Casual Friday Series

Functional Blood Chemistry Series: CBC pt. III

A Biogenetix Clinical Presentation

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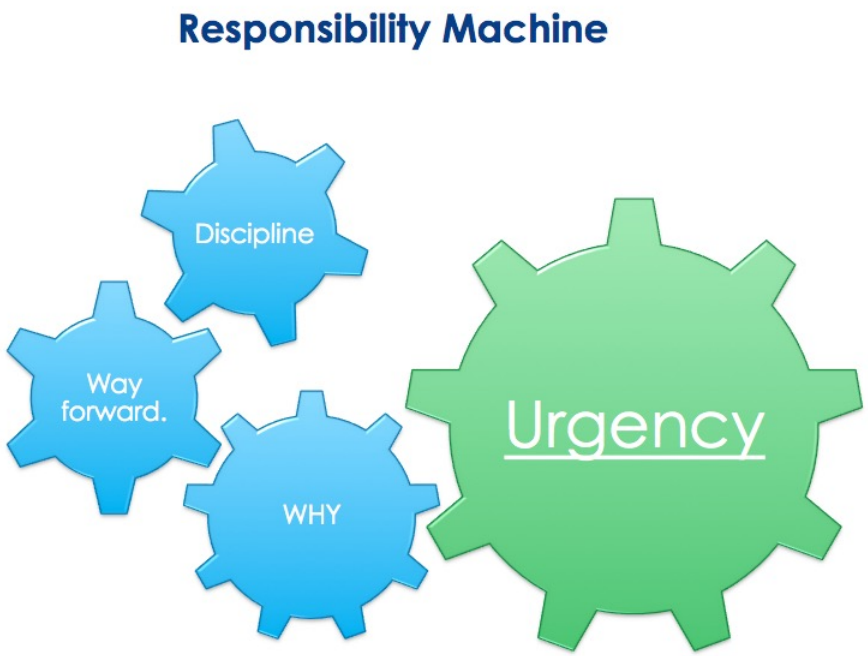
- *The information provided in this presentation is for your consideration only as a practicing health care provider. Ultimately you are responsible for exercising professional judgment in the care of your own patients.*

Applied FM



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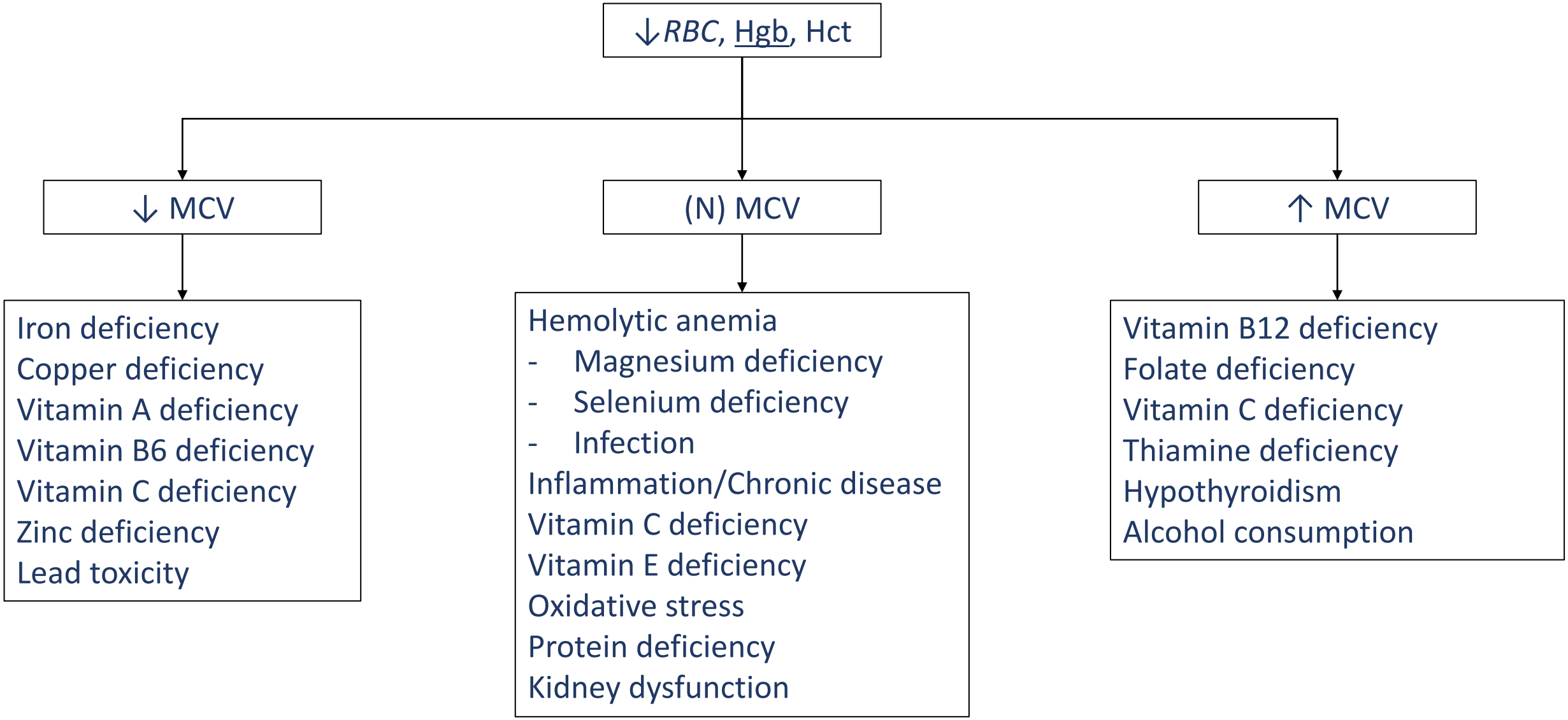
= **Progress.**


