsik
Hemolitik imun
Hemolitik mikroangiopati
Hemolitik makroangiopati
Infeksi malaria
Obat, zat kimia, venom

Leukosit

- Komponen penting dalam sistem pertahanan tubuh
- Melindungi tubuh dari infeksi bakteri, virus, jamur, dan parasite
- Di sirkulasi perifer dibagi menjadi : basofil, eosinofil, netrofil batang, netrofil segmen, limfosit, dan monosit
- Kelainan leukosit berdasarkan jumlah dibagi menjadi :
  - Leukositosis = leukosit > nilai rujukan
  - Leukopenia = leukosit < nilai rujukan



Leukosit

Pasien usia 54 tahun, klinis : Susp. CAP

Parameter	Hasil	Nilai Rujukan	Satuan
Hemoglobin (Hb)	**7,5**	13,2-17,3	g/dL
Hematokrit (Ht)	**22,7**	40-54	%
Eritrosit (RBC)	**2,53**	4,5-5,9	Juta/µL
MCV	90	80-96	fL
MCH	30	28-33	Pg
MCHC	33	33-36	%
Leukosit	**14,27**	4,40-11,0	1000/µL
Basofil	0	0-1	%
Eosinofil	0	2-4	%
Neutrofil	**92**	50-70	%
Limfosit	**5**	20-40	%
Monosit	3	2-8	%
Trombosit	204	150-450	1000/µL

Interpretasi :

- Anemia normokrom normositer
- Leukositosis dominasi neutrofil
- NLR = 18, Sepsis?

Neutrophil-Lymphocyte count Ratio (NLR)

$$NLR = \frac{Absolute\ neutrophil\ count}{Absolute\ lymphocyte\ count}$$

Neutrophil Lymphocyte Ratio (NLR):	Ratio	SIRS severity
Neutrophil count: lymphocyte count	<3	Mild
Neutrophil count: lymphocyte count	3–5	Moderate
Neutrophil count: lymphocyte count	>5	Severe

Diagnostic accuracy of procalcitonin, neutrophil-lymphocyte count ratio, C-reactive protein, and lactate in patients with suspected bacterial sepsis

Lars Ljungstro¨m[1], Anna-Karin Pernestig[2], Gunnar Jacobsson[1,3], Rune Andersson[3,4], Barbara Usener[5], Diana Tilevik[2]*

Table 4. Performance characteristics of single biomarkers for diagnosing verified bacterial sepsis using Sepsis-3 criteria[a].

Biomarker (cut-off)	Sensitivity (95% CI)	Specificity (95% CI)	Accuracy (95% CI)	DOR (95% CI)	PPV (95% CI)	NPV (95% CI)
PCT (2.0 ng/mL)	32.1% (28.3–36.0)	89.5% (87.6–91.4)	69.1% (66.8–71.4)	4.05 (3.10–5.29)	62.9% (57.3–68.5)	70.5% (68.0–72.9)
PCT (10.0 ng/mL)	15.4% (12.4–18.3)	97.4% (96.5–98.4)	68.2% (65.9–70.5)	6.88 (4.38–10.81)	76.8% (69.0–84.6)	67.5% (65.1–69.9)
CRP (20 mg/L)	88.4% (85.8–91.1)	14.4% (12.2–16.5)	40.8% (38.4–43.3)	1.28 (0.93–1.75)	36.4% (33.9–39.0)	69.0% (62.8–75.4)
CRP (100 mg/L)	59.7% (55.6–63.8)	53.3% (50.2–56.4)	55.6% (53.1–58.1)	1.69 (1.37–2.09)	41.5% (38.1–44.9)	70.4% (67.2–73.7)
Lactate (2.5 mmol/L)	29.5% (25.7–33.4)	84.2% (81.9–86.5)	64.6% (62.2–67.1)	2.23 (1.73–2.87)	51.0% (45.4–56.5)	68.2% (65.6–70.9)
Lactate (3.5 mmol/L)	14.9% (11.9–18.0)	95.3% (94.0–96.6)	66.6% (64.2–68.9)	3.54 (2.43–5.18)	63.8% (55.4–72.1)	66.8% (64.3–69.3)
NLCR (3.0)	95.1% (93.3–96.9)	11.7% (9.7–13.7)	41.5% (39.1–44.0)	2.58 (1.67–3.97)	37.5% (35.0–40.0)	81.1% (74.7–87.5)
NLCR (10.0)	64.7% (60.8–68.7)	60.8% (57.9–63.9)	62.2% (59.8–64.6)	2.85 (2.30–3.54)	47.9% (44.3–51.5)	75.6% (72.6–78.6)

