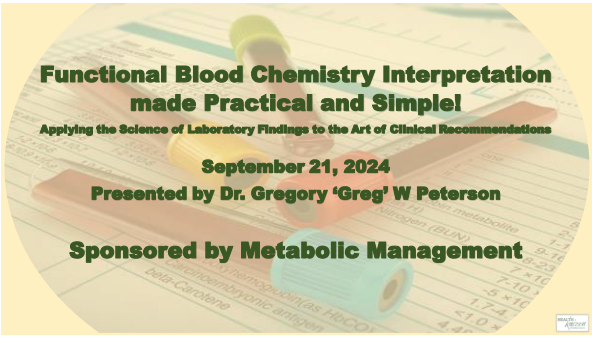


1

Seminar Overview – Goals & Topics

- Understand what a blood panel really means!
- Where to start with the information.
- What to do next with the information.
- Properly utilize the science of the blood chemistry results in your healing art.
- Primary care from a wholistic perspective!

Wellness Promotion - Without A Doubt!!

The Kaizen Way!!

2

Disclaimer

The information presented is presented solely for educational purposes, and it is up to the clinician to determine appropriate intervention and/or appropriate referral to other health care practitioners.

Procedures and products recommended should not be construed as a claim or representation that such procedure or product will constitute a cure.

Treatment and Nutritional recommendations presented may be considered "off-label" per FDA definitions.

Financial Disclosure – Metabolic Management.

3

Disclaimer

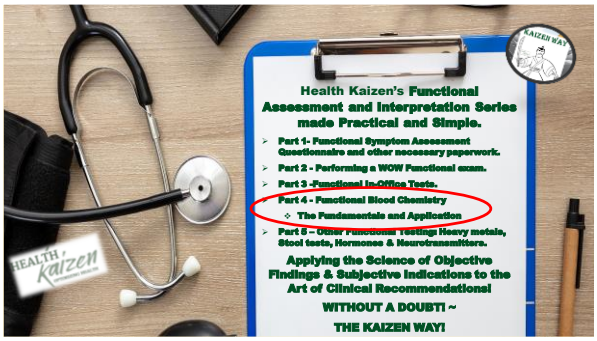
Clinicians must use their own personal judgment, training, knowledge and experience to formulate and direct 'Individualized patient treatment' (Bioindividuality).

Some of the procedures or information presented may be beyond your scope of practice, depending upon your licensure, training, state, etc.. Please consult your state board for clarification before performing new procedures.

Warning – portions of this presentation may contain imperceptibly dry humor, no humor at all or may not even be perceived to be funny at all.

Sometimes thoughts just pop into my head and exit my mouth! - Don't say you weren't warned

4



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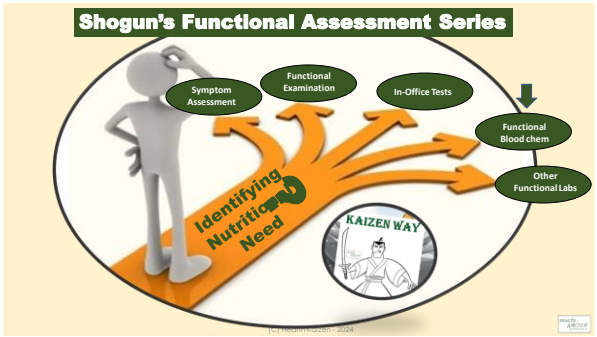

6

6 Key Questions:

- How do we know if the patient may have a deficiency?…… Without A Doubt!
- Does the patient's condition involve a toxin or germ?…… Without A Doubt!
- Will a particular nutrient help their condition?…… Without A Doubt!
- Is the condition corrected to Optimal level?…… Without A Doubt!
- Is the offending mechanism removed?…… Without A Doubt!
- When is the CAUSE corrected?…… Without A Doubt!

The aim of this seminar is how to identify, assess and treat Chronic Degenerative Diseases, Correcting the underlying Biochemical, Functional, and Metabolic Health Issues –

Naturally, Safely and Effectively!……

~ Without A Doubt! ~
The Kaizen Way

7

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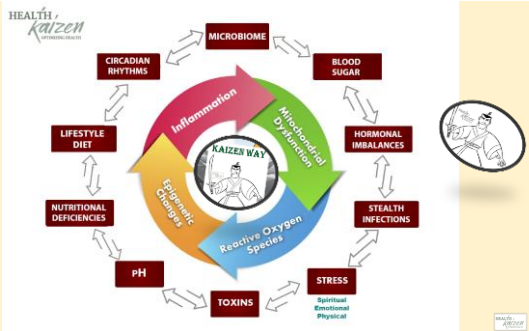
Part 1- Functional Symptom Assessment Questionnaire and other necessary paperwork. (part 4 in recording order).	
Part 2 - Performing a WOW Functional exam. (part 3 in recording order).	
Part 3 - Functional In-Office Tests. (part 2 in recording order).	
Part 4 - Functional Blood Chemistry Interpretation (part 1 in recording order).	

8



9

Why Utilize Functional Blood Testing?

- ✓Excellent diagnostic information
- ✓Is readily accepted by patients
- ✓Relatively inexpensive
- ✓Is acknowledged by the insurance industry
- ✓Supports other clinical findings
- ✓Can indicate a need for additional testing
- ✓Evaluates homeostatic and end-organ pathology
- ✓Can be used as a method of nutritional status assessment
- ✓Documents the effectiveness of your treatment
- ✓Can be very useful as a preventative medicine instrument
- ✓Reveals the functional, biochemical and metabolic state of the patient providing a baseline for subsequent testing and monitoring

10

Why Utilize Functional Blood Testing?

The primary reason for making comprehensive metabolic blood testing available to your patients is that the body's organ systems are subjected to stresses (infections, toxic states, chemical assault, nutritional deficiencies, emotional stress, etc.), this causes cellular changes, leading to biochemical, functional, and metabolic changes followed by clinical manifestations and perhaps pathological conditions that will be reflected in the blood findings early on in the process.

By analyzing, determinations can be made regarding optimal indices levels. And it follows, that specific nutrients (vitamins, minerals, phytochemicals, herbs, enzymes) when targeted to specific organs and organ systems will result in predictable serum changes and improved clinical signs and symptoms in the patient.

11

Tests To Order: "Kaizen Wellness Panel"

- CBC with Differential
- Comprehensive Metabolic Panel (CMP14)
- C-Reactive Protein (CRP)
- Erythrocyte Sedimentation Rate (ESR) or Sed rate
- Ferritin
- GGT
- Hemoglobin A_{1c} (Hgb A_{1c})
- Homocysteine
- Insulin
- Iron
- Lactic Dehydrogenase (LDH)
- Lipid panel
- Magnesium
- Phosphorous
- Thyroid panel with TSH
- Uric acid
- Vitamin D, 25-Hydroxy

12

Huge dataset

Ours is the largest study comparing biomarker profiles measured throughout life among exceptionally long-lived people and their shorter-lived peers to date.
We compared the biomarker profiles of people who went on to live past the age of 100, and their shorter-lived peers, and investigated the link between the profiles and the chance of becoming a centenarian.
Our research included data from 44,000 Swedes who underwent health assessments at ages 64-99 - they were a sample of the so-called Amoris cohort.
These participants were then followed through Swedish register data for up to 35 years. Of these people, 1,224, or 2.7%, lived to be 100 years old. The vast majority (85%) of the centenarians were female.
Twelve blood-based biomarkers related to inflammation, metabolism, liver and kidney function, as well as potential malnutrition and anaemia, were included. All of these have been associated with ageing or mortality in previous studies.
The biomarker related to inflammation was uric acid – a waste product in the body caused by the digestion of certain foods.
We also looked at markers linked to metabolic status and function including total cholesterol and glucose, and ones related to liver function, such as alanine aminotransferase (Alat), aspartate aminotransferase (Asat), albumin, gamma-glutamyl transferase (GGT), alkaline phosphatase (Alp) and lactate dehydrogenase (LD).
We also looked at creatinine, which is linked to kidney function, and iron and total iron-binding capacity (TIBC), which is linked to anaemia. Finally, we also investigated albumin, a biomarker associated with nutrition.

13

Over 70% of Americans have at least 1 chronic health condition.

Chronic diseases cause 7 out of 10 premature deaths—many of which are completely preventable and account for 86% of our nation's healthcare costs.

And 40% have 2 or more.

14

My "Big 3" Focus Today ~

- **Blood Sugar**
- **Inflammation**
- **Microbiome**

15

Blood Sugar Dysregulation

- Glucose
- HgbA1c
- Insulin

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16

How important is healthy blood sugar regulation?

Obtaining and maintaining proper blood sugar metabolism is essential for health!!!! Protracted unhealthy blood sugar has significant effects upon: Blood vessels, eyes, nerves, kidneys and pancreas. It also affects energy levels, blood pressure, cholesterol, triglycerides, overall cardiovascular health, body shape to name a few.

It is estimated that his many as 50% of Americans age 20 years or older may be "prediabetic" sometimes referred to as "insulin resistance." If this condition goes unrecognized and no lifestyle or dietary changes are made, it is quite likely that they will move on to the next stage of diabetes.

No doubt obesity, excess sweets and refined or processed foods, and lack of exercise are major contributors to poor blood sugar metabolism.

Recognizing this "pre-diabetic state" is vitally important to the long-term health of your patients!

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Inflammation:

The Body's Healing 'Fire' Can Turn Harmful When It Burns Too Long

18

Inflammation:

The Body's Healing 'Fire' Can Turn Harmful When It Burns Too Long!

