



همایش سراسری انجمن خون و سرطان کودکان ایران  
با موضوع بیماریهای گلبول سفید در کودکان

چهاردهمین

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White Blood Cell Disorders in Children

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# Approach to Monocytosis

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# Agenda

- **Definition of monocytosis**
- **Chronicity of monocytosis**
- **How to approach to monocytosis**
- **Differentiate neoplastic from non-neoplastic causes**
- **Work-up of patients with monocytosis**
- **Guideline-based approaches**

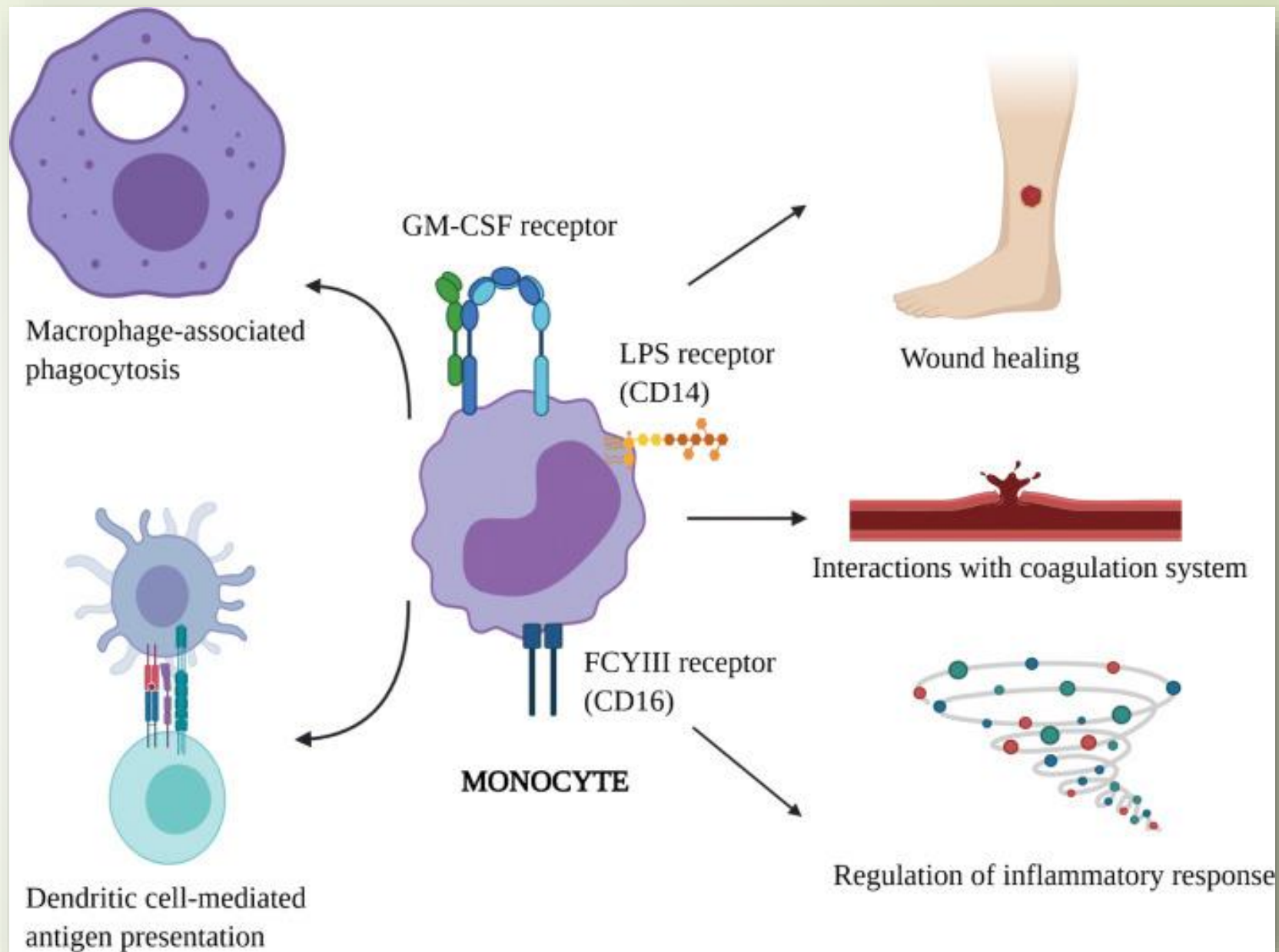
# NL monocyte development and function

- **Monocytes are derived from** a common **granulocyte-monocyte precursor** and progress through the proliferative stages of **monoblasts**, **promonocytes**, and **monocytes** under the influence of **cytokines**, particularly **IL-3**, **IL-6**, and **GM-CSF**, within the marrow space or spleen.