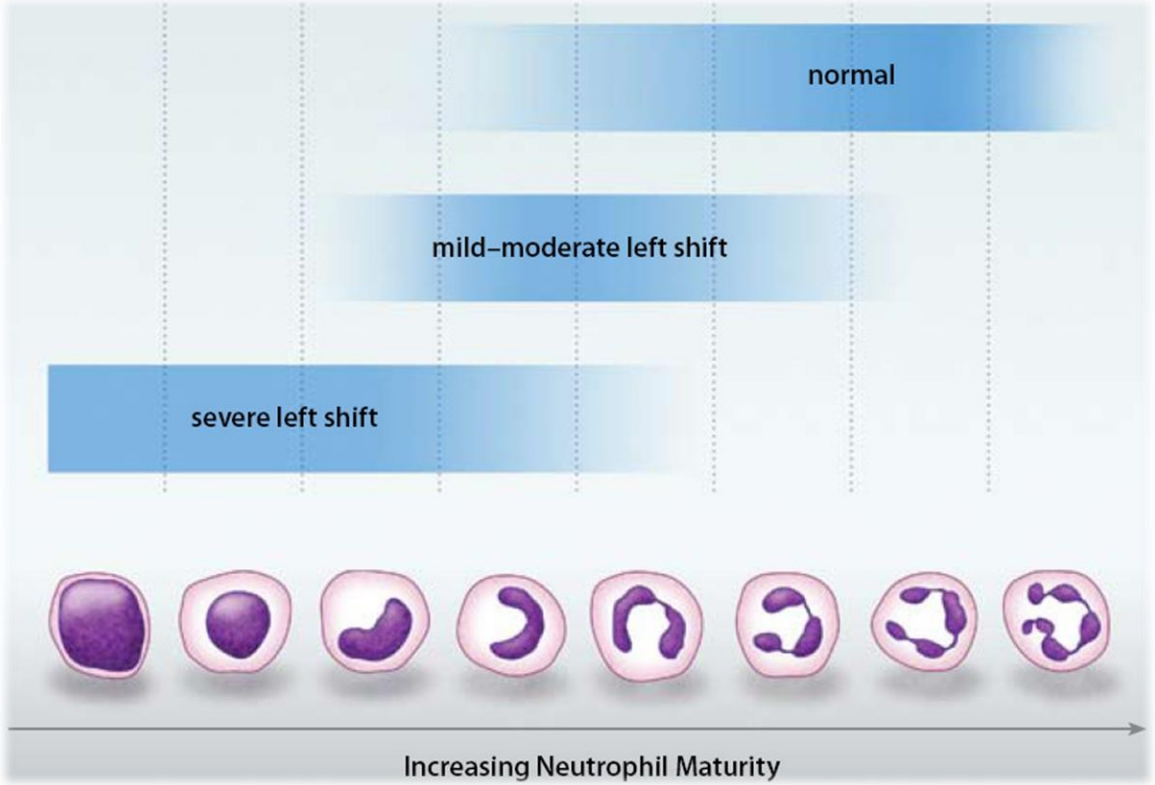
CRP, C-reactive protein; DOR, diagnostic odds ratio; NLCR, neutrophil-lymphocyte count ratio; NPV, negative predictive value; PCT, procalcitonin; PPV, predictive positive value.

