Casual Friday Series

Functional Blood Chemistry Series: CBC

A Biogenetix Clinical Presentation

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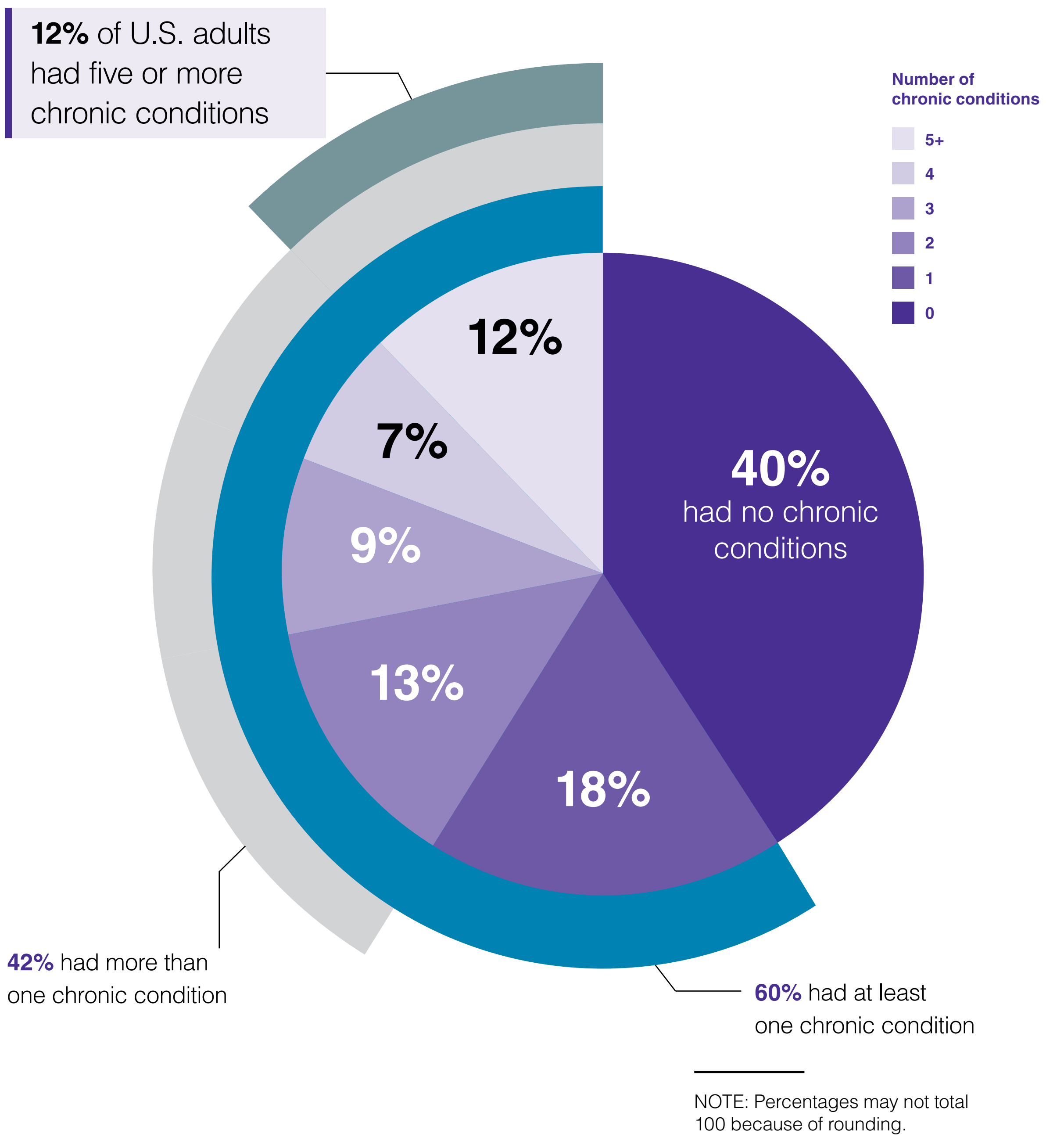
Disclaimer