↓*RBC*, Hgb, Hct
↓ MCV
(N) MCV
↑ MCV
Iron deficiency
Copper deficiency
Vitamin A deficiency
Vitamin B6 deficiency
Vitamin C deficiency
Zinc deficiency
Lead toxicity
Hemolytic anemia
- Magnesium deficiency
- Selenium deficiency
- Infection
Inflammation/Chronic disease
Vitamin C deficiency
Vitamin E deficiency
Oxidative stress
Protein deficiency
Kidney dysfunction
Vitamin B12 deficiency
Folate deficiency
Vitamin C deficiency
Thiamine deficiency
Hypothyroidism
Alcohol consumption

Differentiating Between Destruction and Loss

	Anemia Due to Blood Loss	Anemia of Inflammation	Hemolytic Anemia	Iron Deficiency
RBC	↓	↓	↓	↓
Hgb	↓	↓	↓	↓
Hct	↓	↓	↓	↓
MCV	N	N↓	N↓	↓
MCH	N	N↓	N↓	↓
MCHC	N	N↓	N↓	↓
RDW	N	N	N	↑
Iron	↓		↑	↓
Ferritin	↓	↑	↑	↓
TIBC	↑			↑
Reticulocyte Count	↑	N↓	↑	N↓
Transferrin Receptor		N↓		↑

	Iron Deficiency	Vitamin A Deficiency	Copper Deficiency	Zinc Deficiency	Vitamin B6 Deficiency	Hemolytic Anemia
RBC	↓	↓	↓	↓	↓	↓
Hgb	↓	↓	↓	↓	↓	↓
Hct	↓	↓	↓	↓	↓	↓
MCV	↓	↓	↓	↓	↓	N↓
MCH	↓	↓	↓	↓	↓	N↓
MCHC	↓	↓	↓	↓	↓	N↓
RDW	↑	↑	↑	↑	↑	N
Iron	↓	↑	↓	↑	↑	↑
Ferritin	↓	↑	↓	↑	↑	↑
TIBC	↑	↓	↑	↓	↓	↓
Reticulocyte Count	↓	↓	↓	↓	↓	↑
Transferrin Receptor	↑		↑			
Ceruloplasmin/ Copper			↓			
AST					↓	
ALT					↓	
Neutrophils			↓			
Homocysteine					↑	
Alkaline Phosphatase				↓		

Iron - Elevated

Cause	Reason	Additional Inquiry
Hemosiderosis, hemochromatosis	Genetic conditions clients are likely already aware of. Iron overload.	Client history.
Hemolytic anemia	If RBCs break-down, iron will be released and can increase in the serum.	Evaluate CBC markers.
Liver damage	Liver and spleen are major sources of iron storage. Thus, if there is active liver inflammation iron levels may increase.	Evaluate liver markers.
Vitamin B6 deficiency	If B6 is not available for heme synthesis, iron will not be used and can increase.	Evaluate AST, ALT.

Iron - Decreased

Cause	Reason	Additional Inquiry
Poor intake		Diet journal.
Poor absorption		Diet journal.
Chronic blood loss	Heavy menstruation, GI bleed	Client history. Reticulocytes. CBC.
Chronic disease and/or chronic infection	Iron either becomes depleted or sequestered.	Client history.
Progesterone birth control pills	Association	Client history.

Ferritin - Elevated

Cause	Reason	Additional Inquiry
Hemosiderosis, hemochromatosis	Genetic conditions clients are likely already aware of. Iron overload.	Client history.
Inflammatory diseases	Acute phase reactant.	Evaluate other inflammation markers.
Liver damage	Liver and spleen are major sources of iron storage. Thus if there is active liver inflammation iron levels may increase.	Evaluate liver markers.
Hemolytic anemia, sideroblastic anemia	Iron is being lost or unused from RBCs, thus leading to excess iron.	Evaluate CBC.