[a]Including all episodes fulfilling the Sepsis-3 criteria for bacterial sepsis irrespective severity (i.e., sepsis and septic shock).

https://doi.org/10.1371/journal.pone.0181704.t004

Immature Granulocytes (IGs)

- Sel imatur, prekursor netrofil (Promyelosit, myelosit, metamyelosit)
- Diproduksi di sumsum tulang
- Jumlah sangat sedikit di perifer
- Meningkat pada kondisi inflamasi/infeksi/sepsis



Lanjutan

Evaluation of Immature Granulocyte Count as the Earliest Biomarker for Sepsis

Prabhav Bhansaly[1], Sudhir Mehta[2], Nidhi Sharma[3], Esha Gupta[4], Shaurya Mehta[5], Sweta Gupta[6]

Table 5: Sensitivity, specificity, Youden's index, and DOR

	Biomarkers	*Sensitivity*	*Specificity*	*Youden's index*	*Best criteria*	*DOR*
Period 1	IG#	72.15	43.10	0.15	$0.03 \times 10^3/\mu L$	1.96
	IG%	97.47	18.97	0.16	2.03%	9.02
	Procalcitonin	69.62	41.38	0.11	0.42 ng/mL	1.62
	Lactate	31.96	86.21	0.18	0.3 mmol/L	2.94
Period 2	IG#	89.87	68.97	0.59	$0.06 \times 10^3/\mu L$	19.72
	IG%	88.61	72.41	0.61	0.7%	20.42
	Procalcitonin	74.68	46.55	0.21	0.77 ng/mL	2.57
	Lactate	13.92	93.10	0.07	0.3 mmol/L	2.18
Period 3	IG#	92.41	74.14	0.67	$0.12 \times 10^3/\mu L$	34.91
	IG%	87.34	72.41	0.60	1.22%	18.11
	Procalcitonin	92.41	68.97	0.61	1.78 ng/mL	27.06
	Lactate	64.56	72.41	0.37	1.1 mmol/L	4.78
Period 4	IG#	89.87	82.76	0.73	$0.13 \times 10^3/\mu L$	42.59
	IG%	89.87	77.59	0.67	1.22%	30.72
	Procalcitonin	88.61	81.03	0.69	2.22 ng/mL	33.23
	Lactate	72.22	58.62	0.36	0.9 mmol/L	3.68

Sensitivity, specificity, and best criteria or cutoff value are given for each biomarker in every time period. DOR compares the diagnostic power of biomarkers

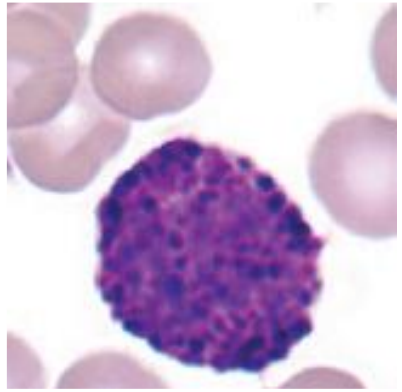
Basofil

- Basophilia (peningkatan jumlah basofil)

  Contoh : reaksi hipersensitivitas akut, infeksi kronis, *Myeloproliferative disorder* (MPD)

- Basopenia (penurunan jumlah basofil)

  Contoh : *hyperthyroidism*, tirotoksikosis, infeksi akut



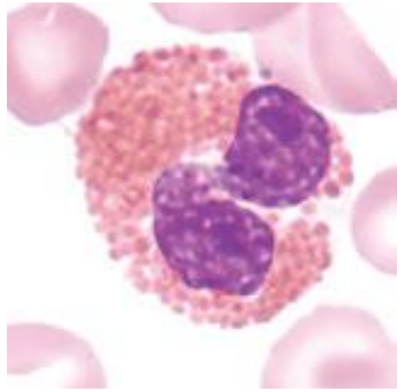
Eosinofil

- Eosinofilia (peningkatan jumlah eosinofil)

  Contoh : alergi, infeksi parasit, hipereosinofilia (eosinofil > 1,5 x 10^9/L selama lebih dari 6 bulan)

- Eosinopenia (penurunan jumlah eosinofil)