- **Uric Acid**
- **Ferritin**
- **C-Reactive protein**
- **Sedimentation Rate**
- **Homocysteine**

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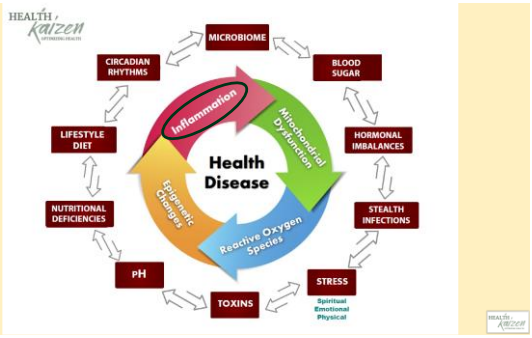

20

CDC Centers for Disease Control and Prevention

PREVENTING CHRONIC DISEASE

PUBLIC HEALTH RESEARCH, PRACTICE, AND POLICY

SPECIAL TOPIC

In Search of a Germ Theory Equivalent for Chronic Disease

Abstract

Introduction

"...for which there is no single underlying etiology. The discovery of a form of low-grade systemic and chronic inflammation ("metaflammation"), linked to inducers (broadly termed "anthropogens") associated with modern man-made environments and lifestyles, suggests an underlying basis for chronic disease that could provide a 21st-century equivalent of the germ theory."

Egger G. In Search of a Germ Theory Equivalent for Chronic Disease. Prev Chronic Dis 2012;9:110301.

21

CDC Centers for Disease Control and Prevention
PREVENTING CHRONIC DISEASE

In Search of a Germ Theory Equivalent for Chronic Disease

“The discovery of a form of otherwise unrecognized inflammation in the early 1990s and its widespread presence in many chronic diseases led to the suggestion that many, if not all, such diseases may have this type of inflammatory basis. If so, . . .

Egger G. In Search of a Germ Theory Equivalent for Chronic Disease. Prev Chronic Dis 2012;9:110301.

22

What Exactly Is Inflammation (and What Is It Not?)

Abstract: <u>In medicine, inflammation is a fuzzy, overused word first coined by the Romans, the intended meaning and precise definition of which varies according to the person and the clinical context. It tends to carry a negative connotation as a response gone awry, like a raging, out-of-control wildfire that requires immediate control and containment lest it destroy all in its path; however, frequently overlooked or lost in the shuffle is the primordial importance of inflammation to health and survival.</u> The precise definition of inflammation matters for several reasons, not least because of the over-liberal use of anti-inflammatory drugs to inhibit inflammation, which may, contrary to prevailing dogma that all inflammation is harmful, act counterproductively to prevent restitutio ad integrum. <u>Using fire as a central analogy, this overview attempts to define inflammation, the better to determine how to manage it, i.e., whether to fan its flames, let it burn out, or suppress it entirely.</u>

Oronsky, B.; Caroen, S.; Reid, T. What Exactly Is Inflammation (and What Is It Not?). Int. J. Mol. Sci. 2022, 23, 14905. https://doi.org/10.3390/ijms232314905

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23

PERSPECTIVE — nature medicine

Chronic inflammation in the etiology of disease across the life span

Indeed, chronic inflammatory diseases have been recognized as the most significant cause of death in the world today, with more than 50% of all deaths being attributable to inflammation-related diseases such as ischemic heart disease, stroke, cancer, diabetes mellitus, chronic kidney disease, non-alcoholic fatty liver disease (NAFLD) and autoimmune and neurodegenerative conditions. <u>Evidence is emerging that the risk of developing chronic inflammation can be traced back to early development, and its effects are now known to persist throughout the life span to affect adulthood health and risk of mortality</u>

Furman, D., Campisi, J., Verdin, E. *et al.* Chronic inflammation in the etiology of disease across the life span. *Nat Med* 25, 1822–1832 (2019). https://doi.org/10.1038/s41591-019-0675-0

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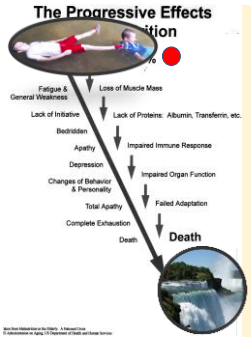
Our goal is to recognize and identify patterns of internal chemistry, toxicity and nutritional deficiencies, which if corrected now will lead to Optimum Health and an improved quality of life.

If left uncorrected, they may become full-blown diseases later. Perhaps, requiring dangerous drugs and/or surgery in an attempt to prolong life, and most likely diminishing quality of life to a mere survival mode.

25



Progression of a Nutrient Deficiency

Biochemical

- Nutritional deficiencies
- Presence of toxins
- Stealth infections
- Stress
- pH
- ?????????????

Symptoms – None (yet)

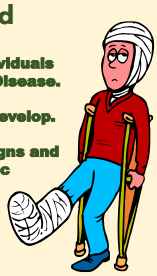
26

The Walking Wounded

The "Walking Wounded" are the unfortunate individuals who have reached a stage between Health and Disease.

Traditional Medicine has to wait for disease to develop.

Natural medicine doctors look for the earliest signs and symptoms of changes in functional and metabolic processes to promote health and prevent diseases from progressing if possible.



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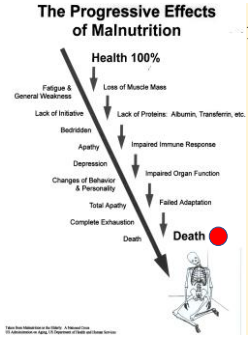

Progression of a Nutrient Deficiency

Pathological

Symptoms:

- "What's wrong with me?"
- Specific disease processes such as an Autoimmune Disease, diabetes, cardiovascular or other organ disease, possibly cancer and eventually -

Death

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The Mighty Microbiome

- **CBC with diff**

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Trillions of microbes have evolved with and continue to live on and within human beings. A variety of environmental factors can affect intestinal microbial imbalance, which has a close relationship with human health and disease. Here, we focus on the interactions between the human microbiota and the host in order to provide an overview of the microbial role in basic biological processes and in the development and progression of major human diseases such as infectious diseases, liver diseases, gastrointestinal cancers, metabolic diseases, respiratory diseases, mental or psychological diseases, and autoimmune diseases.

Baohong Wang, Mingfei Yao, Longxian Lv, Zongxin Ling, Lanjuan Li, The Human Microbiota in Health and Disease, Engineering, Volume 3, Issue 1, 2017, Pages 71-82, ISSN 2095-8099, https://doi.org/10.1016/J.ENG.2017.01.008.

30


European Journal of Clinical Nutrition
PERSPECTIVE
Role of the gut microbiome in chronic diseases: a narrative review
"The gut microbiome, i.e., the community of bacteria and other microorganisms living in the human gut, has been implicated both directly and indirectly (mediating the effects of diet) on human health [1, 2]. The associations between gut microbiome composition and disease status have been widely reported, while recent studies have demonstrated a role for the gut microbiome in influencing remote organs, mucosal, and immune function."
"Differences in gut microbiome composition and function have been associated with a variety of chronic diseases ranging from gastrointestinal inflammatory and metabolic conditions to neurological, cardiovascular, and respiratory illnesses."
European Journal of Clinical Nutrition (2022) 76:489–501; https://doi.org/10.1038/s41430-021-00991-6
Stealth Infections
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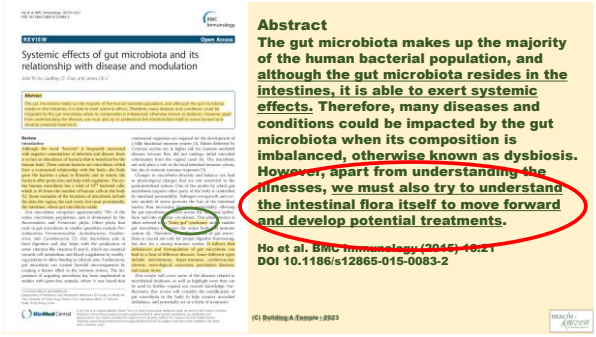
REVIEW
Open Access
Systemic effects of gut microbiota and its relationship with disease and modulation
Abstract
The gut microbiota makes up the majority of the human bacterial population, and although the gut microbiota resides in the intestines, it is able to exert systemic effects. Therefore, many diseases and conditions could be impacted by the gut microbiota when its composition is imbalanced, otherwise known as dysbiosis. However, apart from understanding the illnesses, we must also try to understand the intestinal flora itself to move forward and develop potential treatments.
Ho et al. BMC Immunology (2015) 16:21
DOI 10.1186/s12865-015-0083-2
(C) Building A Temple : 2023

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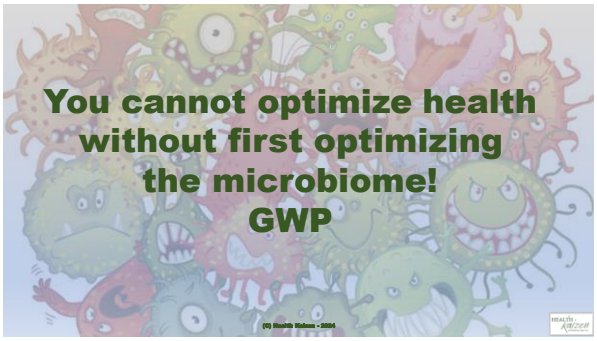
You cannot optimize health without first optimizing the microbiome!
GWP
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The Mighty Microbiome!
"What's Bugging You?
www.healthkaizenlife.com
On-Demand
(Complimentary)

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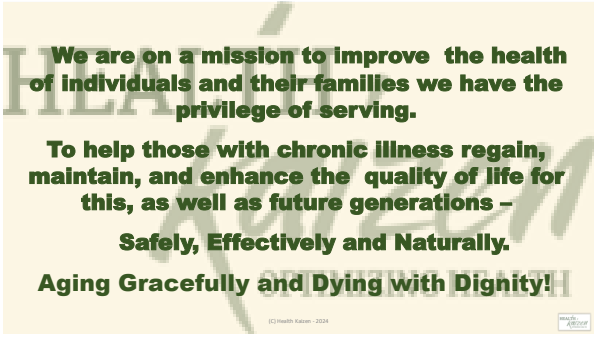
We are on a mission to improve the health of individuals and their families we have the privilege of serving.
To help those with chronic illness regain, maintain, and enhance the quality of life for this, as well as future generations –
Safely, Effectively and Naturally.
Aging Gracefully and Dying with Dignity!
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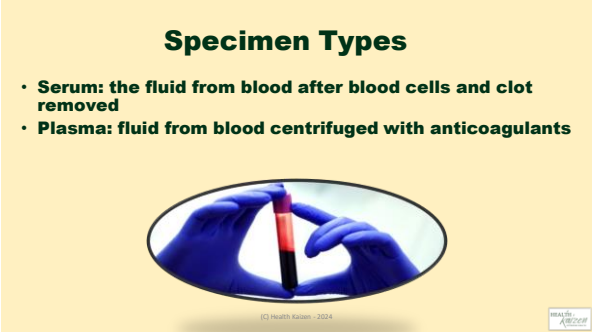
35


Specimen Types
Serum: the fluid from blood after blood cells and clot removed
Plasma: fluid from blood centrifuged with anticoagulants
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Blood Components

Serum is obtained from clotted blood that has not been mixed with an anticoagulant (a chemical that prevents the clotting of blood). This clotted blood is then centrifuged, yielding serum, which contains two types of protein: albumin and globulin.

