

Blood Day for Primary Care

When do I work up an elevated White Blood Cell count?





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Disclosures

- 1. Grant support from Roche, Lundbeck, Gilead and Johnson & Johnson pharmaceuticals
- 2. Advisory boards for Roche, Lundbeck, Gilead and Johnson & Johnson pharmaceuticals
- Participate in clinical trials sponsored by Roche, Gilead and Millenium
- Canadian CLL Research Meeting supported by Roche, Gilead, Lundbeck, Johnson & Johnson and Glaxo-Smith Kline



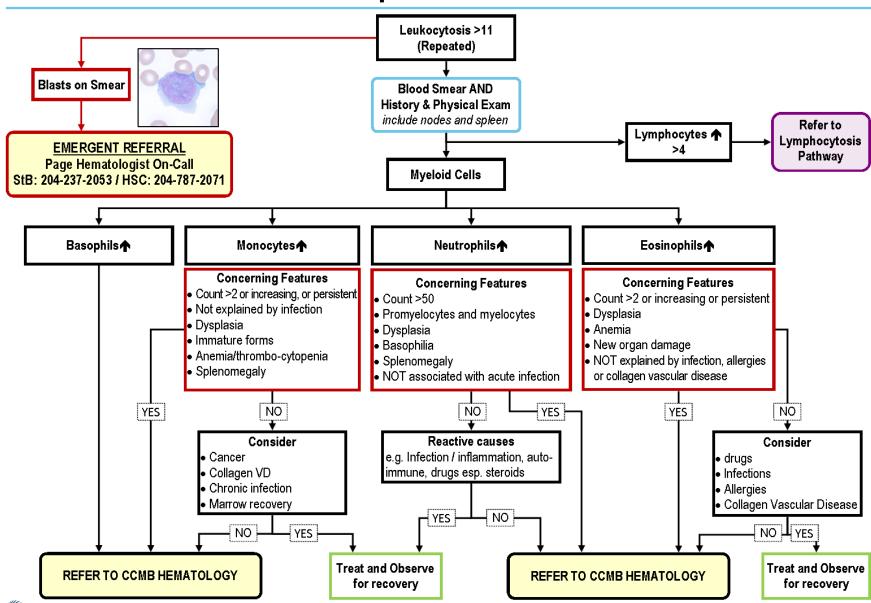


Objectives

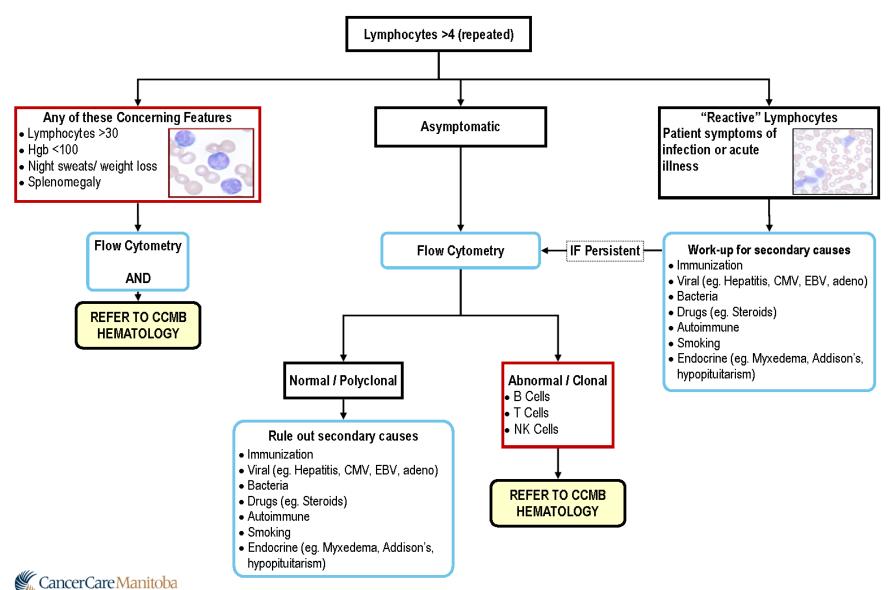
- 1. To know how to work up a case of leukocytosis
- 2. To know what flow cytometry is and how/when to order this test
- 3. To know when to refer a patient with leukocytosis