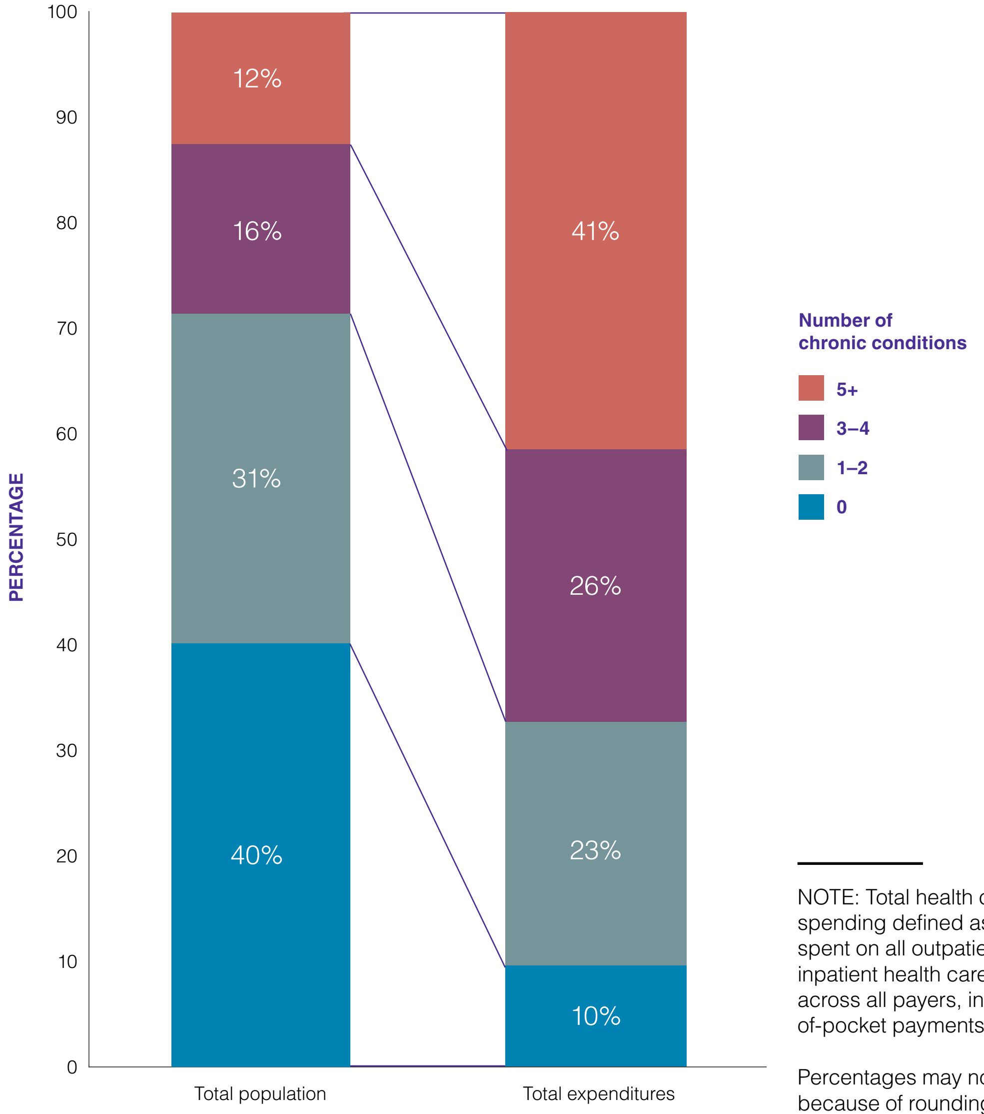
- *Information in this presentation is not intended to diagnose, treat, reverse, cure, or prevent any disease. While this presentation is based on medical literature, findings, and text, The following statements have not been evaluated by the FDA.*
- *The information provided in this presentation is 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.*

As of 2014, 60% of American adults had at least 1 chronic condition, 42% had more than 1 chronic condition.



www.fightchronicdisease.org/sites/default/files/TL221_final.pdf

Figure 2.2. Prevalence and Spending by Number of Chronic Conditions (2014)



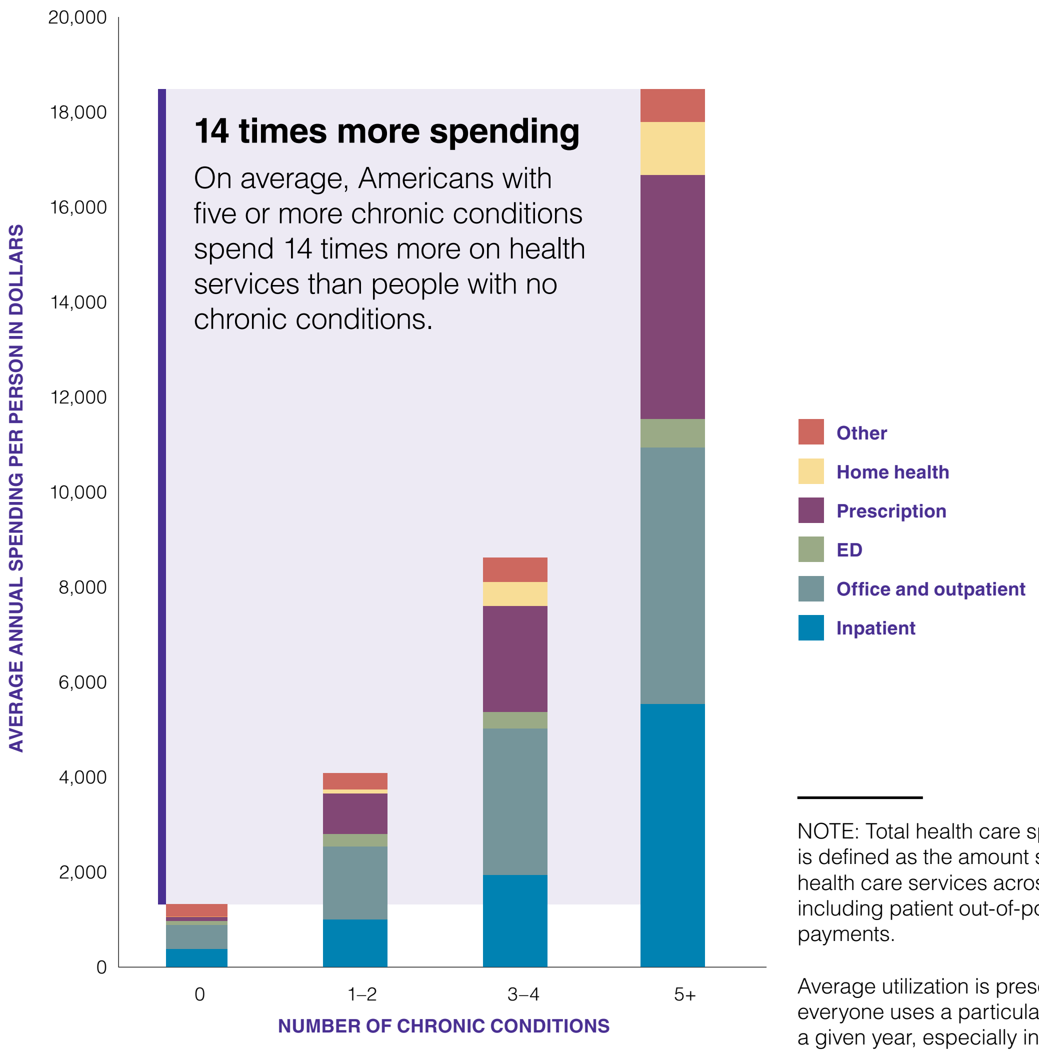
NOTE: Total health care spending defined as the amount spent on all outpatient and inpatient health care services across all payers, including out-of-pocket payments.