Serum is usually collected in mottled red/gray (Tiger), but red-top tubes are occasionally used.

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Blood Components

Plasma is obtained from blood that has been mixed with an anticoagulant in the collection tube and has, therefore, not clotted. This mixed blood is then centrifuged, yielding plasma, which contains albumin, globulin and fibrinogen.

38

Blood Components

Either plasma or serum may be separated from the blood cells by centrifugation.

The essential difference between plasma and serum is that plasma retains fibrinogen (the clotting component), which is removed from serum.

39

Blood Components

There are numerous coagulation factors (factor VIII, factor IX, etc.) involved in the clotting of blood. Several different types of anticoagulants interfere with the activity these factors to prevent clotting. Both anticoagulants and preservatives may be required for plasma specimens. The specified anticoagulant or preservative must be used for the test procedure ordered. The chemical has been chosen to preserve some feature of the specimen and to work with a method used to perform the test.

Blood collected with one anticoagulant is suitable for the test described and may not be considered suitable for other tests. Because and it is or not interchangeable, it is necessary to consult the specimen requirement field of individual test description as to determine the appropriate collection requirements for the test ordered.

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Blood Collection Tube (Vacutainer) Types

Color	Red (plain)	Red (speckled)	Gold	Light blue	Green (dark)	Green (light)	Lavender	Pink	Gray	Royal blue	Royal blue
Additive	None	Clot activator (silica particles)	Clot activator (silica particles) & Gel separator	Sodium citrate 3.2%	Sodium heparin	Lithium heparin (with or without gel)	Potassium EDTA (K2EDTA)	Potassium EDTA (K2EDTA)	Sodium Fluoride & Potassium Oxalate / Sodium Oxalate	None	Potassium EDTA (K2EDTA)
Uses	Chemistry panels (after serum separation)	Chemistry panels (after serum separation)	Chemistry panels (after serum separation)	Coagulation studies (PT, PTT, INR)	Chemistry panels (especially "stat" tests), Blood gas analysis	Chemistry panels (especially "stat" tests), Blood gas analysis	CBC, Blood bank testing	CBC, Blood bank testing	Blood glucose	Trace element and heavy metal testing (less common)	Trace element and heavy metal testing (more common)

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Blood Components

- **Constitutes of blood are approximately 6 to 8% of total body weight.**
- **Average male this represents approximately 5 quarts (2.85 liters).**
- **The fluid portion of blood – serum plasma accounts for 45 to 60% of blood's total weight. This is made up of:**
  - **Water**
  - **Dissolved materials (being carried to the tissues):**
    - **Hormones**
    - **Antibodies**
    - **Enzymes**
  - **Cellular wastes being carried to lungs, liver, and kidneys.**

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Blood Components

The major blood cells are:

- **Red Blood Cells (RBC) or erythrocytes.**
  - **Delicate, round, concave bodies that contain hemoglobin**
  - **Carry oxygen and carbon dioxide.**
  - **RBC production is regulated by oxygenation.**
  - **Erythropoietin is the hormone directly responsible, its production is dependent on kidney function and oxygen levels.**
- **Platelets or thrombocytes**
  - **Involved in with the clotting process and retraction of clots.**
  - **Under the control of thrombopoietin.**

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Blood Components

The major blood cells are:

- **White Blood Cell (WBC) or leukocytes their primary purpose is to fight infection and outside invaders: parasites, bacteria, viruses, fungi, etc.**
  - **Made up of:**
    - ✓ **Neutrophils – neutrophil, granulocyte, polymorphonuclear leukocyte and segmented neutrophil are all interchangeable terms.**
    - ✓ **Lymphocytes**
    - ✓ **Monocytes**
    - ✓ **Eosinophils**
    - ✓ **Basophils**

Stealth Infections

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Except in NY, NJ, and RI

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- *Comprehensive Informational and Educational Resources*

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Metabolic Maintenance Appreciation Offer
Opti Cardio Plus + ESR + Phlebotomy $100

Join PCS and Call Our Office to Schedule Your Test by October 4, 2024
Existing Members Welcome, Too!

349751 Opti-Cardio Plus Components:
Fasting / Avoid Exercise

C-Reactive Protein (CRP), High Sensitivity
Complete Blood Count (CBC) with Differential & Platelet Count
Comprehensive Metabolic Panel (CMP14)
Ferritin
Fibrinogen Activity
GGT
Hemoglobin A1c
Homocysteine
Insulin, Fasting
Iron, Serum
LDH
Lipid Panel with Total Cholesterol/HDL Ratio
Magnesium, Serum
Phosphorus, Serum
TIBC % Saturation
Thyroid Panel with Thyroid-Stimulating Hormone (TSH)
Uric Acid, Serum
Urinalysis, Routine
Vitamin D, 25-Hydroxy

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IMPORTANT

Each commercial lab has its own set of normal values, called Normal Range or Reference Interval or Range on a lab report. These values depend on the equipment or method used, male or female, age, and geographical location. Results that are out of range may or may not represent a problem.

Test results can be affected by several factors, including age, biological sex, pregnant, time of day when the sample was taken, active infections, and food (some test samples need to be taken after fasting for 12 hours). Where normal values for people assigned female at birth (AFAB) and people assigned male at birth (AMAB) are different, they are indicated as F and M.

50

Reference Intervals

"Graham Jones,"* Antony Badrick†

51

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Shogun B & B Series

(Basics & Background)

Laying the Foundation to journey into effective Functional Medicine Examinations, Procedures and Protocol Recommendations.

Part 1 of the Shogun B & B Series – Introduction to Chronic Disease ~ Aging Gracefully and Dying with Dignity	
Part 2 of the Shogun B & B Series – Methylation Made Super Simple ~ Introduction and overview of Methylation	
Part 3 of the Shogun B & B Series – Methylation Made Super Simple ~ Epigenesis and Epimutagens	
Part 4 of the Shogun B & B Series – The Microbiome, Stealth Infections, and Acid/Alkaline Balance	
Part 5 of the Shogun B & B Series – Blood Sugar and pH Regulation	
Part 6 of the Shogun B & B Series – Stress, Adrenals, Thyroid, and the Adrenal/Thyroid Connection	
Part 7 of the Shogun B & B Series – Commonly Encountered Cardiovascular Conditions, Lymphatics, and Toxins	
Part 8 of the Shogun B & B Series – Circadian Rhythms, EMFs, Sleep, and more.	
Part 9 of the Shogun B & B Series – Diet and Lifestyle Modifications	
Part 10 of the Shogun B & B Series – Transformed Weight Management	

These videos are only available to Clinical Mentorship subscribers ~ www.healthkaizenlife.com

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SERUM GLUCOSE

Laboratory range: 70 – 99 mg/dl **Optimal range: 85 – 100**
Will Robinson (WR) range: <60 or >300

Clinical Discussion:
Erratic blood sugar measures maybe indicative of coming diabetes. Adrenals, pancreas, and liver all influence blood sugar levels. Patients with an elevated glucose are not properly utilizing carbohydrates due to an inability of the cells to burn sugar. Glucose tends to be very acidic; this is why diabetics are generally acidic, CO2 will generally be less than 25.

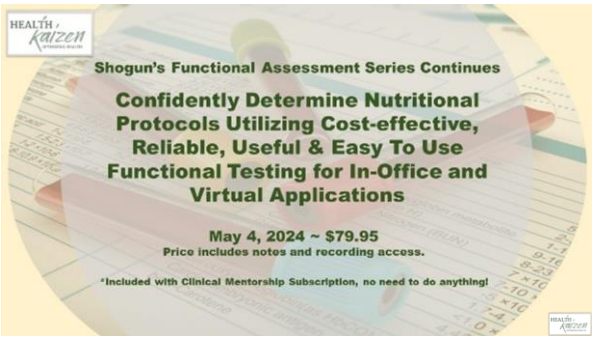
Two hormones, glucagon and insulin tightly regulate blood glucose in the healthy individual. Glucagon accelerates the breakdown of glycogen in the liver which causes an increase in blood glucose levels. Insulin, on the other hand increases cellular membrane permeability allowing for the transport of glucose into the cell for the metabolic needs of the cell.

Getting insulin inside the cell membrane where the actual metabolism takes place requires insulin and the insulin receptors found on the cell membrane. Following the ingestion of a meal with carbohydrates.