- Once mature, monocytes **irreversibly** leave the bone marrow space to **the blood** and further **migrate into tissues** where they differentiate into **tissue-specific macrophages** or **dendritic cells**.
- Monocytes are your **cell's firefighters**

**Immunological Reviews 2014. Vol. 262: 167–178**

## The diverse functions of monocytes in humans

Curr Hematol Malig Rep.  
2021; 16(3): 267–275.





# Monocyte

- Monocytes are large agranular cells that compose **1-9%** of the leukocyte pool. **It is important to calculate the AMC.**
- Monocyte immune functions, including **phagocytosis**, **antigen presentation**, and **cytokine production**.
- Monocytes continue to gradually rise to a peak value of **1500 cells/ $\mu$ l** until **2-week post birth**.
- Monocyte count decreases to below **1000 cells/ $\mu$ l**, which is the WHO threshold for absolute monocytosis,

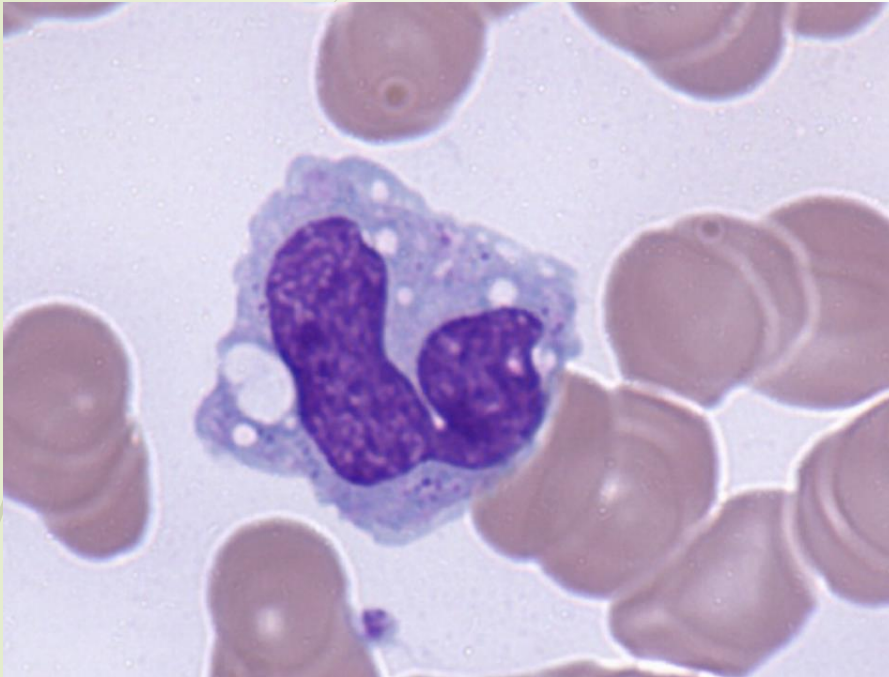
**Current Hematologic Malignancy Reports (2021) 16:267–275**