Ferritin - Decreased

Cause	Reason	Additional Inquiry
Poor intake		Diet journal.
Poor absorption		Diet journal.
Chronic blood loss	Heavy menstruation, GI bleed	Client history.
Chronic disease and/or chronic infection	Iron either becomes depleted or sequestered.	Client history.
Progesterone birth control pills		Client history.

White Blood Cell Count

- Refers to total amount of white blood cells
- The CBC with differential includes the five major types of white blood cells:
  - Neutrophils, lymphocytes, monocytes, eosinophils, basophils
- The WBC count is of limited value without the differential
- In general, an elevated WBC indicates an infection of an acute nature, and a decreased WBC count indicates an infection of a more chronic nature.
  - Decreased WBCs are often seen in autoimmune conditions and pernicious anemia as well.
- Interestingly, high-normal white blood cell counts, along with neutrophils, can indicate possible endothelial dysfunction and peripheral artery disease

White Blood Cell Count

Interfering factors include:

- Stress: epinephrine response can increase white blood cells
- Time of day: lower in the morning, higher in the evening
- Other: age, gender, exercise, pregnancy, pain, temperature and altitude can all affect results
- Early infection/inflammation: Migration out of blood may temporarily lower serum numbers before compensation takes place

ORIGINAL INVESTIGATION

Leukocyte Count as a Predictor of Cardiovascular Events and Mortality in Postmenopausal Women

The Women's Health Initiative Observational Study

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Background: Increasing evidence supports a role for inflammation in the atherosclerotic process. The role of the leukocyte count as an independent predictor of risk of a first cardiovascular disease (CVD) event remains uncer-

L), women in the fourth quartile (6.7-15.0×10⁹ cells/L) had over a 2-fold elevated risk for CHD death (hazard ratio, 2.36; 95% confidence interval, 1.51-3.68), after mul-

deaths, 701 nonfatal myocardial infarctions, 738 strokes, and 1919 deaths from all causes. Compared with women with WBC counts inthe first quartile (2.5-4.7×10⁹ cells/

rently identified by traditional CVD risk factors.

Arch Intern Med. 2005;165:500-508

The WBC count, a stable, well-standardized, widely available and inexpensive measure of systemic inflammation, is an independent predictor of CVD events and all-cause mortality in postmenopausal women. A WBC count greater than 6.7 x 10(9) cells/L may identify high-risk individuals who are not currently identified by traditional CVD risk factors. (Approximately 50% increase in risk.)

INCREASING EVIDENCE SUPPORTS A role for inflammation in the atherosclerotic process.[1,2] Initiation, growth, and complications of atherosclerotic plaques are each judged to be an inflammatory response to vascular injury,[3,4] and inflammatory markers and cytokines originating in the heart, vessel walls, macrophages, adipose tissue, and liver have been associated with the risk of coronary events.[5] In light of the multitude of pathobiological factors involved in inflammation, a large number of targets for measurement have been proposed to identify and monitor the inflammatory process in patients with, or at risk for, coronary heart disease (CHD). These include proinflammatory factors such as oxidized low-density lipoproteins, proinflammatory cytokines (eg, interleukin 1 and tumor necrosis factor-α), adhesion molecules (eg, intercellular adhesion molecule 1 and selectins), inflammatory stimuli with hepatic effects (eg, interleukin 6), or the products of the hepatic stimulation, such as serum amyloid A, C-reactive protein (CRP), and other acute-phase reactants.[6] In addition, indicators of cellular responses to inflammation, such as elevated white blood cell (WBC) count, have also been considered.[6]

For editorial comment see page 487

Author Affiliations are listed at the end of this article. A complete listing of the Women's Health Initiative Research Group is given in a box at the end of this article.

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White Blood Cell Count

Traditional Reference Range:

3.4-10.8 x10E3/uL

Optimal Reference Range

4.5 – 6.5 x10E3/uL

Eur J Epidemiol (2013) 28:735–742
DOI 10.1007/s10654-013-9842-7

CARDIOVASCULAR DISEASE

White blood cell count in young adulthood and coronary artery calcification in early middle age: coronary artery risk development in young adults (CARDIA) study

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We demonstrated that total WBC counts in young adults is associated prospectively with subclinical atherosclerosis measured by CAC 20 years later into middle age, suggesting total WBC and eosinophil counts may be a marker of early-stage atherosclerosis.

ther assessed prospective associations between Y0 WBC and inflammatory biomarkers during the follow-up, and the presence of CAC 15 and 20 years later. In total, 272 and 566 subjects had CAC scores >0 at year (Y) 15 and Y20, respectively. Baseline total WBC counts were cross-sectionally associated with SBP, BMI, and smoking, or HDL-cholesterol ($p \leq 0.01$) at Y0, and prospectively associated young adults was associated prospectively with CAC presence 20 years later after adjusting for age, sex, and race. Results are attenuated when other risk factors are accounted for. Our results suggest the possible early involvement of WBC, particularly eosinophils, in the early stages of atherosclerosis.