> 125 indicates insulin resistance
> 140 on more than 1 fasting reading is virtually diagnostic of diabetes

CPT 00132

54



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SERUM GLUCOSE

DISCUSSION:

***Signs and symptoms*: polyuria, polydipsia, weight loss, fatigue, slow wound healing, and frequent infections.**

***Complications*: Neuropathy, nephropathy, cardiovascular disease, gangrene, skin ulcerations, retinopathy**

***If glucose is elevated, consider the following*:**

1. **Diabetes. A fasting glucose greater than or equal to 140 mg/dL on more than one occasion is considered adequate for the diagnosis of diabetes mellitus. A two-hour postprandial glucose of greater than 200 mg/dL is virtually diagnostic of diabetes mellitus and obviates the need for a glucose tolerance test. Be sure to run a hemoglobin A1c and a simple urinalysis, glucosuria usually does not occur until plasma values reach 180.**
2. **With an elevated cholesterol greater than 220 and triglycerides greater than 150 suspect hyperinsulinemia (Syndrome X).**
3. **With a decreased CO2, less than 25, and an increased anion gap greater than 12, suspect a thiamine deficiency**
4. **Glucose levels may be elevated in response to a poor phlebotomy experience.**
5. **Drugs that may also interfere with glucose levels include: ACTH, corticosteroids, epinephrine, furosomide, thiazides, phenytoin**

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SERUM GLUCOSE

INCREASED (hyperglycemia)	DECREASED (hypoglycemia)
Diabetes – (triglycerides, Hgb A1c increased)	Fasting hypoglycemia
Thiamine (B1) insufficiency	Adrenal hypofunction
Dysinsulinism (Syndrome-X/Metabolic syndrome)	Liver dysfunction
Both hyperthyroidism and hypothyroidism	Hyperinsulinism
Infections	Pregnancy
Chronic nephritis	Addison's disease
Hyperpituitarism	Pancreatic cancer or pancreatitis
Adrenal hyperfunction	Polycystic ovary disease
Cushing's disease	Improper regulation of insulin with IDDM

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SERUM GLUCOSE

Symptoms of Functional or Reactive Hypoglycemia (Low Blood Sugar):

- Irritability if meals are missed.
- Eating to relieve fatigue.
- Increased energy after meals (energy should be consistent before and after meals).
- Craving for sweets between meals.
- Dependency on coffee and sugar for energy.
- Becoming lightheaded if meals are missed.
- Feeling shaky, jittery, or tremulous.
- Feeling agitated and nervous.
- Becoming easily upset.
- Poor memory, forgetfulness.
- Blurred vision.
- May not feel hungry despite needing to eat.

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SERUM GLUCOSE

INCREASED	DECREASED
Alpha lipoic acid	Niacin
Liver, adrenal, pancreas, pituitary extract	Chromium
B - vitamins(B1)	Magnesium
Magnesium	Omega-3 and 6 fatty acids
Muscle extract	
CoQ10	Liver, adrenal, pancreas, pituitary extract
Paleo-Mediterranean diet (KETO)	Paleo- Mediterranean diet

- Berberine – 1 – 4 tid
- GlucoBalance – 2 w meals
- BioGlycozyme - 2 – 3 tid
- Lipoic acid – 1 tid
- Cytozyme H – 1 tid
- ADHS – 3 – 4 bid
- GlucoResolve

- BioGlycozyme - 2 – 3 tid
- Amino Acid Quick Sorb – squirt

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Hemoglobin A1c (Hgb A1c)*

Laboratory range: 4.8 - 5.6% **Optimal range: 4.9 - 5.5**

WR range >8.1(the risk of microalbuminuria IDDM increases dramatically at this level)

Clinical Discussion:

On the individual cellular level Hemoglobin A1c or glycated hemoglobin is not a reversible glucose-protein bond, it is glycated through the life of the red blood cells (approximately 120 days). The formation of new, 'healthy' RBCs is what lowers the A1c. Hemoglobin A1c levels provide a more accurate assessment of the diabetic's blood sugar control as it assesses the past 2 - 3 months.

✓> 8% - action suggested, high risk of developing long-term complications such as retinopathy, nephropathy, neuropathy, cardiopathy, etc.

✓< 7% - current Gold standard - diabetic therapy, some danger of hypoglycemic reaction type I diabetic. Some glucose intolerance individuals and "subclinical" diabetics (Prediabetic) may demonstrate A1c levels in this area.

✓Prediabetes: 5.7 – 6.4

✓Diabetes - >6.4

CPT 83036

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Diabetes, Prediabetes, and Brain Aging: The Role of Healthy Lifestyle

"Diabetes and even prediabetes are associated with accelerated brain aging, especially among men and people with poor cardiometabolic health. However, a healthy lifestyle may counteract this."

Abigail Dove, Jiao Wang, Huijie Huang, Michelle M. Dunk, Sakura Sakakibara, Marc Guitart-Masip, Goran Papenberg, Weili Xu; Diabetes, Prediabetes, and Brain Aging: The Role of Healthy Lifestyle. *Diabetes Care* 2024; dc240860. https://doi.org/10.2337/dc24-0860

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Aim

To investigate the relationship between (pre)diabetes and older brain age, and whether this can be attenuated by modifiable lifestyle factors

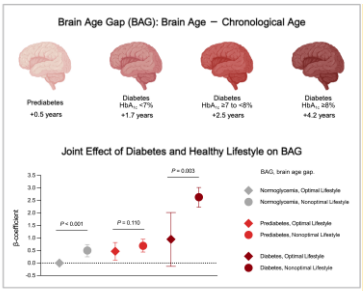
Methods

N = 31,229 UK Biobank participants (40-70y)

Exposures:
- (Pre)diabetes was defined based on medical history and measured HbA_{1c} values
- Healthy lifestyle was defined as no smoking, no heavy drinking, and high physical activity

Outcome:
- Brain age was estimated using a machine learning model based on 1,079 brain MRI phenotypes

Group differences were compared using multivariable linear regression models



Conclusion: Diabetes and even prediabetes are associated with accelerated brain aging, but this may be attenuated by a healthy lifestyle. The results highlight diabetes and prediabetes as ideal targets for lifestyle-based interventions to promote brain health.

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SERUM INSULIN*

Laboratory Range: 0.0-24.9 µIU/ml **Optimum range: < 8**
WR range: >25

Clinical discussion:
Insulin is a peptide hormone, it is secreted by the beta cells of the pancreas in response to glucose levels in the blood. It passes into circulation via the portal vein and the liver. Insulin is generally released in pulses, with the parallel glucose cycle normally about two minutes ahead of the insulin cycle.

The insulin molecule consists of two polypeptide chains, the α-chain with 21 and the β-chain with 30 amino acids. Biosynthesis of the hormone takes place in the β-cells of the islets of Langerhans in the form of single-chain preproinsulin, which is immediately cleaved to give proinsulin. Specific proteases cleave proinsulin to insulin and C-peptide which pass into the bloodstream simultaneously. About half of the insulin, but virtually none of the C-peptide, is retained in the liver.

Circulating insulin has a half-life of three to five minutes and is preferentially degraded in the liver, whereas inactivation or excretion of proinsulin and C-peptide mainly takes place in the kidneys.

CPT 83525

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Definition of Diabetes

- **Type I: Insulin Deficiency is characterized by:**
  - **Destruction of the pancreatic islet cells by some infection or autoimmune reaction**
  - **Typically occurring in a child or adolescent**
- **Type II: Insulin Resistance is characterized by:**
  - **Resistance to insulin at the cellular level with the initial excessive insulin production being unable to clear glucose from the blood stream.**
- **Pre-Diabetes: "Insulin Resistance", "Metabolic Syndrome" is a pre-diabetic condition with excessive insulin production. The glycogenated hemoglobin may be in normal range.**

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SERUM INSULIN

Insulin Resistance, Metabolic Syndrome or Syndrome X

According to the American Heart Association and the National Heart, Lung, and Blood Institute, metabolic syndrome is present if you have two or more of the following signs:

***Signs and symptoms*: Extra weight around the middle and upper parts of the body, central obesity. The body may be described as "apple-shaped."**

- **Blood pressure equal to or higher than 130/85 mmHg**
- **Fasting blood sugar (glucose) equal to or higher than 100 mg/dL**
- **Large waist circumference (length around the waist):**
  - **Men - 40 inches or more**
  - **Women - 35 inches or more**
- **Low HDL cholesterol:**
  - **Men - under 40 mg/dL**
  - **Women - under 50 mg/dL**
- **Triglycerides equal to or higher than 150 mg/dL**

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SERUM INSULIN

Symptoms of insulin resistance (high blood sugar):

- **Constant hunger.**
- **Fatigue after meals.**
- **Hormonal issues.**
- **General fatigue.**
- **Craving for sweets not relieved by eating them.**
- **Must have sweets after meals.**
- **Waist girth equal to or larger than hip girth.**
- **Frequent urination.**
- **Increased appetite and thirst.**
- **Difficulty losing weight.**
- **Migrating aches and pains.**

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Metabolic Syndrome

The term "Metabolic Syndrome" refers to the clustering of risk factors associated with cardiovascular disease (CVD) and type 2 diabetes.

Pre-Diabetes: " Insulin Resistance", "Metabolic Syndrome" is a pre-diabetic condition with excessive insulin production. The glycogenated hemoglobin may be in normal range.

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SERUM INSULIN

Etiology of Elevated Fasting Insulin: **Obesity is the most common cause.**

Dangers of Elevated Fasting Insulin:

- **Retention of sodium; increased B.P.; fluid retention**
- **Increased plaque in the arteries**
- **High correlation between high insulin & certain types of cancer**
- **Aging, memory problems, immune suppression, obesity, & heart disease**

With Elevated Fasting Insulin consider the following:

- **Berberine HCl**
- **Exercise. Insulin sensitivity is improved with even moderate exercise.**
- **The following minerals have been shown to help: magnesium, chromium, vanadium, and zinc**
- **The following B vitamins will help: Biotin, and inositol**

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ScienceDirect

Biomedical Journal

Short review

The etiology of oxidative stress in insulin resistance

Samuretha Harrik, Walter H. Hou

Insulin resistance is a prevalent syndrome in developed as well as developing countries. It is the predisposing factor for type 2 diabetes mellitus, the most common end stage development of metabolic syndrome in the United States. Previously, studies investigating type 2 diabetes have focused on beta cell dysfunction in the pancreas and insulin resistance, and developing ways to correct these dysfunctions. However, in recent years, there has been a profound interest in the role that oxidative stress in the peripheral tissues plays to induce insulin resistance. The objective of this review is to focus on the mechanism of oxidative species generation and its direct correlation to insulin resistance, to discuss the role of obesity in the pathophysiology of this phenomenon, and to explore the potential of antioxidants as treatments for metabolic dysfunction.