# Monocytosis

- Racial differences are only minimal,
- Slightly lower absolute monocyte counts in Blacks and Asians compared to Caucasians
- persistent monocytosis as an absolute monocyte count  $> 1 \times 10^9/L$  with monocytes accounting for  $> 10\%$  of leukocytes  
**persisting for  $> 3$  months**

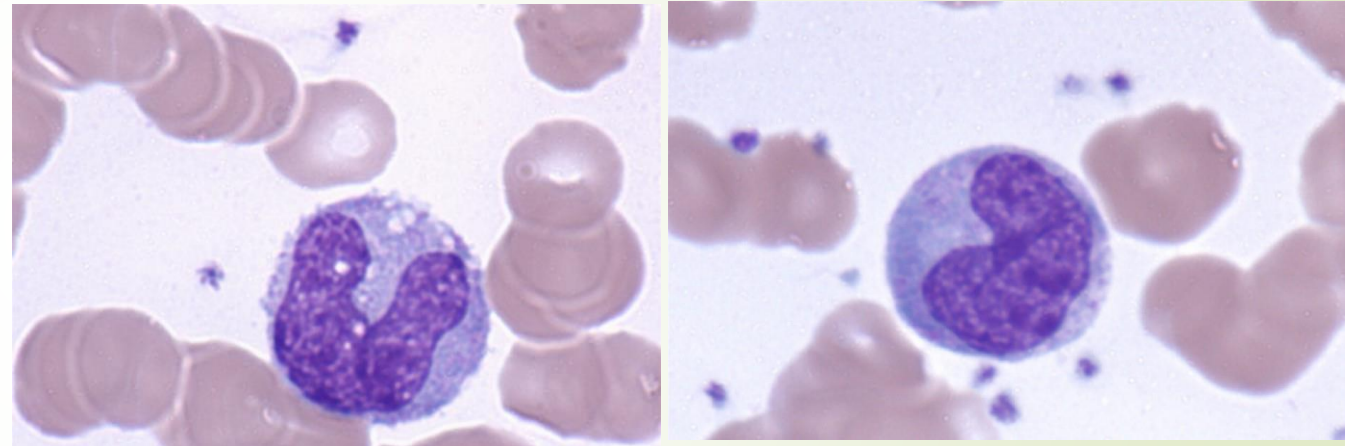
Immunological Reviews 2014. Vol. 262: 167–178

# Monocyte Morphology



Typical monocyte with a folded nucleus, fine azurophilic granulation in pale, gray-blue cytoplasm.

- Nucleus may have a "kidney-bean" shape or a cerebriform appearance.
- Nucleus may have a folded appearance.