Work-Up of LEUKOCYTOSIS



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George IT. Hematology, 475-484, 2012 (Adapted) Feb.6, 2015: ©Hematology DSG FINAL (Johnston)
Pathways are subject to clinical judgment and actual practice patterns may not always follow the proposed steps in this pathway.



George IT. Hematology, 475-484, 2012 (Adapted) Feb.6, 2015: ©Hematology DSG FINAL (Johnston)

ActionCancerManitoba George IT. Hematology, 47
Pathways are subject to clinical judgment and actual practice patterns may not always follow the proposed steps in this pathway.



Secondary lymphocytosis

- Immunization
- 2. Viral (eg hepatitis, CMV, EBV, adeno)
- 3. Bacterial
- 4. Drugs, eg, steroids
- 5. Autoimmune
- 6. Smoking
- 7. Endocrine (myxedema, Addison's, hypopituitarism)

May be B cell, T cell or NK cell





Malignant Lymphocytosis

1. B cell

- 1. Chronic lymphocytic leukemia (CLL)/small lymphocytic lymphoma (SLL)
- 2. Lymphomas with leukemic involvement

2. T cell

- 1. Large granular lymphocytic leukemia
- 2. Lymphomas with leukemic involvement

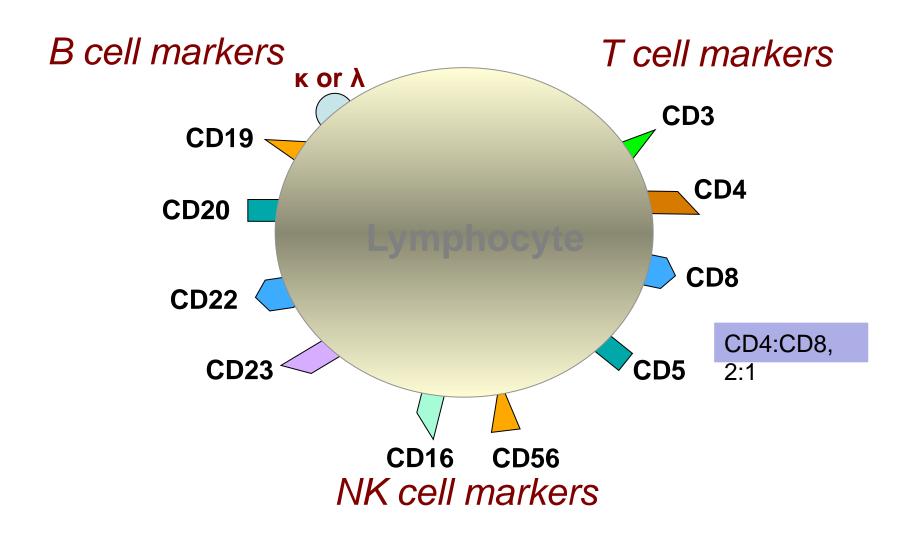
3. NK cells

1. NK cell leukemia

Andrews et al. Leuk Lymph, 49:1731, 2008



Flow cytometry for lymphocytes



- About 150 cluster differentiation (CD) markers to differentiate blood cell of origin
- Performed at HSC or St B. Ensure you state what you are looking for!