Keywords White blood cell count · Coronary artery calcification · Atherosclerosis

Electronic supplementary material The online version of this article (doi:10.1007/s10654-013-9842-7) contains supplementary material, which is available to authorized users.

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Neutrophils

The most abundant and most motile of all white blood cells

Neutralizes an invader by phagocytosis

- Contains a number of enzymes and pyrogens that can also cause damage to host cells

Optimal range: 50-60%

Neutrophils

Elevated

- Generally due to bacterial infection and/or inflammation

Decreased

- Copper deficiency
  - Low hemoglobin/RBC, ferritin may be elevated, possible ataxia; high zinc intake (>50mg/day)
- B12 or folate deficiency
- Elevations in other types of white blood cells

Interfering factors: stress, excitement, fear, anger, joy and exercise temporarily cause increase neutrophils.

Lymphocytes

Lymphocytes contain a wide variety of white blood cells including B-cells, T-cells and Natural Killer Cells

The lymphocyte count does not differentiate between these – more specific testing is required to identify the lymphocyte subsets

Optimal range: 30-35%

Lymphocytes

Elevated

- Viral infections
- Crohn's disease
- Other inflammatory/autoimmune diseases
- Hypoadrenalism (cortisol suppresses lymphocytes, so low cortisol may cause elevation – check sodium and potassium)

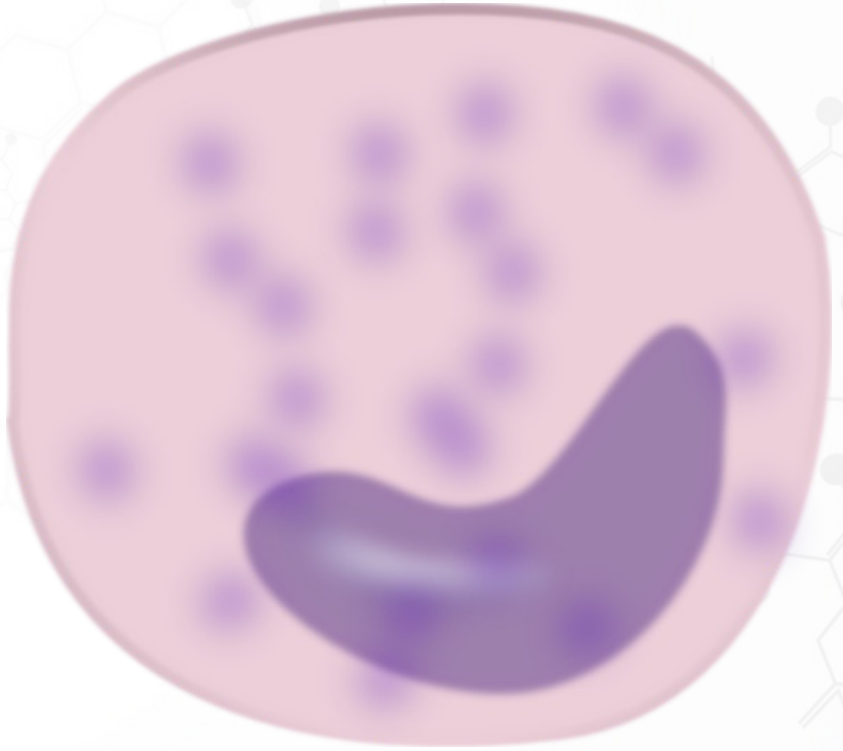
Decreased

- Zinc deficiency
- Elevations of other white blood cells

Interfering factors: Exercise, emotional stress and menstruation can cause increase in lymphocytes.

Monocytes

- Monocytes leave circulation within 16-36 hours and become macrophages
- Macrophages remove foreign substances via phagocytosis
  - They also participate in the destruction of old red blood cells, denatured proteins, microorganisms, and dead cells
- Macrophages can become Antigen Presenting Cells (APCs) and deliver an antigen to lymphocytes
- Optimal range: <6%



Monocytes

Elevated

- Generalized, systemic inflammation
- Collagen disease, such as Rheumatoid Arthritis
- Ulcerative colitis
- Recovery state after an infection or trauma
- One study showed that a white blood cell count of 5.5 with high-normal monocytes (6.1%) was associated with non-alcoholic fatty liver disease