ASH | Image Bank



# Morphology

1-Monocyte

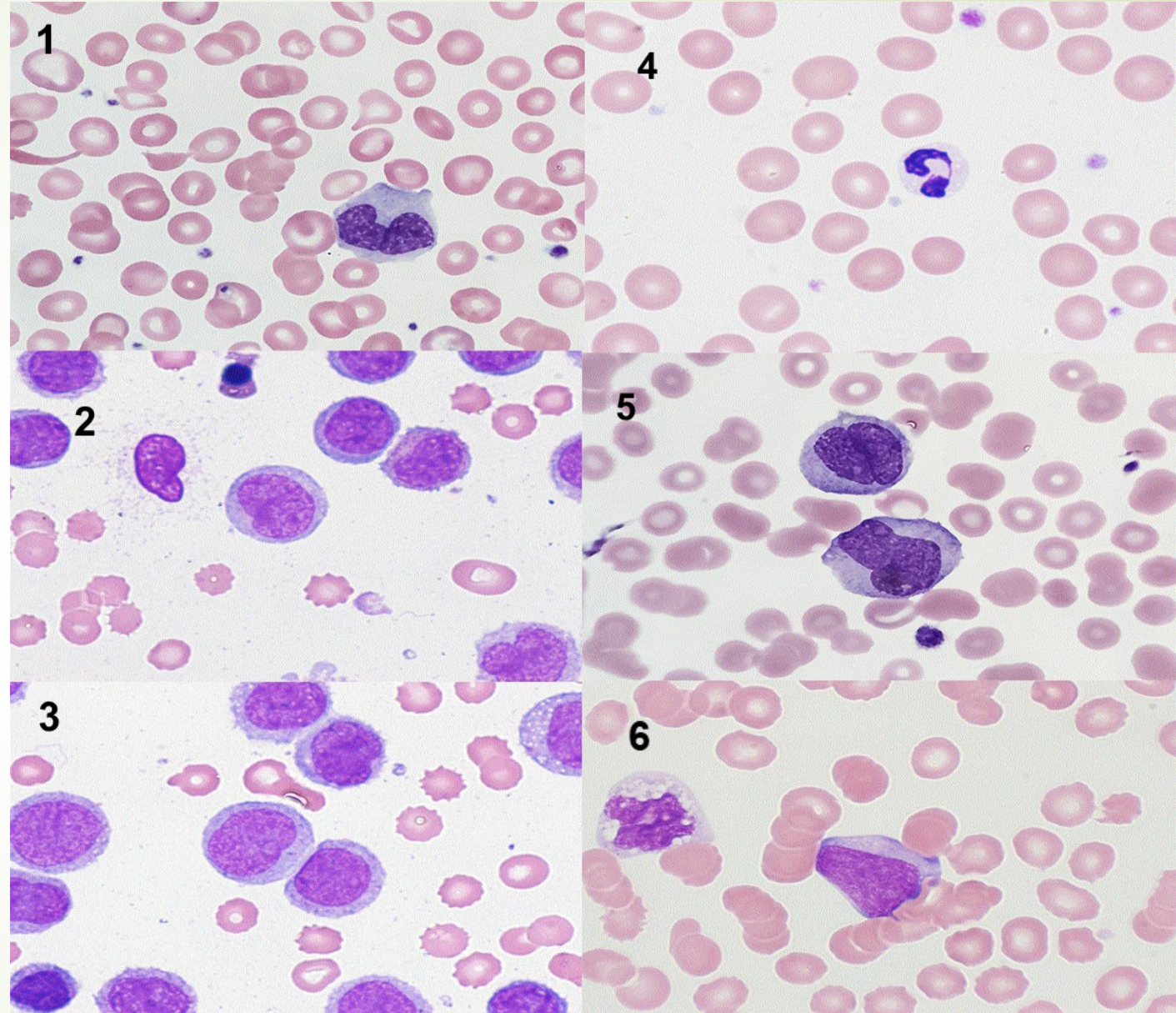
2- Promonocyte

3-Monoblasts

4-CMML with hypolobated  
hyperchromatic nucleus & hypo granular  
cytoplasm

5-abnormal monocyte

6-myeloblast in AML





# Cytochemical stains of Monocyte

- In clinical practice, it can be quite **difficult** to apply morphologic criteria when distinguishing reactive or dysplastic monocytes from promonocytes or monoblasts. As such, **interobserver variability can be quite high.**
- Monocytic cells at all stages of maturation characteristically show strong and diffuse **cytoplasm** positivity for the nonspecific esterases (NSE), alpha-naphthyl acetate, and alpha-naphthyl butyrateic, while **granulocytic lineage cells are negative or very weakly positive for these stains.**

# Flow cytometric analysis of Monocyte

- Most normal monocytes express moderate intensity CD45 with strong CD33, CD13, CD36, CD4, CD14, CD64, CD11b, CD11c, dim CD15, and HLA-DR.
- “classical” CD14++ CD16– monocytes usually account for approximately 90% of monocytes in healthy adults
- “intermediate” CD14+ CD16+
- “nonclassical” CD14– CD16+
- CD56, one of the more commonly expressed aberrant antigens in both reactive and neoplastic conditions
- It is also worth emphasizing that markers of immaturity detected by flow cytometry and/or immunohistochemistry, such as CD34 and/or CD117, are not reliably expressed on monoblasts or promonocytes