Biomedical journal 40(2017) 257-262

69

Biochimica et Biophysica Acta

Is Alzheimer's disease a Type 3 Diabetes? A critical appraisal☆

Kamesh Kandimalla*, Vani Thirumala**, P. Hemachandra Reddy***

"Recently researchers proposed the term 'Type-3-Diabetes' for Alzheimer's disease (ad) because of the shared molecular and cellular features among Type-1-Diabetes, Type-2-Diabetes and Insulin resistance associated with memory deficits and cognitive decline in elderly individuals."

"Interestingly, insulin also plays a crucial role in the formation amyloid plaques. In this review, we discussed significant shared mechanisms between AD and diabetes and we also provided therapeutic avenues for diabetes and AD. This article is part of a Special issue entitled: Oxidative Stress and Mitochondrial Quality in Diabetes/Obesity and Critical Illness Spectrum of Diseases - edited by P. Hemachandra Reddy.

Biochimica et Biophysica Acta 1863 (2017) 1078–1089
https://dx.doi.org/10.1016/j.bbadis.2016.08.018
0925-4439/© 2016 Elsevier B.V. All rights reserved.

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International Journal of Molecular Sciences

Alzheimer's Disease as Type 3 Diabetes: Common Pathophysiological Mechanisms between Alzheimer's Disease and Type 2 Diabetes

Abstract: **Globally, the incidence of type 2 diabetes mellitus (T2DM) and Alzheimer's disease (AD) epidemics is increasing rapidly and has huge financial and emotional costs.**

AD and T2DM are interlinked with insulin resistance, neuroinflammation, oxidative stress, advanced glycosylation end products (AGEs), mitochondrial dysfunction and metabolic syndrome. Beta-amyloid, tau protein and amylin can accumulate in T2DM and AD brains. Given that the T2DM patients are not routinely evaluated in terms of their cognitive status, they are rarely treated for cognitive impairment.

Studies suggesting AD as a metabolic disease caused by insulin resistance in the brain also offer strong support for the hypothesis that AD is a type 3 diabetes.

Michailidis M, Moraitou D, Tata DA, Kalinderi K, Papamitsou T, Papaliagkas V. Alzheimer's Disease as Type 3 Diabetes: Common Pathophysiological Mechanisms between Alzheimer's Disease and Type 2 Diabetes. Int J Mol Sci. 2022 Feb 28;23(5):2687. doi: 10.3390/ijms23052687. PMID: 35269827; PMCID: PMC891048

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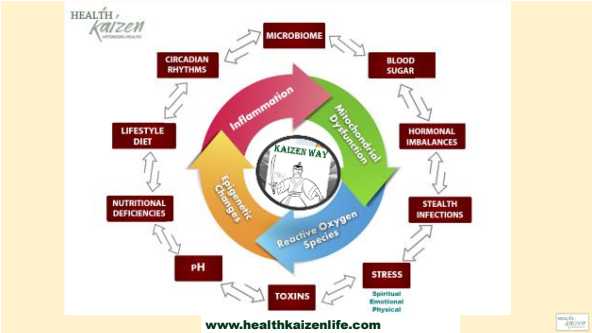


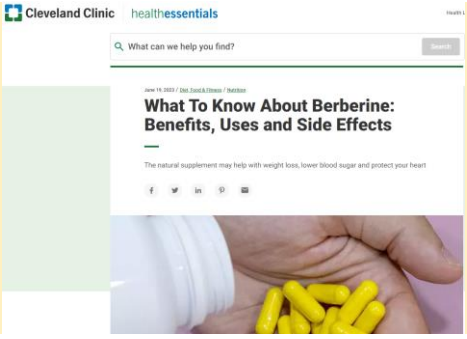
72

The Failure of Traditional Medicine

Traditionally trained physicians have been taught to treat Blood Sugar Dysregulation based on numbers alone – Glucose & HgbA1C.

DIABETES MELLITUS GIVES US A CHANCE TO THROW AWAY THE PROTOCOLS AND TREAT THE 'CAUSE'.

73



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75

Is Berberine Superior to Metformin in Management of Diabetes Mellitus and its Complications?

"**Berberine scores over metformin as a antidiabetic** by certain pharmacological mechanism like alpha glucosidase reductase inhibition, **release of GLP 1**, **modification of gut microbiota**, inhibition of enzyme dipeptidyl pepetidase 4 **and as a insulin mimetic.** Lipid lowering action and effect on polycystic ovarian disease is more superior with berberine than metformin. **Thus it can be concluded that berberine can be superior to metformin in management of diabetes and in prevention of its complications.**"

International Journal of Pharmacognosy and Phytochemical Research 2015; 7(3); 543-553

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molecules

Berberine, a Herbal Metabolite in the Metabolic Syndrome: The Risk Factors, Course, and Consequences of the Disease

"**Berberine is a plant alkaloid possessing scientifically determined mechanisms of the prevention of the development of atherosclerosis, type 2 diabetes, and obesity, as well as cardiovascular complications and cancer.** It positively contributes to elevated levels of fasting, postprandial blood glucose, and glycosylated hemoglobin, while decreasing insulin resistance. It stimulates glycolysis, improving insulin secretion, and inhibits gluconeogenesis and adipogenesis in the liver; **by reducing insulin resistance**, berberine also **improves ovulation**. The **anti-obesity action** of berberine has been also well-documented."

Och, A.; Och, M.; Nowak, R.; Podgórska, D.; Podgórski, R. Berberine, a Herbal Metabolite in the Metabolic Syndrome: The Risk Factors, Course, and Consequences of the Disease. Molecules 2022, 27, 1351. https://doi.org/10.3390/molecules27041351

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Novo Nordisk CEO: Wegovy will lower, not raise, healthcare costs

Employers and employees spent more than $400 billion on obesity care in 2023; Novo Nordisk's CEO said weight loss drug Wegovy can reduce these costs — an inverse of critics' expectations.

For months, U.S. lawmakers have slammed Novo Nordisk's monthly list prices of Ozempic ($969) and Wegovy ($1,349) because the drugs can be 10 to 15 times cheaper in other countries. The Denmark-based company has previously said the reason for these price disparities is because of America's complex pharmaceutical industry.

"Unfortunately, even when we lower our prices, patients in the United States often don't receive the savings — this is a problem," a spokesperson told *Becker's* in July. The company has said it receives about 60% of U.S. list prices after pharmacy benefit managers take rebates and fees.

CEO Lars Fruergaard Jørgensen told *NBC Nightly News* the two medications are reducing overall healthcare costs. As the drugs help people lose weight, employers and employees might see reduced medical costs, disability payments, workers' compensation and absenteeism.

"We are actually providing products that's actually helping take that cost burden off," Mr. Jørgensen told the news outlet, adding that more than 80% of insured Americans pay $25 or less for a month's supply.

Business Group on Health recently surveyed 125 companies that cover 17.1 million workers across multiple industries about projected healthcare costs for 2025. About 79% of employers said they have seen increased interest in obesity medications and 96% said they are concerned about the long-term cost implications.

The companies expect an 8% increase in employers' healthcare costs, partly because of GLP-1 medications. Multiple organizations have already trimmed GLP-1 coverage for their employees because of rising costs.

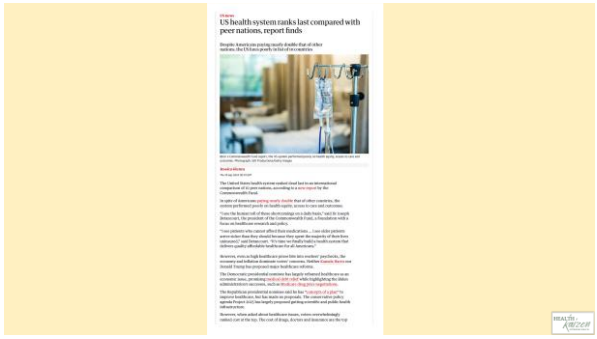
Mr. Jørgensen is slated to testify at a Health, Education, Labor and Pensions Committee hearing on Sept. 24 about Ozempic and Wegovy's prices.

Subscribe to the following topics: employeeshealthcare costsobesityemployerswegovy
Latest articles on GLP-1s:
The specialty where weight loss drug adherence isn't a problem
The GLP-1 questions facing health systems
Ozempic and cancer: What to know

https://www.beckershospitalreview.com/glp-1s/novo-nordisk-ceo-wegovy-will-lower-not-raise-healthcare-costs.html

8/27/24

78



US health system ranks last compared with peer nations, report finds

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Original Article

Berberine, a Natural Plant Product, Activates AMP-Activated Protein Kinase With Beneficial Metabolic Effects in Diabetic and Insulin-Resistant States

These findings suggest that berberine displays beneficial effects in the treatment of diabetes and obesity at least in part via stimulation of AMPK activity.