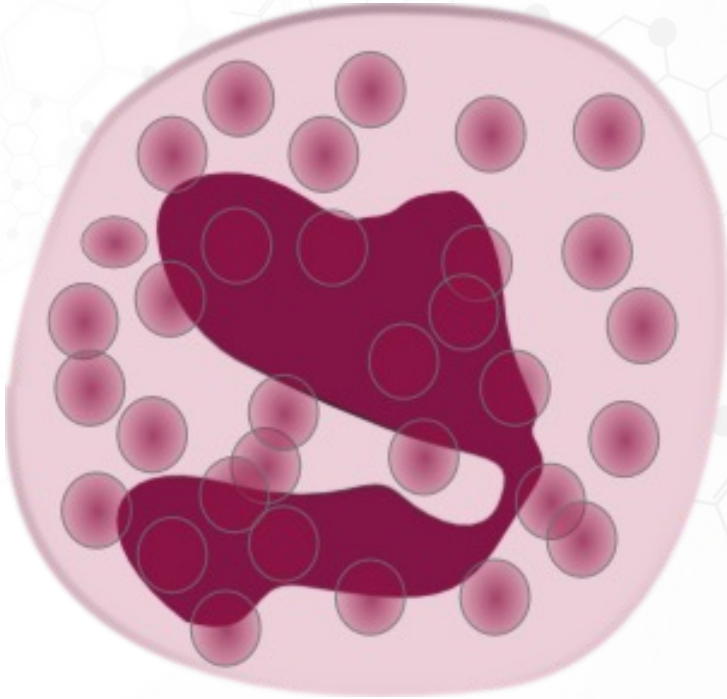
  Kim, Hack-Lyoung, Goh Eun Chung, In Young Park, Jin Man Choi, Se-Min Hwang, Jeong-Hoon Lee, and Donghee Kim. 2011. "Elevated Peripheral Blood Monocyte Fraction in Nonalcoholic Fatty Liver Disease." The Tohoku Journal of Experimental Medicine 223 (3): 227–33.

Eosinophils

Eosinophils are also phagocytic immune cells and become active in the later stages of inflammation.

They are found in large numbers in the intestines and lungs.

Optimal range: <3%



Eosinophils

One study suggested eosinophils may be elevated in primary biliary cirrhosis, which can also raise HDL levels.

Thus, if they are both elevated, consider primary biliary cirrhosis.

Eosinophil levels also tend to correlate with platelet counts and fibrinogen.

Eosinophils

Elevated

- Allergies, asthma
- Parasitic infection, tapeworms
- Hypoadrenalism
- Chronic skin disease, such as eczema
- Ulcerative colitis, Crohn’s
- Aspirin sensitivity

Decreased

- Significantly elevated cortisol

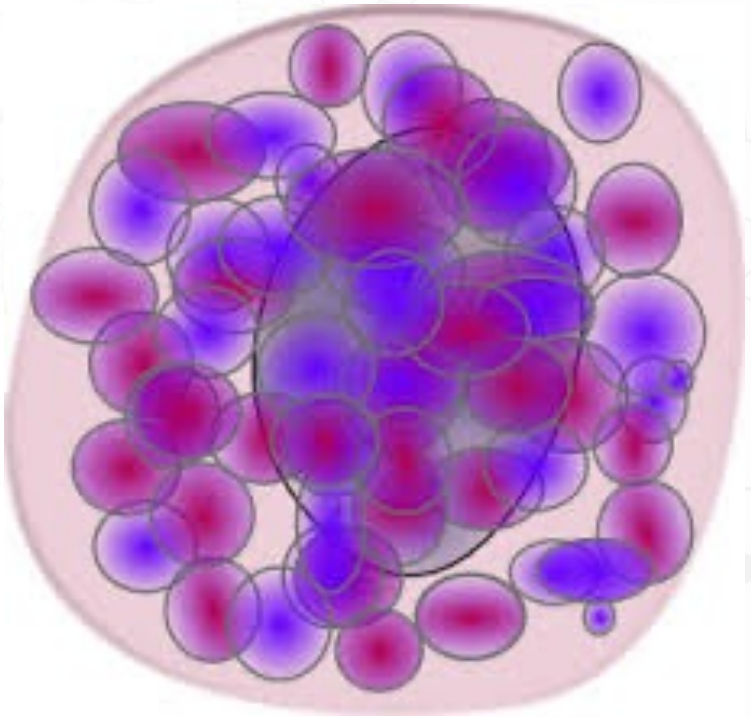
Interfering factors: Lowest in the morning. Stress and high cortisol can lower numbers.

Basophils

Basophils contain a large number of granules containing heparin, histamine, leukotriene, serotonin, etc.