Percentages may not total 100 because of rounding.

Americans with 5 or more chronic conditions make up 12% of the population, but account for 41% of all health related expenses.

www.fightchronicdisease.org/sites/default/files/TL221_final.pdf

Patients with 5 or more chronic conditions spend 2x as much as those with 3-4, and **14x** as much as someone without any chronic condition at all.

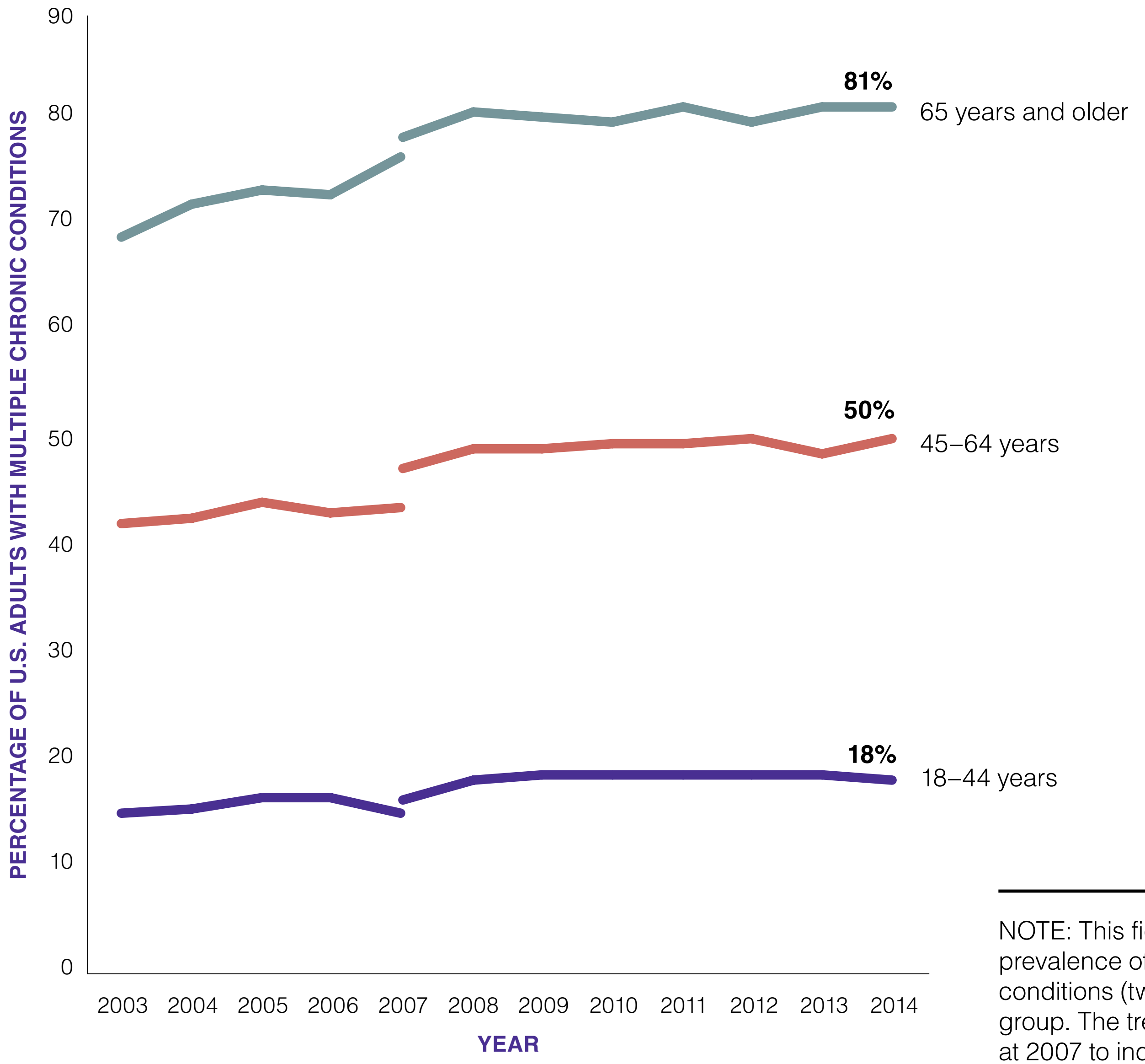


NOTE: Total health care spending is defined as the amount spent on health care services across all payers, including patient out-of-pocket payments.

Average utilization is presented; not everyone uses a particular service in a given year, especially inpatient stays and ED visits.

www.fightchronicdisease.org/sites/default/files/TL221_final.pdf

Figure A.1. Prevalence of Multiple Chronic Conditions (2003–2014)



NOTE: This figure documents the prevalence of multiple chronic conditions (two or more) by age group. The trend lines break at 2007 to indicate that MEPS changed its approach to the chronic disease questions.

www.fightchronicdisease.org/sites/default/files/TL221_final.pdf

Chronic Conditions and Lifespan

0 chronic conditions: 67+22.6 additional years
5 chronic conditions: 67+14.9 additional years
10 chronic conditions: 67+5 additional years

Med Care. 2014 Aug;52(8):688-94. doi: 10.1097/MLR.0000000000000166.
Multiple chronic conditions and life expectancy: a life table analysis.
DuGoff EH1, Canudas-Romo V, Buttorff C, Leff B, Anderson GF.