**Int J Lab Hematol. 2018 Apr;40(2):107-114**

# Etiology of Monocytosis

## Infection

- Kala-azar
- Malaria
- TB
- Rocky Mountain spotted fever
- Subacute bacterial endocarditis
- Syphilis
- infectious mononucleosis
- **COVID-19**

## Autoimmune and inflammatory disorders

- Inflammatory bowel disease
- Myositis
- Rheumatoid arthritis
- Sarcoidosis
- Systemic lupus erythematosus
- ITP

## Marrow stress

- Bone marrow recovery from transient neutropenia
- Cyclic neutropenia
- Hemolytic anemia
- Severe chronic neutropenia
- Sickle cell anemia



# Etiology of Monocytosis (cont...)

## Malignancy

- AML
- Cutaneous myeloid dendritic dysplasia
- Histiocytic medullary reticulosis
- Lymphoid and plasma cell malignancies, esp. Hodgkin lymphoma
- MDS
- MPN, esp. CMML and JMML
- Solid tumors, for example, carcinoma

## Iatrogenic Causes

- Antipsychotics, for example, ziprasidone
- Corticosteroids
- Cytokine therapy, for example, G-CSF, GM-CSF
- Radiation therapy

## Other

- Chronic stress
- Lipoidoses, for example, NiemannPick disease
- Myocardial infarction
- Postsplenectomy
- Tetrachloroethane poisoning
- Exercise

# Signs and Symptoms of monocytosis

- **Monocytes can settle in the spleen or liver, enlarging these organs**
- **pain in the upper left part of the abdomen**
- **early satiety**
- **pain in the upper right part of the abdomen**

# Stepwise investigation

## Initial steps to investigate monocytosis

- Confirm the presence of monocytosis by PBS
- Assess the AMC
- Assess for other CBC abnormalities
- Duration of monocytosis
- Evaluate size of spleen, liver, and lymph nodes
- Past medical history

## Next steps to take

- BM examination
- Flow cytometry
- Immunohistochemistry/cytochemistry
- Cytogenetic studies
- Molecular genetic testing