They are associated with inflammation and hypersensitivities

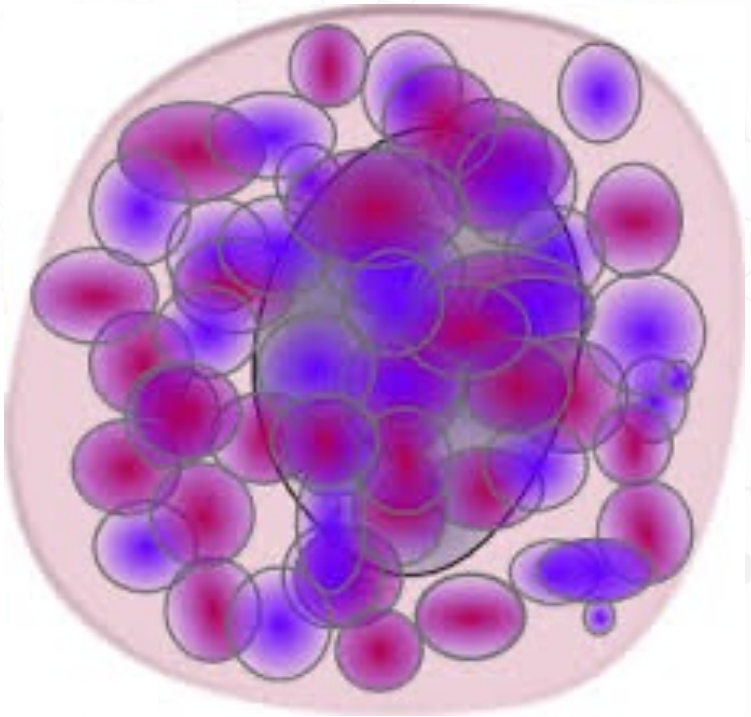
Tissue basophils are called mast cells.



Basophils

Elevated

- Inflammation, allergy
- Chronic hemolytic anemia
- Hypothyroidism



Platelet Count

Platelets, also known as thrombocytes, are small, anucleated, cell fragments found in the blood.

Their lifespan is about 7-10 days.

Platelets are involved in the clotting cascade and contain a number of chemicals that they release, when activated, that promotes clotting.

They are also necessary for vascular integrity and vasoconstriction

Low levels of platelets can cause increased bleeding; elevated levels can increase clotting