Yun S. Lee, Woo S. Kim, Kang H. Kim, Myung J. Yoon, Hye J. Cho, Yun Shen, Ji-Ming Ye, Chul H. Lee, Won K. Oh, Chul T. Kim, Cordula Hohnen-Behrens, Alison Gosby, Edward W. Kraegen, David E. James, Jae B. Kim; Berberine, a Natural Plant Product, Activates AMP-Activated Protein Kinase With Beneficial Metabolic Effects in Diabetic and Insulin-Resistant States. *Diabetes* 1 August 2006; 55 (8): 2256–2264. https://doi.org/10.2337/db06-0006

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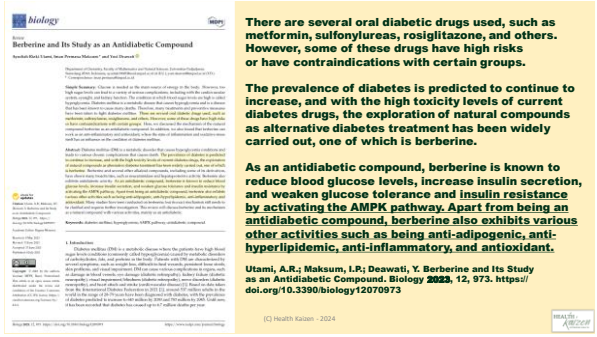

biology

Review

Berberine and Its Study as an Antidiabetic Compound

There are several oral diabetic drugs used, such as metformin, sulfonylureas, rosiglitazone, and others. However, some of these drugs have high risks or have contraindications with certain groups.

The prevalence of diabetes is predicted to continue to increase, and with the high toxicity levels of current diabetes drugs, the exploration of natural compounds as alternative diabetes treatment has been widely carried out, one of which is berberine.

As an antidiabetic compound, berberine is known to reduce blood glucose levels, increase insulin secretion, and weaken glucose tolerance and insulin resistance by activating the AMPK pathway. Apart from being an antidiabetic compound, berberine also exhibits various other activities such as being anti-adipogenic, anti-hyperlipidemic, anti-inflammatory, and antioxidant.

Utami, A.R.; Maksum, I.P.; Deawati, Y. Berberine and Its Study as an Antidiabetic Compound. Biology 2023, 12, 973. https://doi.org/10.3390/biology12070973

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Signal Transduction and Targeted Therapy

ARTICLE

Berberine treats atherosclerosis via a vitamine-like effect down-regulating Choline-TMA-TMAO production pathway in gut microbiota

Trimethylamine-N-oxide (TMAO) derived from the gut microbiota is an atherogenic metabolite

Oral BBR decreased TMAO production in animal intestine, lowered blood TMAO and interrupted plaque formation in blood vessels in the HFD-fed hamsters. Moreover, 21 patients with atherosclerosis exhibited the average decrease of plaque score by 3.2% after oral BBR (0.5 g, bid) for 4 months (*P < 0.05, n = 21); whereas the plaque score in patients treated with rosuvastatin plus aspirin, or clopidogrel sulfate or ticagrelor (4 months, n = 12) increased by 1.9%. TMA and TMAO in patients decreased by 38 and 29% in faeces (*P < 0.05; *P < 0.05), and 37 and 35% in plasma (*P < 0.001; *P < 0.05), after 4 months on BBR. BBR might treat atherosclerotic plaque at least partially through decreasing TMAO in a mode of action similar to that of vitamins**

Signal Transduction and Targeted Therapy (2022) 7:207 ; https://doi.org/10.1038/s41392-022-01027-6

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How important is healthy blood sugar regulation?

Obtaining and maintaining proper blood sugar metabolism is essential for health!!!! Protracted unhealthy blood sugar has significant effects upon: Blood vessels, eyes, nerves, kidneys and pancreas. It also affects energy levels, blood pressure, cholesterol, triglycerides, overall cardiovascular health, body shape to name a few.

It is estimated that his many as 50% of Americans age 20 years or older may be "prediabetic" sometimes referred to as "insulin resistance." If this condition goes unrecognized and no lifestyle or dietary changes are made, it is quite likely that they will move on to the next stage of diabetes.

No doubt obesity, excess sweets and refined or processed foods, and lack of exercise are major contributors to poor blood sugar metabolism.

Recognizing this "pre-diabetic state" is vitally important to the long-term health of your patients!

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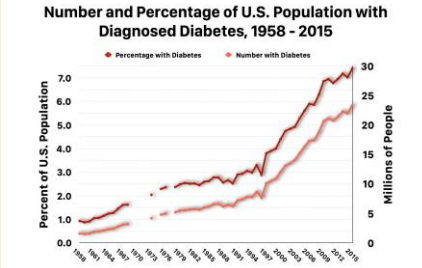

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SERUM URIC ACID*

Laboratory Range: 3.0 – 7.2 mg/dL (F) 3.8 – 8.4 (M) Optimal Range: 4 - 6
WR range – > 9.0 indicate severe hyperuricemia and requires immediate medical attention.
Values < 3.0 mg/dL generally indicates either a need for B12 or molybdenum.

Clinical Discussion:
Uric acid is synthesized in the liver and transported to and stored in the kidneys. Generally, you will see an increase in uric acid along with creatinine and BUN in renal dysfunctions and occasionally with liver dysfunction. It is the end product of purine (protein), nucleic acid, and nucleoprotein metabolism. Exogenous purines are absorbed from the intestines after digestion has separated them from the larger nucleoprotein's that have been consumed in the diet.

Uric acid excretion is dependent upon glomerular flow rates, filtration, and epithelial integrity. Uric acid dissolves poorly and water and stones will readily precipitate from urine with a high uric acid concentration. Urate crystals are commonly deposited in soft tissue and especially in the joints leading to gouty arthritis.

Reduced oxygen levels also result in increased uric acid levels. Alcohol, processed meats and purines (pork, shellfish, organ meats, and high fructose corn syrup are the biggest culprits) also increase urine uric acid levels.

CPT 84550

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Purines are one of the most common chemical compounds on the planet. There are two kinds of purines: endogenous and exogenous. Exogenous purines are absorbed by the body through the foods that you eat, whereas, endogenous purines are made directly by the body itself.

Uric acid forms when purines are broken down in the digestive system. Eating too many purines can cause a buildup of uric acid in the body. If uric acid remains in the body for too long, it can crystallize and cause a number of health risks. Therefore, it's important to moderate the number of purines that you consume. Health risks may arise if either occurs, such as:

- **Gout**
- **Dementia**
- **Kidney disease**
- **Diabetes**

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Foods low in purines:

- **Eggs**
- **Nuts**
- **Legumes**
  - **Garbanzo beans (chickpeas)**
  - **Lima beans**
  - **Red beans**
  - **Pinto beans**
  - **Avoid – white beans, soybeans, split peas, black-eyed peas**
- **Any type of fruit**
- **Vegetables (excluding asparagus, cauliflower, spinach, mushrooms, and green peas)**
- **Poultry**
- **Salmon, and herring**
- **Lemons and cherries will reduce inflammation caused by uric acid.**

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Serum Uric Acid

INCREASED (hyperuricemia)	DECREASED (hypouricemia)
-Gout	-Suspect poor enzymation
-Dysbiosis	
-Dementia	
-Heavy metal toxicity	-Molybdenum deficiency-if MCV is less than 88 and low MCH deficiency is even more probable
-Hypertension	
-CHF	
-Rheumatoid arthritis	-If along with elevated MCV, MCH, MCHC and RDW suspect a B12 and or folate deficiency
-Renal insufficiency-acute or chronic nephritis	- Vitamin D deficiency
-Atherosclerosis-if ESR and basophils are elevated	-Chronic folate and/or vitamin B12 anemia
-Urinary obstruction	-pregnancy
-Cancer-accompanied by massive and rapid destruction of cell nuclei	- Heavy-metal toxicity
-Asthma	- Excessive use of salicylates
-Pernicious anemia	
-Hyperparathyroidism	
-Polycythemia	
-Diabetes	

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Serum Uric Acid

INCREASED	DECREASED
30-40 black cherries daily or 2 glasses of black cherry juice	Molybdenum
Folate	Folate/B12
Lithium	Broad-spectrum digestive enzymes
HCl	B complex
Pancreatic enzymes	Chymotrypsin particularly if increased cholesterol and triglycerides
B12	
Pantothenic acid	
Low purine diet	

- Li-Zyme Forte
- 5-MTHF Forte Plus
- Carbamide Plus
- Intenzyme Forte
- Hydrozyme

- Mo-Zyme Forte
- B12-2000 Lozenges
- Intenzyme Forte

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High-normal Uric Acid Linked With Mild Cognitive Impairment In The Elderly

Science Daily **January 3, 2007 — Researchers at the Johns Hopkins and Yale university medical schools have found that a simple blood test to measure uric acid, a measure of kidney function, might reveal a risk factor for cognitive problems in old age. Of 96 community-dwelling adults aged 60 to 92 years, lowest scores on tests of mental processing speed, verbal memory and working memory those with uric-acid levels at the high end of the normal range had the.**

The findings appear in the January issue of Neuropsychology, which is published by the American Psychological Association (APA). *High-normal uric acid levels, defined in this study as 5.8 to 7.6 mg/dL for men and 4.8 to 7.1 mg/dL for women, were more likely to be associated with cognitive problems* even when the researchers controlled for age, sex, weight, race, education, diabetes, hypertension, smoking and alcohol abuse. These findings suggest that older people with serum (blood) uric-acid levels in the high end of the normal range are more likely to process information slowly and experience failures of verbal and working memory, as measured by the Wechsler Adult Intelligence Scale and other well-established neuropsychological tests.

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Review Article

The Influence of Serum Uric Acid Level on Alzheimer's Disease: A Narrative Review

Mengyuan Qiao, Chongli Chen, Yuqing Liang, Yuxi Luo, and Wenbin Wu

1. Introduction

2. Method

As a powerful antioxidant in the human body, uric acid (UA) has been the subject of increasing research that focused on its influence on Alzheimer's disease (AD) in recent years.

This paper reviews recent advances in the study of SUA and AD which offers the possibility of new biomarker, new prevention, and treatment strategies for Alzheimer's disease.

Qiao M, Chen C, Liang Y, Luo Y, Wu W. The Influence of Serum Uric Acid Level on Alzheimer's Disease: A Narrative Review. Biomed Res Int. 2021 Jun 2;2021:5525710. doi: 10.1155/2021/5525710. PMID: 34124244; PMCID: PMC8192189.