April 2018

Goldman Sachs asks in biotech research report: 'Is curing patients a sustainable business model?'

”…where the success of [its] hepatitis C franchise has gradually exhausted the available pool of treatable patients," the analyst wrote. "In the case of infectious diseases such as hepatitis C, curing existing patients also decreases the number of carriers able to transmit the virus to new patients, thus the incident pool also declines … Where an incident pool <u>remains stable</u> (eg, in cancer) the potential for a cure poses less risk to the sustainability of a franchise."

https://www.cnbc.com/amp/2018/04/11/goldman-asks-is-curing-patients-a-sustainable-business-model.html?__twitter_impression=true

People are not commodities…
unless THEY CHOOSE TO BE.

How do you transition them?

re·spon·si·bil·i·ty

/rəˌspänsəˈbilədē/

noun

the state or fact of having a duty to deal with something or of having control over someone.
synonyms: authority, control, power, leadership
"a job with greater responsibility"

- the state or fact of being accountable or to blame for something.
  "the group has claimed responsibility for a string of murders"
  synonyms: blame, fault, guilt, culpability, liability
  "they denied responsibility for the bomb attack"
- the opportunity or ability to act independently and make decisions without authorization.
  "we would expect individuals lower down the organization to take on more responsibility"

Work the Responsibility Machine

Responsibility Machine

Functional Medicine Diagnostic Workup

Applied FM

Responsibility Machine

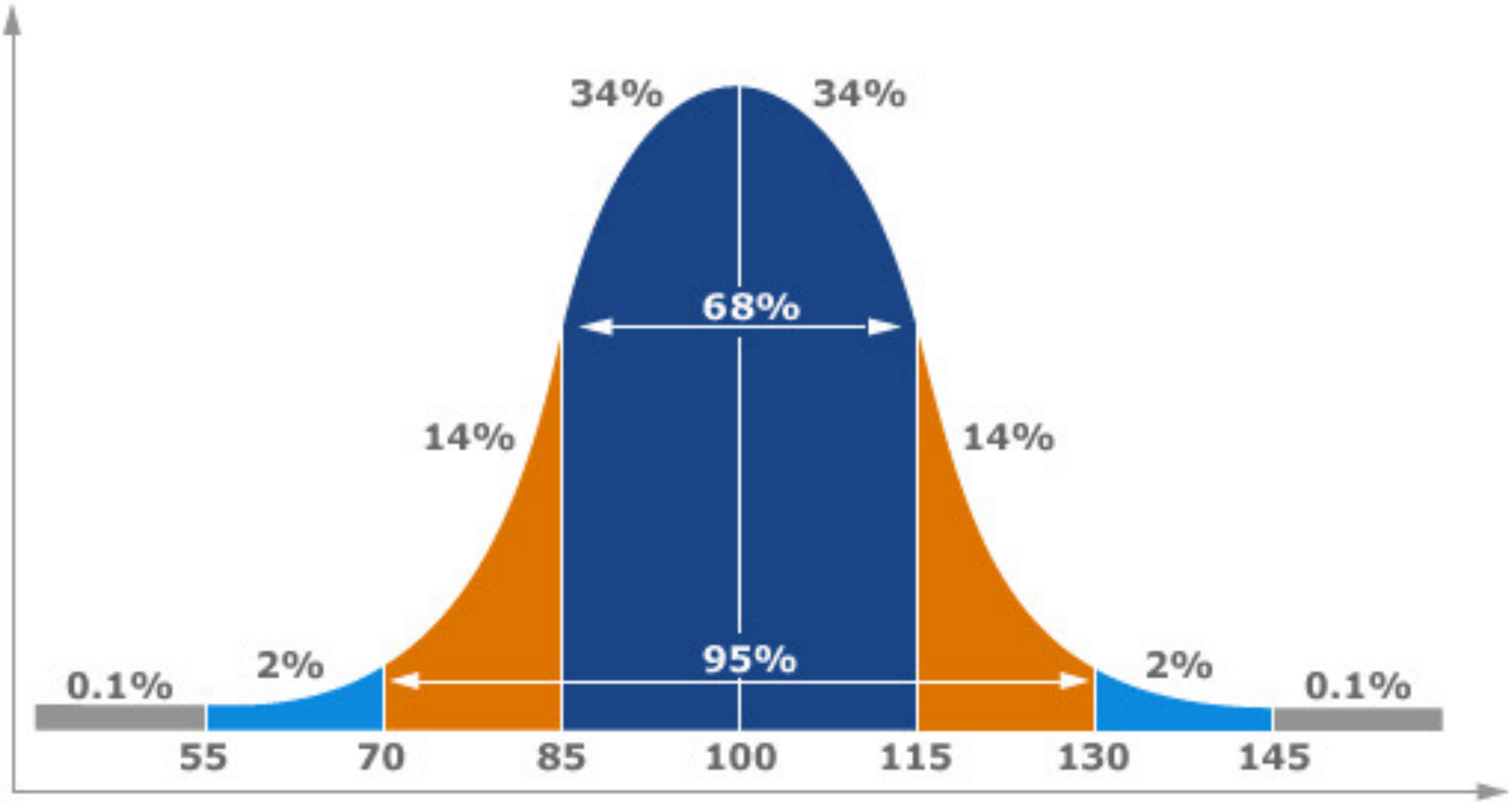
\+

Functional Medicine Diagnostic Workup

=

Progress.