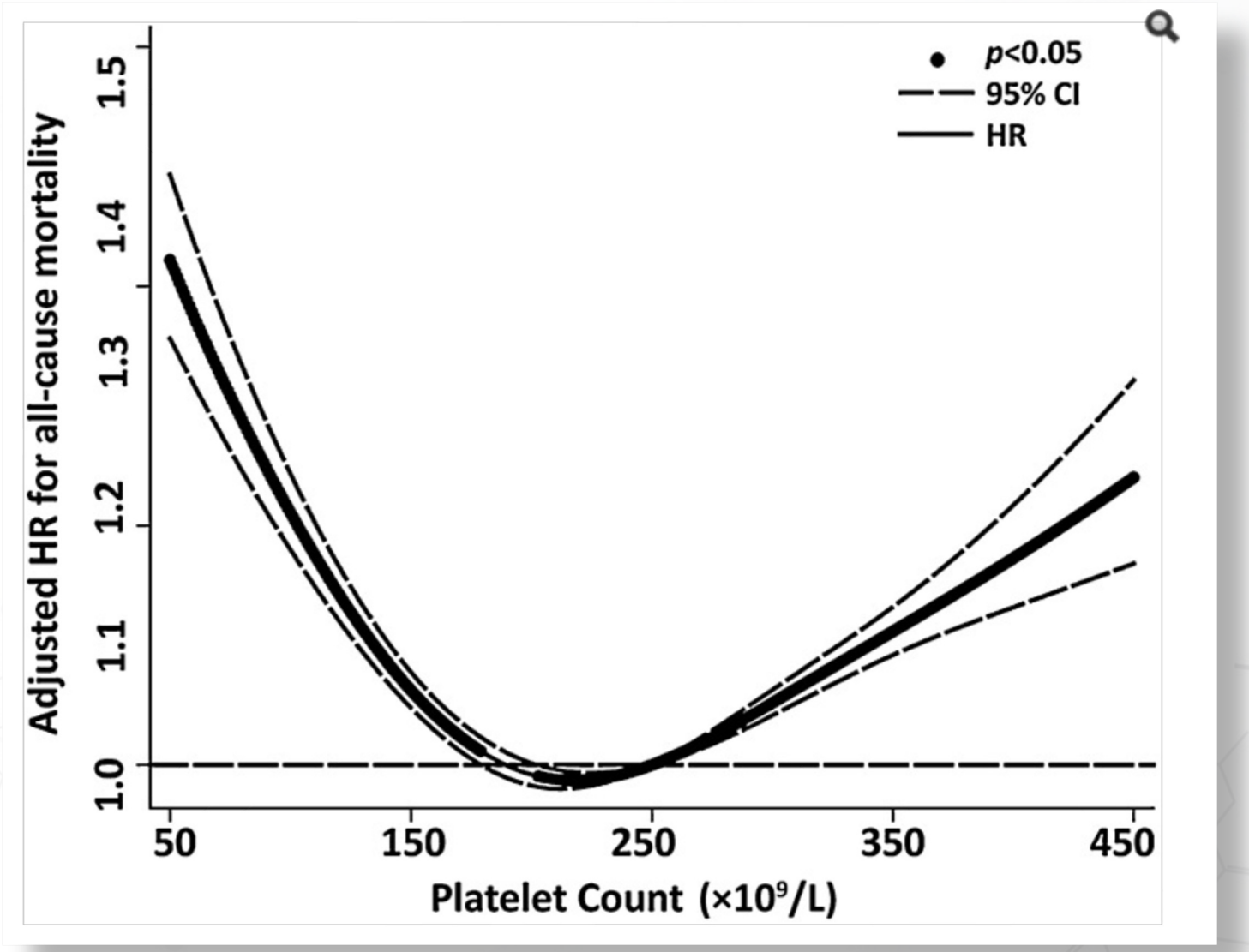
Platelet Count

Traditional Reference Range

140-400 x $10^3/mm^3$

Optimal Reference Range

225-275 x $10^3/mm^3$



Tsai, Ming-Tsun, Yung-Tai Chen, Chi-Hung Lin, Tung-Po Huang, Der-Cherng Tarng, and Taiwan Geriatric Kidney Disease Research Group. 2015. "U-Shaped Mortality Curve Associated with Platelet Count among Older People: A Community-Based Cohort Study." Blood 126 (13): 1633–35. doi:10.1182/blood-2015-06-654764.

Platelet Count - Increased

Cause	Reason	Additional Inquiry
Iron deficiency anemia	Mechanism unknown. Possibly due to increased erythropoietin levels.	*Should be noted that some references show low platelets in severe iron deficiency anemia.
Collagen diseases (rheumatoid arthritis, lupus)		
Hemolytic anemia and/or blood loss	Increased production of all blood cells	Evaluate CBC.
Stress, infection, inflammation	Increased thrombosis during inflammation.	Malignancy can be considered with persistent elevation outside lab limits

*

Platelet count - Decreased

Cause	Reason	Additional Inquiry
Alcoholism	Poor liver function, leading to decreased thrombopoietin.	Evaluate liver markers.
Liver dysfunction	The liver produces thrombopoietin, which stimulates platelet production. Therefore, poor liver function can lead to low thrombopoietin levels.	Evaluate liver markers.
Certain viral and bacterial infections	Observation.	Evaluate WBC, lymphocytes.
Pernicious anemia	Poor nuclear function, including megakaryocytes.	
Bleeding	Blood loss can lead to decrease of all blood cells, including platelets.	Client history. CBC.

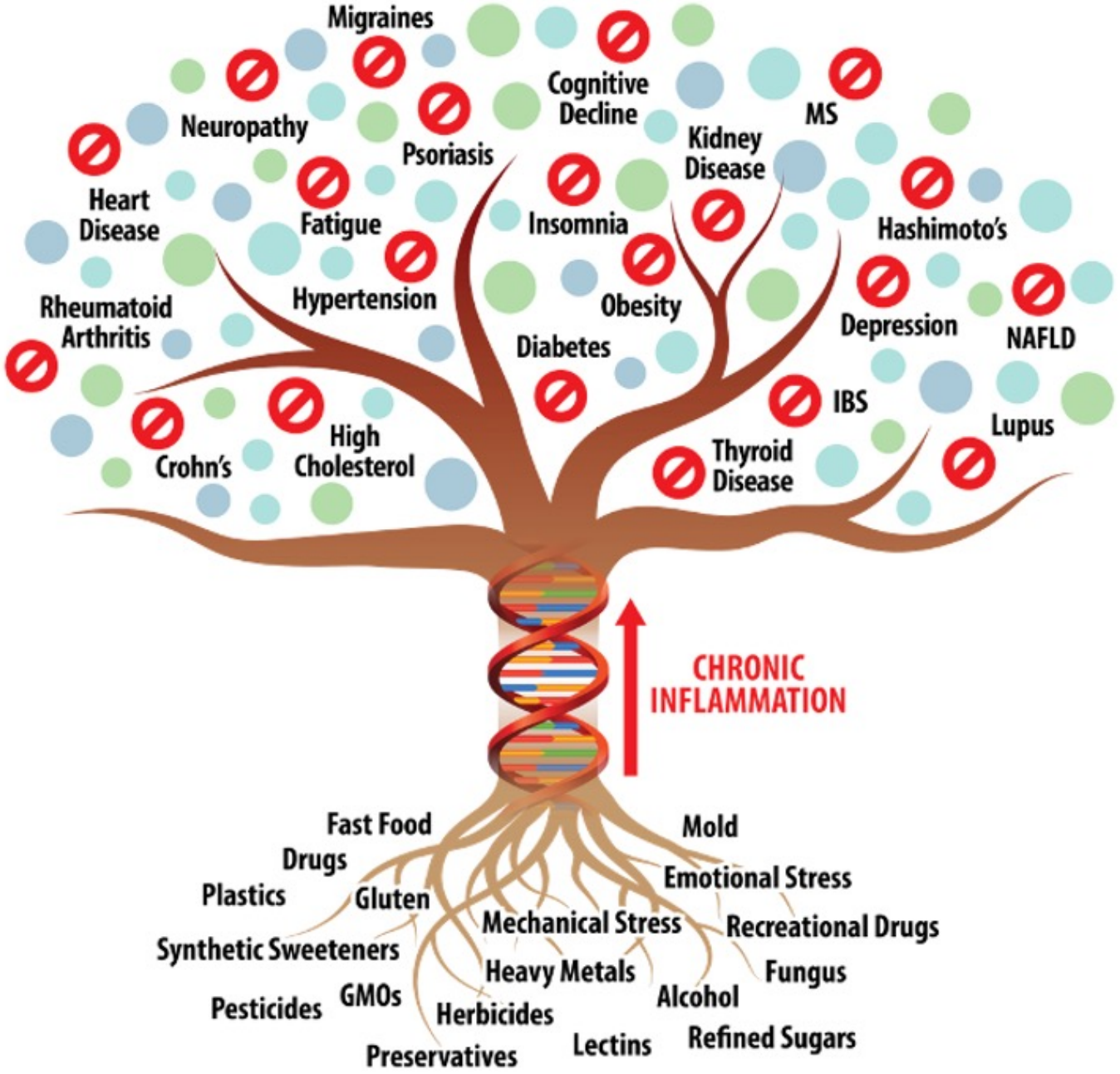
	Test	Current Result and Flag		Previous Result and Date	Units	Reference Interval
	WBC [01]	7.1			x10E3/uL	3.4-10.8
▼	**RBC** [01]	**3.54**	**Low**		x10E6/uL	3.77-5.28
▼	**Hemoglobin** [01]	**9.6**	**Low**		g/dL	11.1-15.9
▼	**Hematocrit** [01]	**31.8**	**Low**		%	34.0-46.6
	MCV [01]	90			fL	79-97
	MCH [01]	27.1			pg	26.6-33.0
▼	**MCHC** [01]	**30.2**	**Low**		g/dL	31.5-35.7
	RDW [01]	15.3			%	11.7-15.4
	Platelets [01]	301			x10E3/uL	150-450
	Neutrophils [01]	80			%	Not Estab.
	Lymphs [01]	10			%	Not Estab.
	Monocytes [01]	6			%	Not Estab.
	Eos [01]	3			%	Not Estab.
	Basos [01]	0			%	Not Estab.