93

Higher serum uric acid is associated with poorer cognitive performance in healthy middle-aged people: a cross-sectional study

Abstract

Age-related cognitive impairment can occur many years before the onset of the clinical symptoms of dementia. Uric acid (UA), a metabolite of purine-rich foods, has been shown to be positively associated with improved cognitive function, but such association remains controversial.

Our findings support previous studies suggesting an inverse association between high sUA levels and cognitive function in elderly and extend the evidence for such a role to middle-aged participants. Further prospective studies are warranted to investigate the relationship between UA and cognition.

Khaled Y, Abdelhamid AA, Al-Mazroey H, Almannai AK, Fetais S, Al-Srami AS, Ahmed S, Al-Hajri N, Mustafa A, Chivese T, Djoudri L. Higher serum uric acid is associated with poorer cognitive performance in healthy middle-aged people: a cross-sectional study. Intern Emerg Med. 2023 Sep;18(6):1701-1709. doi: 10.1007/s11739-023-03337-1. Epub 2023 Jun 17. PMID: 37330420; PMCID: PMC10504193.

94

Berberine attenuates uric acid-induced cell injury by inhibiting NLRP3 signaling pathway in HK-2 cells

Abstract

Hyperuricemia (HUA) is a common chronic metabolic disease that can cause renal failure and even death in severe cases.

From the data, BBR significantly reversed the up-regulation of inflammatory factors (IL-1β, IL-18) and LDH.

Collectively, our results suggested that BBR can alleviate cell injury induced by UA. The underlying unctionary (sic) mechanism may be through the NLRP3 signaling pathway.

Zheng J, Gong S, Wu G, Zheng X, Li J, Nie J, Liu Y, Chen B, Liu Y, Su Z, Chen J, Li Y. Berberine attenuates uric acid-induced cell injury by inhibiting NLRP3 signaling pathway in HK-2 cells. Naunyn Schmiedebergs Arch Pharmacol. 2023 Oct;396(10):2405-2416. doi: 10.1007/s00210-023-02451-3. Epub 2023 May 17. PMID: 37193772; PMCID: PMC10497693.

95

Anti-Inflammatory Diet and Dementia in Older Adults With Cardiometabolic Diseases

IMPORTANCE Inflammation has been proposed as a mechanism linking cardiometabolic diseases (CMDs) to increased risk of dementia. However, whether an anti-inflammatory diet can support brain and cognitive health among people with CMDs is unclear.

CONCLUSIONS AND RELEVANCE In this cohort study, people with CMDs and an anti-inflammatory compared with proinflammatory diet had a significantly lower hazard ratio of dementia, larger gray matter volume, and smaller white matter hyperintensity volume.

***JAMA Network Open*. 2024;7(8):e2427125. doi:10.1001/jamanetworkopen.2024.27125**

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What is in the Comprehensive Metabolic Panel?

Test includes:

- ALT/SGPT
- Albumin:Globulin (A:G) ratio
- Albumin, serum
- Alkaline phosphatase, serum
- AST/SGOT
- Bilirubin, total
- BUN
- BUN: Creatinine ratio
- Calcium, serum
- Carbon dioxide, a total
- Chloride serum
- Creatinine
- eGFR calculation
- Globulin, total
- Glucose, serum
- Potassium, serum
- Protein, total, serum
- Sodium, serum

CPT 80053

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Why is the Comprehensive Metabolic Panel used?

As a general health screen that provides information on the kidneys, liver, acid-base balance, blood glucose level, and blood proteins. It's used to evaluate organ function and check for conditions like diabetes, liver disease, and kidney disease. It is routinely ordered as part of blood workup for physical examination or medical exam especially one where symptoms are vague. Abnormal test results are then followed up with more specific tests before a final diagnosis is made.

Albumin, ALP, ALT, AST, bilirubin, BUN, calcium, carbon dioxide, chlorine, creatinine, glucose, potassium, sodium, total protein

If you are interested in two or more individual CMP components, it is generally better to order the entire CMP as it offers more information.

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Blood Urea Nitrogen (BUN):

Laboratory Range: 8 - 27 mg/dL **Optimal Range: 12 - 17**

WR range - >45 mg/deciliter indicates a serious metabolic problem (uremia) and requires immediate medical attention

Clinical Discussion

Blood urea is a by-product in the process of protein degradation/utilization, serum levels reflect a balance between protein metabolism and the clearance/excretion of urea. Therefore, increased BUN is the result of either increased production or decreased excretion. Urea as formed almost entirely by the liver from both protein metabolism and protein digestion. It is removed almost entirely by the kidneys; however notable amounts travel from the liver to the colon and are acted upon by the gut microflora to recirculate nitrogen.

BUN is an excellent tool for determining renal dysfunction in the early stages. It will also assess amino acid and protein need during pregnancy. It is important that the BUN be performed only after a 12 hour fast since there is an increase in blood values after ingestion of protein.

****Be aware of the sign of 88. This is where the BUN value falls to 8, and a serum protein value climbs to 8, thus making the sign of 88.This scenario creates a favorable environment for the future development of free radical pathology.**

CPT 84520

99

Uric Acid vs Urea

What is Uric Acid?

Uric acid is a product of the breakdown of purines, which are substances found in our own body cells as well as in many foods. When cells die and get recycled, or when we munch down on purine-rich foods, our body gets to work processing these purines, and uric acid is born. While this compound can be a friend, acting as an antioxidant. It has a notorious side, when it accumulates in excess, uric acid can crystallize in joints, resulting in the painful condition known as gout. The term 'uric acid' refers to solid form of this acid, while 'urate' is its name when it is in it soluble form in the blood.

What is Urea?

Urea often takes the spotlight in discussions about bodily waste, and for a good reason. When we indulge in protein-rich meals, the body breaks these proteins down, resulting in the production of ammonia. Given its toxic nature, ammonia isn't something our bodies want to hold on to. Therefore, the liver steps in to detoxify the body. It transforms ammonia into urea, a compound our system can tolerate.

From its formation in the liver, urea embarks on a journey through the bloodstream, pays a visit to the kidneys, and finally gets escorted out via the urine. This process ensures we effectively eliminate the surplus nitrogen that results from protein metabolism and causes ammonia production.

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Uric Acid vs Urea

Origins: Urea originates from the breakdown of proteins, while uric acid is a byproduct of purine metabolism. Urea is produced in the liver whereas uric acid is mainly produced in the kidneys.

Functions: Both serve as a mechanism to expel waste from the body. Urea gets rid of excess nitrogen to prevent ammonia toxicity caused by the breakdown of proteins, whereas uric acid acts as an antioxidant and protects our cells from damage.

Toxicity: Urea is relatively non-toxic and is safely eliminated through urine. High levels of urea can be caused by kidney failure and may cause nausea and weakness, though in such cases there are other toxins at play as well. Similarly, at normal levels, uric acid can be beneficial, but excessive amounts can cause gout or kidney stones.

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Blood Urea Nitrogen (BUN):

INCREASED	DECREASED
Urinary tract infection	Protein malnutrition
Chronic Renal Dysfunction	Dysbiosis
Amyloidosis	Acute liver destruction
Malignant hypertension	Acute hepatic insufficiency
Bleeding gastric ulcer	Pregnancy
Addison's disease	Nephrosis-patient is losing everything through the kidney
Starvation	Chronic wasting disease
Congestive heart failure	Amyloidosis
Collagen/vascular diseases	
Metallic poisoning of the kidneys	
Polycystic kidney	
Nephritis acute or chronic	

The following drugs may increase BUN: Alkaline antacids, antimony salts, arsenicals, cephaloridine, furesomide, gentamicin, kanamycin, neomycin, methyldopa.

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Blood Urea Nitrogen (BUN):

An Increased or Decreased BUN can be a serious finding indicating consequential liver damage.

Considerations:

- **Elevated BUN and protein levels consider increased protein metabolism.**
- **Decreased BUN and uric acid for edema.**
- **Decreased BUN and increased T3, T4, and T7-suspect iodine deficiency**
- **Increased BUN may be due to anterior pituitary dysfunction.**
- **Decreased BUN with low urinary specific gravity-suspect posterior pituitary dysfunction.**
- **Elevated BUN with normal creatinine usually indicates a non-renal cause of uremia.**

Whether elevated or decreased, the clinician must determine the underlying cause and clinically address it.

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Drugs that can increase BUN measurements include:
Allopurinol, Aminoglycoside, Amphotericin B, Aspirin (high doses), Bacitracin Carbamazepine, Cephalosporins, Chloral hydrate, Cisplatin, Colistin, Furosemide, Gentamicin, Guanethidine, Indomethacin, Methicillin, Methotrexate, Methyldopa, Neomycin, Penicillamine, Polymyxin B, Probenecid, Propranolol, Rifampin, Spironolactone, Tetracyclines, Thiazide diuretics, Triamterene, Vancomycin,

Drugs that can decrease BUN measurements include: Chloramphenicol, and Streptomycin

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Blood Urea Nitrogen (BUN):

INCREASED	DECREASED
• Treat UTI per usual protocols	Posterior pituitary extract
• Dysbiosis is common	Liver extract
• Anterior pituitary extract	Dysbiosis
• Liver extract	Kidney extract
• Kidney extract	Eliminate gluten grains
• Omega-3 fatty acids	Eliminate gluten grains if indicated
• If indicated recommend appropriate digestive support (Hypochlorhydria is very common)	

Remember, acute renal failure requires immediate medical attention and hospitalization most likely. In either case, whether elevated or decreased, the clinician must determine the underlying cause and address it clinically.

Dietary interventions including eliminating citrus (except lemon), dairy products, alcohol, grains, processed foods, hydrogenated fats and oils, refined carbohydrates and caffeine containing foods. A high complex carbohydrate diet of fruits and vegetables until the renal dysfunction is resolved is recommended.