Raw Data



Optimal Range

A tighter set of ranges designed to help:

1. Identify underlying physiological issues that can help explain symptoms
2. Evaluate health rather than disease
   - Catch potentially more serious disease processes earlier

Sodium

Laboratory ref range:

135 – 145 mmol/L

Optimal ref range:

139 – 142 mmol/L

Sensitivity

- Ability of a test to detect a positive test in every patient with a given disease
- A test with 100% sensitivity will be positive in every patient with a specific disease
- 90% sensitivity will not accurately identify 10% of individuals with a specific disease (false negative)
- The higher the sensitivity, the lower the chance of false negatives.
- PKU test is highly sensitive for infants with PKU. PSA test for prostate issues has a low sensitivity (~40%)

Specificity

- Percent of negative results in people without the disease
- Helps predict false positives
- Refers to how well a test successfully (specifically) identifies a given disease (only found in people with the disease)
- A test with 90% specificity may be positive in 10% of the people that *do not* have the disease
- The lower the specificity, the higher the chance for false positives

“The Heart Attack Test” (THAT test)

Used on 200 people who have had a heart attack.
196 people tested positive (98% sensitivity)

- Four false negatives (people had it, but weren’t identified)

Used on 200 people who did *not* have a heart attack
20 people tested positive (90% specificity)

- Identified the disease 10% of the time even though the disease wasn’t present

The majority of blood chemistry markers, when out of range, merely point to a list of possibilities

Combining this information with history, intake, signs/symptoms, and other data can help narrow to a list of *probabilities*

Rarely will a lab test dictate the course of treatment

Offers additional insights

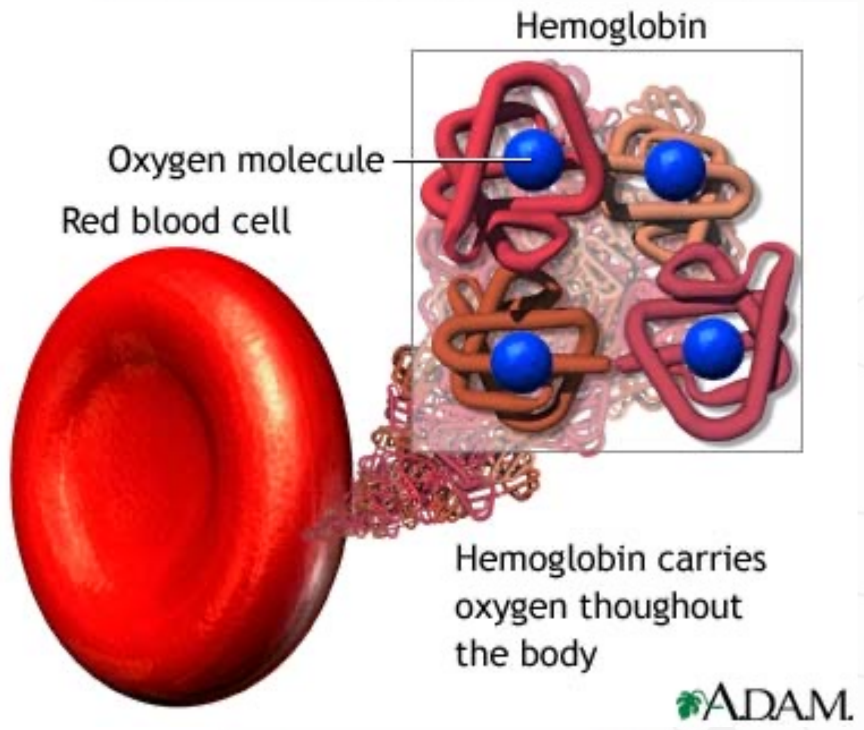
CBC (Complete blood Count)

- Red blood cell count
- Hemoglobin
- Hematocrit
- MCV
- MCH
- MCHC
- RDW
- White blood cell count
- Platelet count

c/ Differential

- Neutrophils
- Lymphocytes
- Monocytes
- Eosinophils
- Basophils

- Red blood cells are anucleated cells, produced in bone marrow and have a life span of approximately 120 days.
- They have a phospholipid membrane
- Contain 280 *million* molecules of hemoglobin
- Contain cytosol and enzymes (PPP and glycolysis)



Red Blood Cell Count

Number of red blood corpuscles per volume of blood.

Traditional Reference Range:

Male: 4.5-5.9 X 10^6 cells/uL

Female: 4.1-5.1 X 10^6 cells/uL

Optimal Reference Range:

Male: 4.8-5.5 X 10^6 cells/uL

Female: 4.4-4.8 X 10^6 cells/uL

Hemoglobin

Hemoglobin measurement is the amount of hemoglobin per unit of blood.

Traditional Reference Range:

- Men: 14.0-17.4 g/dL
- Women: 12.0-16.0 g/dL

Optimal Reference Range

- Men: 14.5-16 g/dL
- Women: 13-14.5 g/dL

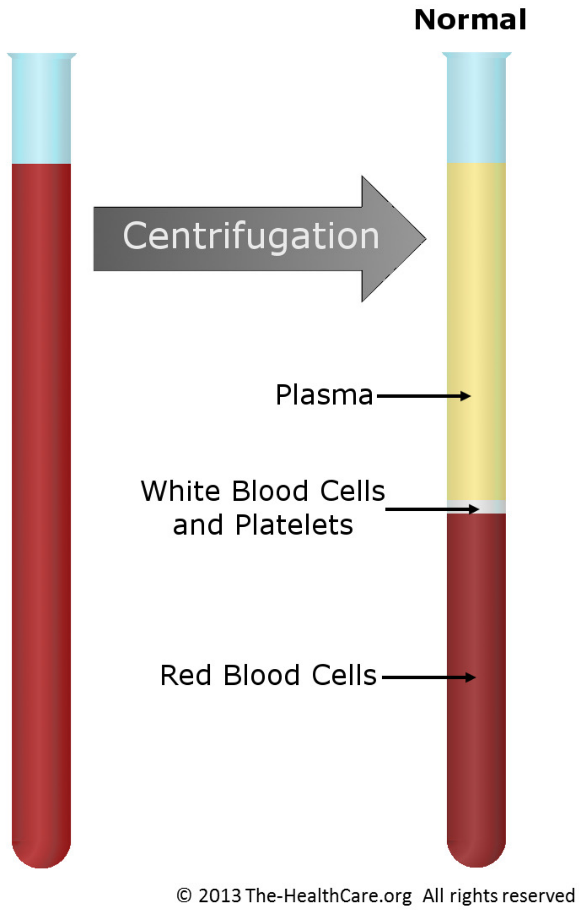
Hematocrit (Packed Cell Volume)