Flow Cytometry

	CD19	CD5	CD23	CD10	CD25	CD79b	FMC7	CD103
CLL	++	++	++	-	+/-	-	-/+	-
Follicullar lymphoma	++	-/+	-/+	++	-	++	++	-
Mantle cell lymphoma	++	++	1	-/+	ı	++	++	-
Marginal zone lymphoma	+	-	+/-	-	1	++	+	-
Hairy cell leukemia	+++		-	-	+++	+	+++	+++
Lymphoplasmacyto id lymphoma	++	-	-	-	-/+	+	+	-
Marginal zone lymphoma	+	-	+/-	-	-	++	+	-

Cells must be monoclonal for kappa or lambda light chains!



Typical Referral

Homato.	logy
CBC	

Toot	03/12/2014	REFERENCE	UNITS
Name	11:00	RANGE	
WBC	9.6	4.5-11-0	x10E9/L
REC	3,43 L	4.4-5.9	x10E12/L
RB	92) L	140-180	g/L
HCT	0.304 L	0.4-0.52	L/L
NCV	58.6	90-98	fL
MCH	26.8	26-34	pg
NCHC	303 L	320-365	9/1
90%-CV	19.5 H	11.4-14 4	9
PLT	—— 180	140-440	x10E9/L
MPV	9.2 I	9.4-12.4	±L
2 NEOTS	2.0	1,9-5,4	x10E9/L
4 LYMPHS	6.8 H	1.3-3.2	x10E9/L

Hematology CBC

Tost	03/12/2014	REFERENCE	UNITS	
Nwno	11:00	RANGE		

HEMATOPATHOLOGIST SMEAR REVIEW

SEE COMMENT

HEMATOPATHOLOGIST INTERPRETATION: RECOMMEND RECOLLECTION OF PERIPHERAL BLOOD FOR FLOW CYTOMETRY IMMUNOPHENOTYPIC ANALYSIS TO RULE OUT A LYMPHOPROLIFERATIVE DISORDER REVEWED BY DR. PING SUN (PH:204-258-1114, PAGER:204-935-2908).

Lab # NK66134-8 Collected on 18 Dec 14 at 08:05

Your reference -

Copies sent to: IMMUNOLOGY LAB - HSC

RESULTS

REFERENCE

UNIT

Blood Phenotyping FLOW CYTOMETRY COMMENT:

The sample contains 50% lymphocytes. 20% are T cells CD4/8=3, 7% NK cells, and the rest are K+dim, CD20+dim, CD19+, CD5+, CD23+, CD43+, CD79b+dim, CD38-, ZAP70- B cells. Phenotypic findings are consistent with chronic lymphocytic leukemia. Morphological and clinical correlation required. The ZAP-70 results (% of CLL cells in which ZAP-70 expression is detected) provided are to be interpreted and used at the discretion of the requesting physician . Method adapted from Rassenti et al N Engl J Med 2004 August 26; 351(9):893-901.

Flow Cytometry Signed By: Dr. Carmen Morales

- To be malignant cells need to be monoclonal, ie, either kappa (K) or lambda (L)
- CD19+, CD5+ and CD23+ is diagnostic for CLL cells
- ZAP-70 and CD38 are prognostic markers
- Pt has CLL





Immunophenotype for 71 Normal Individuals >50 years with Lymphocytes >4

Diagnosis	%
Normal	41%
CLL immunophenotype	38%
Other lymphomas	7%
NK cells	7%
T-cell LGL	7%

Likelihood of being abnormal increases with:

- patient age
- lymphocyte count

Andrews JM et al. Leuk Lymph 49:1731, 2008





Take-Home Message

- If blasts on smear phone 'hematologist-on-call' at SBGH or HSC
- Most leukocytosis are transient and are a response to infection, inflammation or drugs
- Mild peripheral lymphocytosis is common in older patients and cause can be diagnosed by flow cytometry





Interactive Question

- Question: An asymptomatic 72 year old man is found on routine blood work to have a lymphocyte count of 56.
 Physical exam normal. What would be your next option:
 - a) Screen for EBV and HIV
 - b) Bone marrow
 - c) CT scans of chest and abdomen
 - d) Flow cytometry 🗸





Questions?

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