# Monocytosis with various conditions

**Monocytosis with cytopenias**

**Monocytosis with cytoses**

**Monocytosis with neutropenia**

**Monocytosis with atypical lymphocyte**

**Monocytosis with dysplasia**

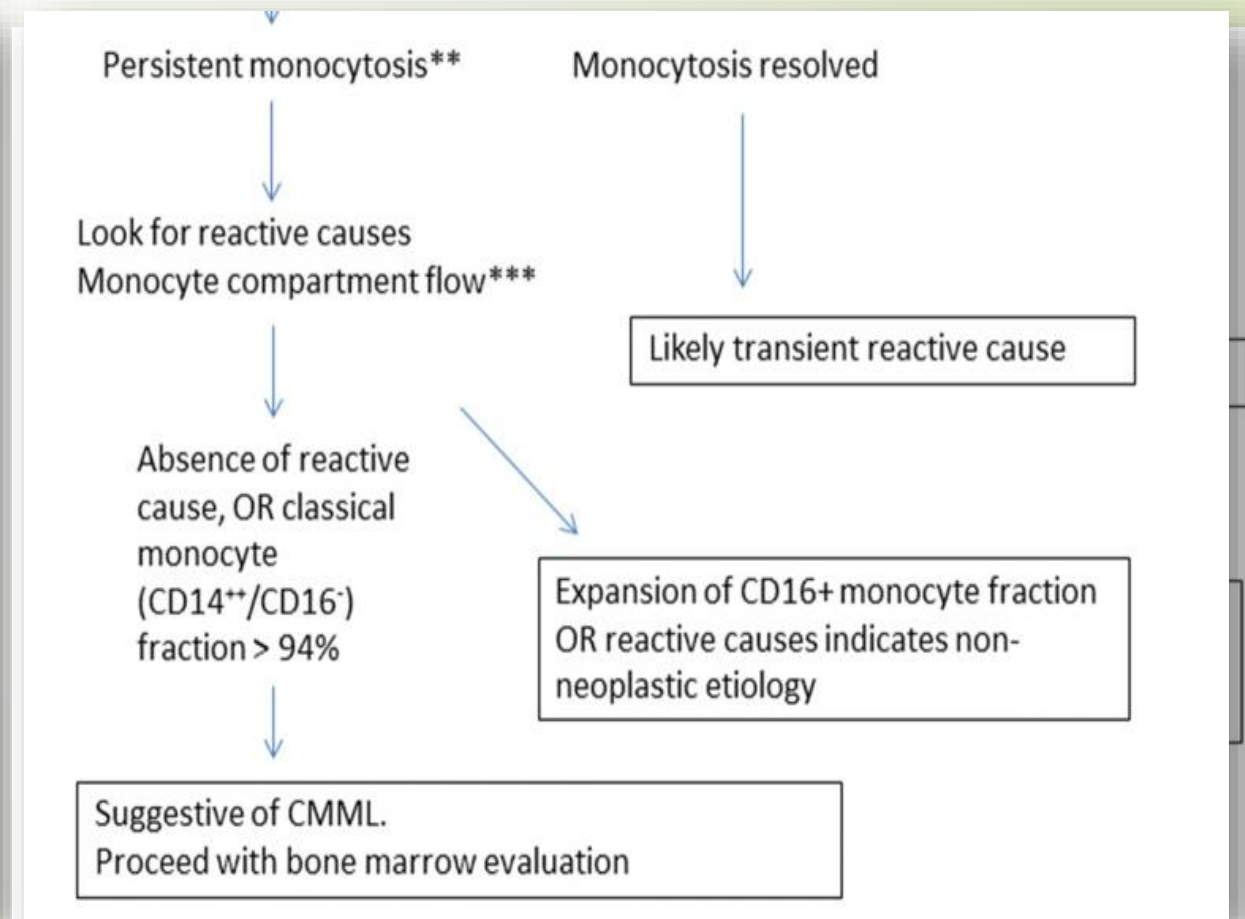
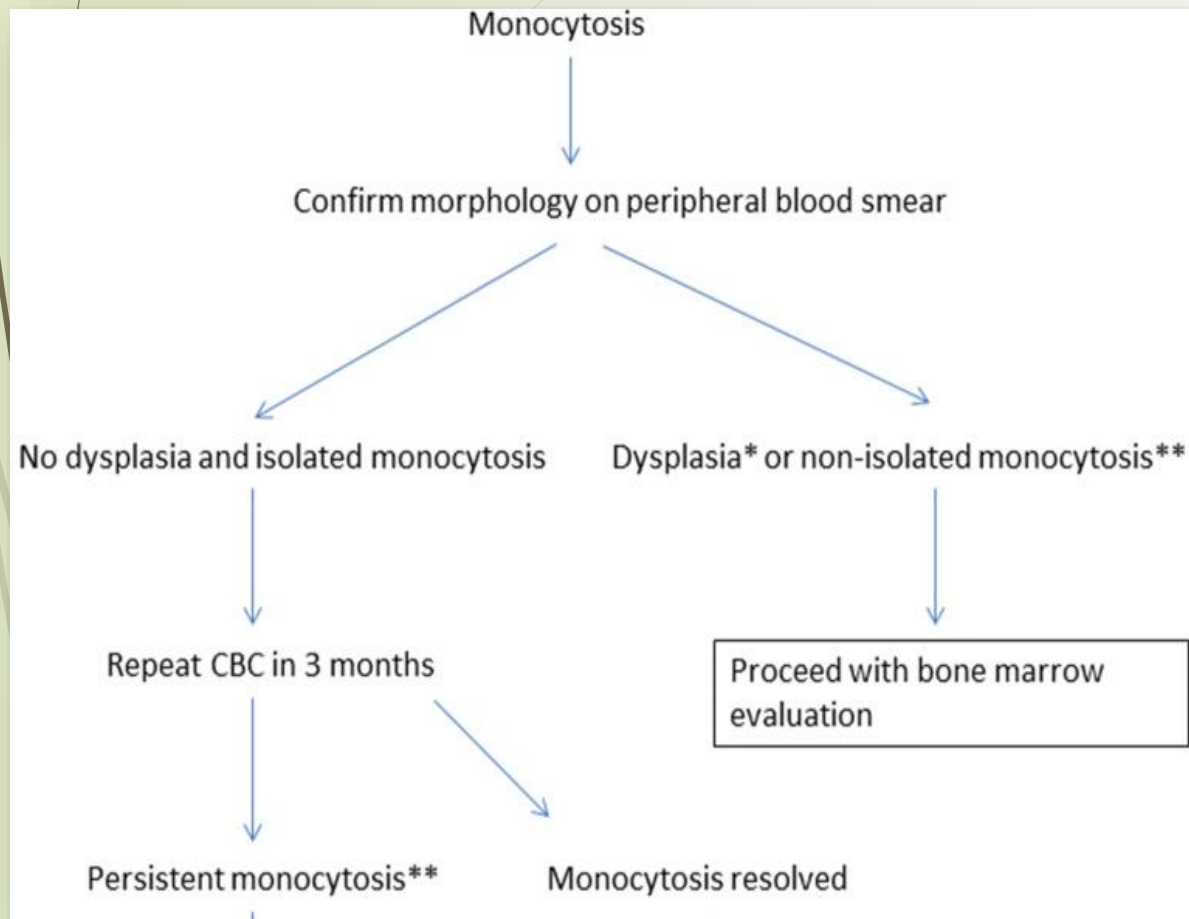
**Monocytosis with thrombocytopenia**