Hematocrit means “to separate blood”.

Percentage of volume of blood composed of red blood cells

Usually about three times the value of hemoglobin

(Size and shape of RBC can alter this)



Hematocrit (Packed Cell Volume)

Traditional Reference Range

- Men: 42-52% or 0.42-0.52
- Women: 36-48% or 0.36-0.48

Optimal Reference Range

- Men: 44-49%
- Women: 39-45%

Hematocrit can be misleading. For example, small RBC can be more tightly packed and thus create a lower hematocrit. On the other hand, large red blood cells may not pack as well creating a falsely normal hematocrit despite having anemia.

Fewer, large RBC = normal hematocrit

RBC, Hemoglobin, Hematocrit - Elevated

Cause	Reason	Additional Inquiry
Dehydration	RBC can appear elevated due to hemoconctration, or a decrease in plasma volume.	Evaluate other dehydration markers (albumin, BUN, Na/K, specific gravity).
Elevated testosterone	Testosterone can increase RBC production.	Evaluate testosterone signs, symptoms and markers.
Poor oxygenation	High altitude, smoking, poor lung function (eg asthma) could create relative hypoxia (low oxygen) in the body and increase RBC production to compensate.	Client history.
Thiamin deficiency	In a rat study, thiamine deficiency increased EPO and red blood cell production (past 30 days).	Evaluate other thiamin deficiency markers, including CO2 and anion gap (low CO2, increased anion gap).
Insulin resistance	Insulin has been found to regulate erythropoiesis. Increased insulin has been shown to increase RBC production.	Evaluate markers of glucose regulation.

RBC, *Hemoglobin*, Hematocrit - Decreased

Cause	Reason	Additional Inquiry
Anemia	Production, destruction or loss of RBC.	Evaluate other CBC markers.
Liver disease	Dilution due to volume overload, shortened RBC survival, poor response by bone marrow.	Evaluate liver markers.
Hypothyroidism	Decreased nutrient absorption and/or decreased EPO production.	Evaluate thyroid markers (free T3).
Exercise	Endurance exercise, during intense training, has been shown to decrease hemoglobin 3-8%.	Client history.
Arginine deficiency	Arginine deficiency has been shown to decrease hematopoetic stem cell differentiation and proliferation.	Nutritional history (including excess lysine).
Protein deficiency	Decreases EPO production.	Evaluate diet history.
Inflammation	Infection, inflammation, cytokine dysregulation. Increased destruction and/or decreased production (TNFa, IL-6, INFg).	Evaluate markers of infection and infection.

Infections Known To Cause Hemolytic Anemia

Aspergillus

Bacillus anthracis

Babesia microti and *Babesia divergens*

Bartonella bacilliformis

Campylobacter jejuni

Clostridium perfringens(Welchii)

Coxsackievirus

Cytomegalovirus

Diplococcus pneumoniae

Epstein-Barr virus

Escherichia coli

Fusobacterium necrophorum

Haemophilus influenzae

Hepatitis A

Hepatitis B

Hepatitis C

Herpes simplex virus

Human immunodeficiency virus

Influenza A virus

Leishmania donovani

Leptospira interrogans serovar *ballum* and/or *Leptospira kirschneri* serovar *butembo*

Mumps virus

Mycobacterium tuberculosis

Mycoplasma pneumoniae

Neisseria intracellularis

Parvovirus B19

Plasmodium falciparum

Plasmodium malariae

Plasmodium vivax

Rubella virus

Rubeola virus

Salmonella

Shigella

Streptococcus

Toxoplasma

Trypanosoma brucei

Varicella virus

Vibrio cholerae

Yersinia enterocolitica

RBC, *Hemoglobin*, Hematocrit - Decreased

Cause	Reason	Additional Inquiry
Vitamin E deficiency	Not used in human erythropoiesis, except when following a low calorie and/or low protein diet.	Evaluate nutritional history.
Magnesium deficiency	Causes increased iron absorption, uptake and storage, but appears to increase RBC fragility.	Evaluate magnesium status (high-normal serum iron).
Zinc deficiency	Causes poor hemoglobin synthesis, as well as increased RBC fragility (hemolysis).	Evaluate diet history as well as other zinc deficiency symptoms and markers (eg alkaline phosphatase).
Copper deficiency	Copper is required to keep iron in its usable (ferric) state. Thus low copper leads to microcytic hypochromic anemia, which is unresponsive to iron.	Low ceruloplasmin and/or serum copper. Possibly low neutrophils.
Selenium deficiency	Selenium mitigates oxidative stress. Leads to defective RBC differentiation, increased fragility, etc.	Evaluate diet history.
Vitamin B6 deficiency	Necessary to synthesize hemoglobin. Leads to microcytic anemia (sideroblastic).	Alcohol consumption. Diet history. Other vitamin B6 markers (low AST and/or ALT).
Vitamin A deficiency	Because iron and ferritin are likely normal, appears to be a iron transport issue. Also involved with EPO.	Diet history. Symptoms of vitamin A deficiency (night blindness).