  Contoh : Terapi steroid (*Cushing's syndrome*), inflamasi akut/sepsis



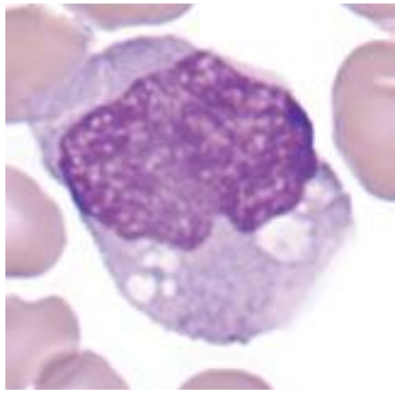
Monosit

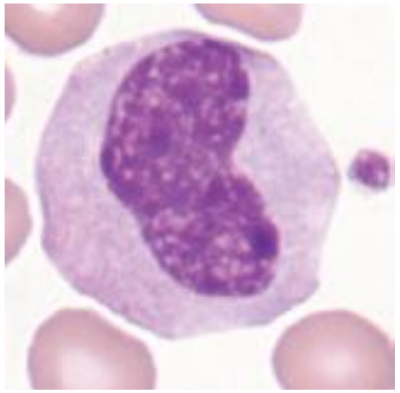
- Monositosis (peningkatan jumlah monosit)

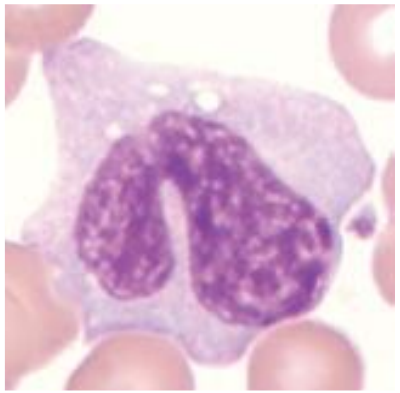
  Contoh : artritis rematoid, SLE, infeksi kronis (TBC, *subacute bacterial endocarditis*), keganasan

- Monositopenia (penurunan jumlah monosit)

  Contoh : terapi steroid, infeksi HIV, TB milier, infeksi EBV

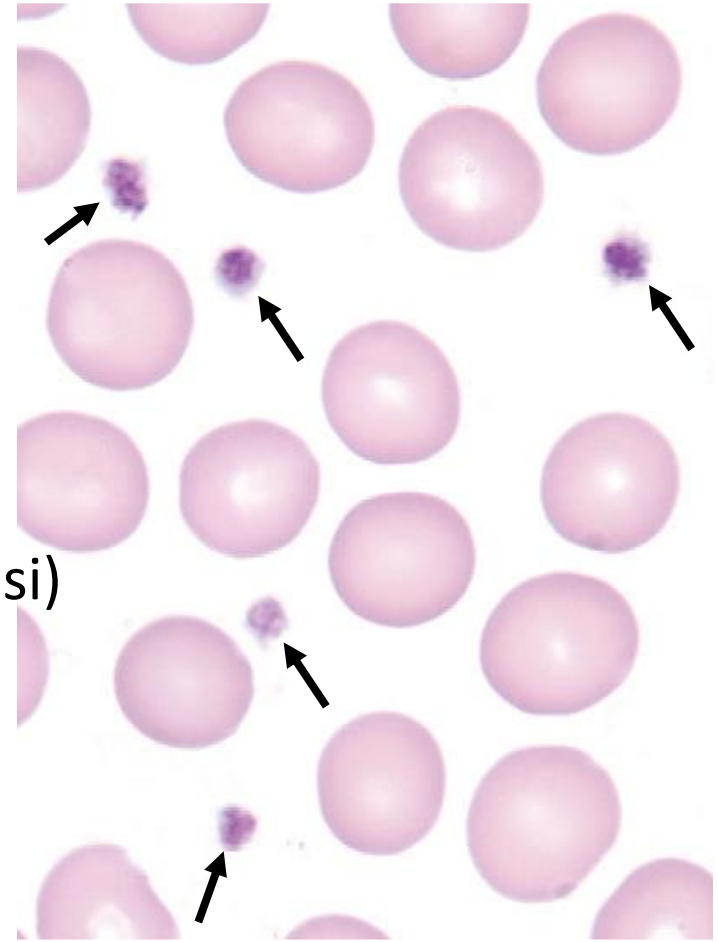






Trombosit/*Platelet*

- Struktur *discoid* yang diselaputi membran
- Berasal dari pecahan sitoplasma megakariosit
- Diameter ± 2-3 µm, masa hidup di sirkulasi 7-10 hari
- Berperan dalam hemostasis (adhesi, reaksi pelepasan, dan agregasi)
- Kelainan trombosit : jumlah dan fungsi