	Test	Current Result and Flag		Previous Result and Date	Units	Reference Interval
	Iron Bind.Cap.(TIBC)	326			ug/dL	250-450
	UIBC [01]	307			ug/dL	118-369
▼	**Iron** [01]	**19**	**Low**		ug/dL	27-139
	Ferritin [01]	99			ng/mL	15-150

	Test	Current Result and Flag		Previous Result and Date	Units	Reference Interval
	WBC [01]	5.7			x10E3/uL	3.4-10.8
▼	**RBC** [01]	**3.35**	**Low**		x10E6/uL	3.77-5.28
	Hemoglobin [01]	11.5			g/dL	11.1-15.9
▼	**Hematocrit** [01]	**33.2**	**Low**		%	34.0-46.6
▲	**MCV** [01]	**99**	**High**		fL	79-97
▲	**MCH** [01]	**34.3**	**High**		pg	26.6-33.0
	MCHC [01]	34.6			g/dL	31.5-35.7
	RDW [01]	12.8			%	11.7-15.4
▲	**Platelets** [01]	**526**	**High**		x10E3/uL	150-450
	Neutrophils [01]	50			%	Not Estab.
	Lymphs [01]	37			%	Not Estab.
	Monocytes [01]	7			%	Not Estab.
	Eos [01]	5			%	Not Estab.
	Basos [01]	1			%	Not Estab.

Test	Current Result and Flag	Previous Result and Date	Units	Reference Interval
Iron Bind.Cap.(TIBC)	278		ug/dL	250-450
UIBC [01]	193		ug/dL	118-369
Iron [01]	85		ug/dL	27-139
Iron Saturation	31		%	15-55

	AST (SGOT) [01]	29			IU/L	0-40
▲	**ALT (SGPT)** [01]	**35**	**High**		IU/L	0-32


Migraines
Neuropathy
Psoriasis
Cognitive Decline
MS
Kidney Disease
Heart Disease
Fatigue
Insomnia
Hashimoto's
Hypertension
Obesity
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Rheumatoid Arthritis
Diabetes
IBS
Lupus
Crohn's
High Cholesterol
Thyroid Disease
CHRONIC INFLAMMATION
Fast Food
Mold
Drugs
Emotional Stress
Plastics
Gluten
Mechanical Stress
Recreational Drugs
Synthetic Sweeteners
Heavy Metals
Fungus
Pesticides
GMOs
Herbicides
Alcohol
Preservatives
Lectins
Refined Sugars

The Wedge Protocol