Combined Issues – The Art of Blood Chemistry Analysis

Influences to raise RCB count (dehydration, high testosterone, insulin resistance) combined with influences to decrease RBC count (anemia, hypothyroidism), can result in a normal RBC on a blood chemistry.

Similarly, influences to raise hematocrit (macrocytosis, dehydration) combined with influences to lower hematocrit (anemia), can result in normal hematocrit on a blood chemistry.

Mean Corpuscular Volume (MCV)

- Estimate of the average RBC size (volume) measured in micrometers (femtoliter, fL)
- Most clinically useful (versus MCH or MCHC)
- Calculation

MCV = Hct (%) X 10/RBC

- Elevated MCV indicates larger than normal RBCs and decreased MCV indicates smaller than normal RBCs

Traditional Reference Range
80-96 fL/cell
Optimal Reference Range
84 – 92 fL/cell

Mean Corpuscular Volume (MCV)

Interfering Factors	
Elevated	**Decreased**
Hyperglycemia	
Increased reticulocytes	
Increased WBC count	

It is also critical to understand that <u>mixed</u> red blood cells – some large, some small – can lead to a <u>normal</u> MCV

Mean Corpuscular Hemoglobin (MCH)

The mean corpuscular hemoglobin is a measure of the average weight of hemoglobin per RBC.

It is calculated by:

MCH = hemoglobin (g/dL) X 10/red blood cell count

Traditional Reference Range

26-34 pg/cell

Optimal Reference Range

28-32 pg/cell

Mean Corpuscular Hemoglobin Concentration (MCHC)

Measures the average concentration of hemoglobin in the red blood cells.

Good at monitoring therapy as it uses hemoglobin and hematocrit in its calculation

MCHC = hemoglobin (g/dL) X 100/hematocrit (%)

Traditional Reference Range

32-36 g/dL

Optimal Reference Range

33-35 g/dL

MCV, MCH, MCHC – Elevated - Macrocytic

Cause	Reason	Additional Inquiry
B12 and/or folate deficiency	Poor intake (vegetarians), impaired absorption (intrinsic factor, HCL), parasites, increased requirements (hyperthyroidism, pregnancy), enzyme deficiencies (MTHFR), poor protein binding.	Diet history. Other markers including genetic markers, MMA, homocysteine.
Vitamin C deficiency	Strong relationship with RBC folate.*	Diet history and other vitamin C symptoms and markers (alk phos, bleeding gums)
Alcohol	Result from nutritional deficiencies, chronic GI bleeding, hepatic dysfunction, or direct toxic effects of alcohol on erythropoiesis.	History.
Thiamin deficiency	Causes marked macrocytosis, likely due to decrease in nucleic acid synthesis (PPP).	Evaluate other thiamin deficiency markers, including anion gap.

MCV, MCH, MCHC – Normal - Normocytic

Cause	Reason	Additional Inquiry
Hemolytic anemia	Excess breakdown. Normal RBC production, but less RBC, hemoglobin, hematocrit	Normal RDW can help confirm hemolytic anemia. Also increased K and or Mg.
Kidney dysfunction	Decreased EPO production.	Kidney markers (BUN, creatinine, electrolytes, cystatin-C, urinalysis)
Anemia of Inflammation	Poor red blood cell production, but those that are created are normal size and color.	Additional markers such as transferrin binding receptor can differentiate anemia of inflammation. Also CRP, ESR, acute phase reactants
Vitamin E deficiency	Not used in human erythropoiesis, except when following a low calorie and/or low protein diet.	Evaluate nutritional history.
Magnesium deficiency	Causes increased iron absorption, uptake and storage, but appeared to increase RBC fragility.	Evaluate magnesium status (high-normal serum iron).
Selenium deficiency	Selenium mitigates oxidative stress. Leads to defective RBC differentiation, increased fragility, etc.	Evaluate diet history.
Oxidative stress	ROS suppress EPO synthesis.	Evaluate markers of oxidative stress (bilirubin, uric acid, GGT)
Vitamin C deficiency	Scurvy often results in normocytic anemia. Reduces vitamin E (lipid peroxidation), increased ROS, etc.	Diet history and other vitamin C symptoms and markers (alk phos, bleeding gums)

MCV, MCH, MCHC – Decreased - Microcytic

Cause	Reason	Additional Inquiry
Iron deficiency	Poor intake, malabsorption, increased iron loss (bleeding), increased iron requirements	Ferritin, TIBC, transferrin binding receptor.
Vitamin B6 deficiency	Necessary to synthesize hemoglobin. Leads to microcytic anemia (sideroblastic).	Alcohol consumption. Diet history. Other vitamin B6 markers (low AST and/or ALT).
Copper deficiency	Copper is required for converting iron into its useable form for transportation and heme synthesis.	Low ceruloplasmin and/or serum copper. Possibly low neutrophils. High zinc intake.
Zinc deficiency	Causes poor hemoglobin synthesis, as well as increased RBC fragility (hemolysis).	Diet journal. Decreased taste acuity, low hormones (testosterone), skin issues all can indicate zinc deficiency. Zinc tally test. Low alkaline phosphatase.
Vitamin A deficiency	Because iron and ferritin are likely normal, appears to be a iron transport issue. Also involved with EPO.	Diet history. Symptoms of vitamin A deficiency (night blindness).
Vitamin C deficiency	Interactions with iron.	Diet history and other vitamin C symptoms and markers (alk phos, bleeding gums)

Red Cell Distribution Width (RDW)