**Monocytosis with splenomegaly**

## Assessment and Recommendation

AMC $\geq 1 \times 10^9/L$	+	+	+
RMC $\geq 10\%$	+	$\pm$	$\pm$
Granulocytic dysplasia	+	-	-
Promonocytes	$\pm$	-	-
Blasts	+	$\pm$	-
Cytopenias	+	-	-
Left-shifted neutrophilia	$\pm$	$+^{b,e}/-$	$\pm$
Basophilia	-	$+^b/-$	-
Eosinophilia	$+^a/-$	$+^f/-$	$\pm$
Thrombocytosis	-	$+^{d,e}/-$	$\pm$
Polycythemia	-	$+^c/-$	-
Splenomegaly	+	+	-
History of recent chemotherapy, infection, inflammatory disease, trauma, and malignancy	-	-	$\pm$
<b>Assessment</b>	Possible neoplasm such as MDS/MPN (CMML); AML w/ monocytic differentiation; myeloid neoplasm with PDGFRB <sup>a</sup>		Possible neoplasm such as MPN with monocytosis (eg, CML <sup>b</sup> , PV <sup>c</sup> , ET <sup>d</sup> , PMF <sup>e</sup> ); systemic mastocytosis <sup>f</sup>
<b>Recommendation</b>	Bone marrow examination with appropriate ancillary studies (eg, chromosome analysis, FISH, molecular testing, flow cytometry)		Likely reactive
			Close clinical correlation and follow-up [If persistent and unexplained, then consider bone marrow examination]

# Guideline-based approach to monocytosis





# Take home message

**In monocytosis, we should differentiate neoplastic from non-neoplastic causes**

**If suspicious to neoplastic cause BM examination**

**If monocytosis is persistent BM examination**

**Monocytosis itself is only a symptom and doesn't require treatment. Treating the underlying cause will resolve the monocytosis.**



**Thanks.**

**Dr.N.Shakibazad**  
**Approach to Monocytosis**