Lanjutan

	F/8th	M/50th		
Parameter	**Hasil**	**Hasil**	**Nilai Rujukan**	**Satuan**
Hemoglobin (Hb)	10,8	**9,1**	12,0-15,0	g/dL
Hematokrit (Ht)	33,2	**27,4**	35,0-49,0	%
Eritrosit (RBC)	4,2	**3,1**	4,0-5,4	Juta/µL
MCV	85	82,9	80-94	fL
MCH	27	27,5	26-32	Pg
MCHC	35,1	33,5	32-36	%
Leukosit	6,0	**2,3**	4,50-13,5	rb/µL
Trombosit	**12**	**4**	150-450	rb/µL

Interpretasi :

- Trombositopenia

Etiopatologi :

- Hipoproduktif (produksi berkurang)
- Hiperdestruktif (penghancuran bertambah)

Pemeriksaan lanjutan untuk menentukan penyebab trombositopenia :

- Indeks *Platelet* : PCT, PDW, MPV, P-LCR, IPF

Indeks Trombosit

Parameter	**Nilai Rujukan**	**Satuan**
Plateletcrit (PCT)	0,17-0,32	%
Platelet Distribution Width (PDW)	9-13	%
Mean Platelet Volume (MPV)	7,2-11,2	fL
Platelet Large Cell Ratio (P-LCR)	17,5-42,3	%
Immature Platelet Fraction (IPF)	0,8-6,03	%

Lanjutan

F/8th

Parameter	Hasil	Nilai Rujukan	Satuan
Trombosit	12 ↓	150-450	ribu/µL
PCT	0,12 ↓	0,17-0,32	%
PDW	16 ↑	9-13	%
MPV	13 ↑	7,2-11,2	fL
P-LCR	48 ↑	17,5-42,3	%
IPF	8,3 ↑	0,8-6,03	%

Interpretasi :

Kasus F/8th

- PCT ↓ : persentase trombosit dalam darah menurun
- PDW ↑: terdapat berbagai variasi ukuran trombosit di perifer
- MPV ↑ : rerata ukuran trombosit meningkat
- P-LCR ↑ : jumlah trombosit berukuran besar meningkat
- IPF ↑ : respons sumsum tulang terhadap trombositopenia baik

Kesimpulan : trombositopenia terjadi karena peningkatan destruksi trombosit (trombositopenia hiperdestruktif)

Lanjutan

M/50th

Parameter	Hasil	Nilai Rujukan	Satuan
Trombosit	4 ↓	150-450	ribu/µL
PCT	0,01↓	0,17-0,32	%
PDW	6 ↓	9-13	%
MPV	14,7 ↑	7,2-11,2	fL
P-LCR	56,7 ↑	17,5-42,3	%
IPF	0,52 ↓	0,8-6,03	%

Interpretasi :