- Indication of the variation in red cell size, called anisocytosis.
- Red blood cells normally have some variation in size, hence having a traditional reference range of 11.5-14.5%

Optimal reference range is <12%

- The RDW is helpful in identifying an anemia of nutrient deficiency versus other types, such as blood loss, hemolysis, etc
- Generally speaking, when RDW is normal and anemia is present, it is likely *not* due to nutrient deficiency. If RDW is elevated and anemia is present, it is likely due to nutrient deficiency (eg iron, B12, folate, B6, etc).
- If no anemia is present, RDW might be used as an inflammatory marker

Anemia

RBC, *hemoglobin*, hematocrit – if decreased, suggest anemia (inability to optimally deliver oxygen to cells of the body)

MCV, MCH, MCHC – suggest the cause or type of anemia

RDW – can help indicate whether the anemia is of a nutrient deficiency or not

Anemia

1. Production

   Nutrient deficiencies, lack of production stimulus

2. Destruction

   RBC are being broken down more rapidly than they can be produced

   - Nutrient deficiency, infection

3. Loss

   Red blood cells are being lost via abnormal bleeding

↓ *RBC*, Hgb, Hct

↓ MCV

- Iron deficiency
- Copper deficiency
- Vitamin A deficiency
- Vitamin B6 deficiency
- Vitamin C deficiency
- Zinc deficiency
- Lead toxicity

(N) MCV

- Hemolytic anemia
  - Magnesium deficiency
  - Selenium deficiency
  - Infection
- Inflammation/Chronic disease
- Vitamin C deficiency
- Vitamin E deficiency
- Oxidative stress
- Protein deficiency
- Kidney dysfunction

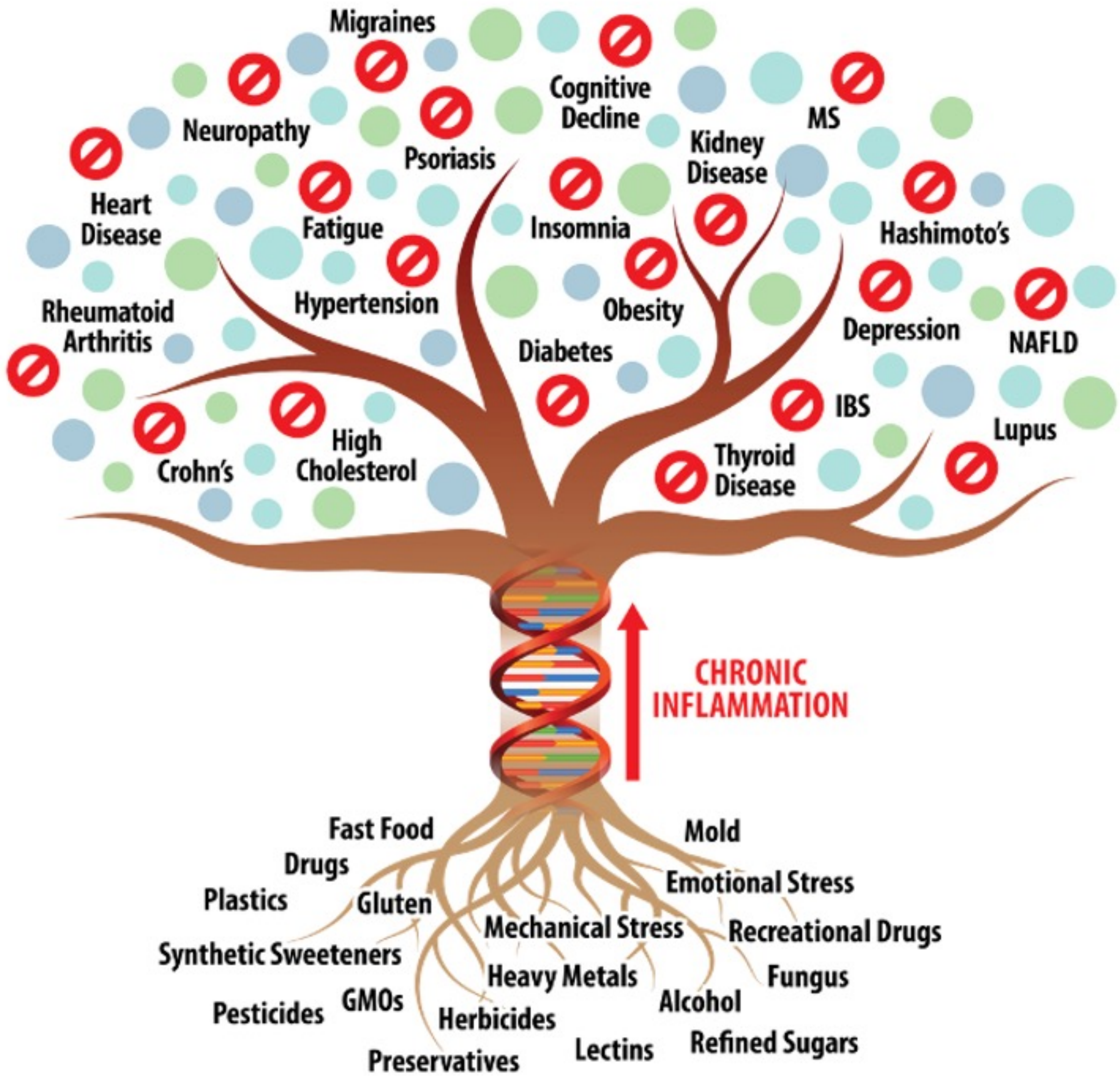
↑ MCV

- 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	N		↓			
Homocysteine					↑	
Alkaline Phosphatase				↓		


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

The Wedge Protocol