Kasus M/50th

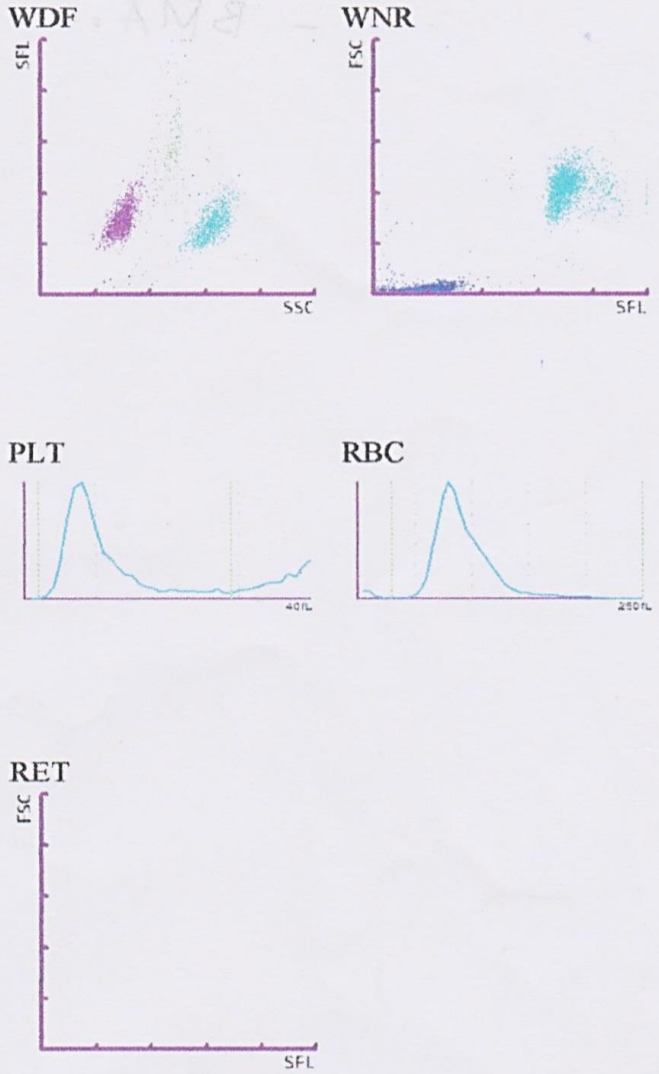
- PCT ↓ : persentase trombosit dalam darah menurun
- PDW ↓ : ukuran trombosit di perifer hampir sama
- MPV ↑ : rerata ukuran trombosit meningkat
- P-LCR ↑ : jumlah trombosit berukuran besar meningkat
- IPF ↓ : respons sumsum tulang terhadap trombositopenia kurang adekuat

Kesimpulan : trombositopenia terjadi karena peningkatan destruksi trombosit (trombositopenia hipoproliferatif)

PARAMETERS				NILAI RUJUKAN			
HGB	8.8	-	[g/dL]	L	13,3	-	16,6
				P	11,0	-	14,7
RBC	2.88	-	[10^6/uL]		3,69	-	5,46
HCT	25.7	-	[%]	L	41,3	-	52,1
				P	35,2	-	46,7
MCV	89.2		[fL]		86,7	-	102,3
MCH	30.6		[pg]		27,1	-	32,4
MCHC	34.2	+	[g/dL]		29,7	-	33,1
RDW-SD	59.9	+	[fL]		41,2	-	53,6
RDW-CV	19.8	+	[%]		12,2	-	14,8
NRBC%	0.3		[%]				
NRBC#	0.01		[10^3/uL]				
WBC	3.34	-	[10^3/uL]		3,37	-	10
EO%	0.0	*	[%]		0,6	-	5,4
BASO%	0.3		[%]		0,3	-	1,4
NEUT%	40.7	*	[%]		39,8	-	70,5
LYMPH%	52.1	*	[%]		23,1	-	49,9
MONO%	6.9	*	[%]		4,3	-	10,0
EO#	0.00	*	[10^3/uL]				
BASO#	0.01		[10^3/uL]				
NEUT#	1.36	*	[10^3/uL]				
LYMPH#	1.74	*	[10^3/uL]				
MONO#	0.23	*	[10^3/uL]				
IG%	0.6	*	[%]				
IG#	0.02	*	[10^3/uL]				
PLT	58	-	[10^3/uL]		150	-	450
PDW	10.1		[fL]		9,6	-	15,2
MPV	10.6		[fL]		9,2	-	12,0
P-LCR	26.6		[%]		19,7	-	42,4
PCT	0.06	-	[%]		0,19	-	0,39
RET#			[10^6/uL]		0,034	-	0,100
RET%			[%]		0,80	-	2,21
IRF			[%]		3,2	-	13,3
LFR			[%]		87,1	-	98,3
MFR			[%]		3,1	-	11,8
HFR			[%]		0,1	-	1,4
RET-He			[pg]		31,9	-	37,3

LED

SCATTERGRAM / HISTOGRAM



HCT


TERIMA KASIH