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Blood Urea Nitrogen (BUN):

INCREASED	DECREASED
• Treat UTI per usual protocols	Posterior pituitary extract
• Anterior pituitary extract	Liver extract
• Liver extract	Kidney extract
• Kidney extract	Eliminate gluten grains
• Omega-3 fatty acids	Eliminate gluten grains if indicated
• If indicated recommend appropriate digestive support (Hypochlorhydria is very common)	Treat dysbiosis

- Renal Plus – 2 – 3 tid
- Argizyme – 2 – 3 tid
- Cytozyme KD – 2 – 3 tid
- Carbamide Plus – 2 – 3 tid
- Co-Q Zyme 100 – 1 bid
- Bio-3B-G – 2 tid
- Hydrozyme or Betaine Plus HP

- Protein
- Hydrozyme or Betaine Plus HP
- Renal Plus – 2 – 3 tid

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Creatinine

Laboratory Range: 0.57 – 1.00(F) 0.76 - 1.27 mg/dL(M) Optimal Range: 0.7-1
WR range - >2.5 mg/dL Indicates a serious metabolic problem and requires immediate medical attention

Clinical Discussion:
Serum creatinine provides a rough approximation of glomerular filtration. Levels are proportional to lean body muscle mass and is unaffected generally by diet or physical activity. Both BUN and creatinine are often ordered to follow renal problems, Creatinine rises less quickly than BUN. Concentration a creatinine generally will not become abnormal until about half or more of the nephrons have stopped functioning and chronic progressive renal disease is more advanced. Not as sensitive to protein intake as BUN.

Creatinine may be slightly lower in children and pregnant women. Creatinine has a diurnal variation with the lowest values at approximately 7 AM with repeat values around 7 PM.

CPT 82565

107

Creatinine

INCREASED WITH:	DECREASED WITH
Renal obstruction/destruction	Hypochlorhydria
Renal hypertension	Reduced muscle mass in adult
Early nephritis	Amyotonia congenita-usually children
Benign prostatic hypertrophy	
Uterine dysfunction	
Intestinal obstruction	
Congestive heart failure	
Starvation/dehydration	
Uncontrolled diabetes	

If high with an increased percentage of monocytes, a normal BUN and electrolyte, then benign prostatic hypertrophy is possible. A creatinine at 1.2 or higher and symptoms such as urinary urgency, frequency, nocturia, hesitancy, intermittency with decreased urinary stream size and force, especially in males over 45 years of age this is quite suggestive of BPH.

Elevated levels will occur when the body is clearing heavy metals if they are being pushed too fast. Do not do heavy-metal detoxification if creatinine is greater than 1.1.

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Creatinine

INCREASED	DECREASED
Vitamins A, C and E	Muscle extract
Kidney extract	Choline
Selenium	Inositol
L-carnitine	Vitamin E
	Selenium
	Dimethyl glycine
	L-carnitine

- Renal Plus – 2 – 3 tid
- Cytozyme KD – 2 – 3 tid
- Argizyme – 2 – 3 tid
- Carbamide Plus – 2 – 3 tid
- Bio-3B-G – 2 tid
- Hydrozyme or Betaine Plus HP

- Protein
- Hydrozyme or Betaine Plus HP

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Glomerular Filtration Rate (eGFR)

Laboratory Range: >59mL/min1.73

The glomerular filtration rate (GFR) shows how well the kidneys are filtering. An estimated 37 million adults in the United States may have chronic kidney disease (CKD) but nearly 90% are unaware of their condition. When found early, people can take important steps to protect their kidneys.

- eGFR of 90 or higher is in the normal range
- eGFR of 60 - 89 may mean early-stage kidney disease
- eGFR of 15 - 59 may mean kidney disease
- eGFR below 15 may mean kidney failure

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Glomerular Filtration Rate (eGFR)

There are four stages of CKD. Each stage reflects the level of decrease in the volume of blood that the kidneys can filter in one minute, also known as the estimated glomerular filtration rate (eGFR). CKD is diagnosed when abnormalities of kidney function are present for more than three months.

Symptoms associated with CKD:

- ✓ Dry, itchy skin
- ✓ Need to urinate more often–especially at night
- ✓ Puffiness around the eyes–especially in the morning
- ✓ Swollen feet and ankles
- ✓ Difficulty sleeping
- ✓ Poor appetite
- ✓ Muscle cramps at night
- ✓ Fatigue and low energy
- ✓ Difficulty concentrating

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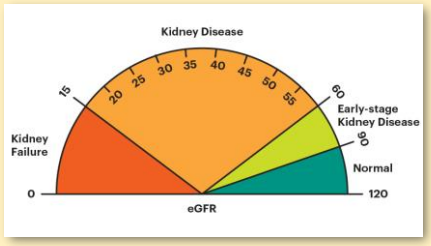
Glomerular Filtration Rate (eGFR)

What is a normal eGFR number?

In adults, the normal eGFR number is ideally greater than 90. eGFR declines with age, even in people without kidney disease.

Age (years)	Average eGFR
20–29	116
30–39	107
40–49	99
50–59	93
60–69	85
70+	75

112



113

BUN/Creatinine Ratio

Laboratory Range: 10 – 24 (F) 12 – 28 (M) Optimal Range: 13 - 17
WR range – a ratio >30 indicates possible renal dysfunction. A ratio > 35 for indicates renal dysfunction, but could be upper gastrointestinal bleeding. Check with hemoccult

The BUN/creatinine ratio is useful in assessing patients that have chronic renal dysfunction; however the ratio may be skewed when high normal BUN is present with a low normal creatinine or a high normal creatinine for low normal BUN. Therefore, the ratio is generally not as valuable diagnostically as the individual values for BUN and creatinine.

If BUN and creatinine both arise where BUN is 10 X creatinine in the presence of an elevated uric acid, the patient is most likely experiencing renal failure and requires immediate medical attention. If however, the BUN rise is exponential and the creatinine is remaining stationary, the patient may be experiencing atherosclerosis, perirenal azotemia (no calcium, could kill the patient), or internal bleeding.

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BUN/Creatinine Ratio

INCREASED

- Catabolic states - including fever, tissue trauma, burns, internal bleeding, circulatory failure leading to fall in renal blood flow and then to shock and acute CHF
- Acute and chronic renal failure
- Urinary tract obstruction-(BPH)
- High-protein diet
- Diabetes insipidus

DECREASED

- Suspect edema due to posterior pituitary dysfunction-look for low sodium and chloride. This is due to in inappropriate secretion of antidiuretic hormone which is produced in the hypothalamus and stored in the posterior pituitary and when released increases wandering absorption by the kidneys, thus increasing the fluid content of the body and decrease in the BUN/creatinine ratio
- Pregnancy
- Low protein-high carbohydrate diet
- Hypochlorhydria

If BUN and creatinine both arise where BUN is 10 X creatinine in the presence of an elevated uric acid, the patient is most likely experiencing renal failure and requires immediate medical attention. If however, the BUN rise is exponential and the creatinine is remaining stationary, the patient may be experiencing atherosclerosis, prerenal azotemia (no calcium, could kill the patient), or internal bleeding
Azotemia has three classifications, (pre, renal, post) depending on its causative origin, but all three types share a few common features. They are characterized by a decrease in the glomerular filtration rate (GFR) of the kidneys and increases in blood urea nitrogen (BUN) and serum creatinine concentrations.

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ORIGINAL ARTICLE

Berberine ameliorates chronic kidney disease through inhibiting the production of gut-derived uremic toxins in the gut microbiota

Libin Pan, Hang Yu, Jie Fu, Jiachun Hu, Hui Xu, Zhengwei Zhang, Mengmeng Bu, Xinyu Yang, Haojian Zhang, Jinyue Lu, Jiandong Jiang*, Yan Wang*

Abstract At present, clinical interventions for chronic kidney disease are very limited, and most patients rely on dialysis to sustain their lives for a long time. However, studies on the gut-kidney axis have shown that the gut microbiota is a potentially effective target for correcting or controlling chronic kidney disease.

These findings suggest that berberine may be a therapeutic drug with significant potential to ameliorate chronic kidney disease through the gut-kidney axis.

Libin Pan, Hang Yu, Jie Fu, Jiachun Hu, Hui Xu, Zhengwei Zhang, Mengmeng Bu, Xinyu Yang, Haojian Zhang, Jinyue Lu, Jiandong Jiang, Yan Wang,
Berberine ameliorates chronic kidney disease through inhibiting the production of gut-derived uremic toxins in the gut microbiota, Acta Pharmaceutica Sinica B, Volume 13, Issue 4, 2023, Pages 1537-1553,
ISSN 2211-3835, https://doi.org/10.1016/j.apsb.2022.12.010.

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SERUM SODIUM

Laboratory Range: 134 - 144 mmol/L **Optimal Range: 139 - 144**
WR range – below 125 mmol/L or above 150 mmol/L

Clinical Discussion
Sodium is the primary acidifying mineral of the body and is antagonistic to potassium. It is the most abundant cation in the extracellular fluid. It is important in osmotic regulation of extracellular fluid balances, acid-base balance and renal, cardiac and adrenal function. It is required for maintenance of the sodium-potassium pump; adrenal function which also controls the level. Sodium pumps water and nutrients into the cell wall and is primarily under the control of the adrenal cortex. Chloride pumps water and nutrients through the cell wall and the potassium essentially moves them about inside the cell.

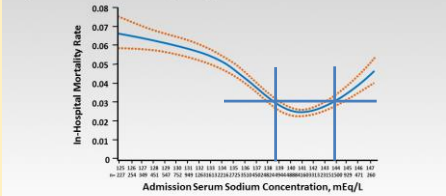
To determine electrolyte balance - Anion gap = [Na+] - [Cl-] - [HCO3-](CO2)

Decreased serum sodium (hyponatremia) on admission to the hospital is associated with a poor prognosis. It may manifest in lethal neurological complications (water intoxication with brain edema).

CPT 84295

117

Relationship Between Serum Sodium Levels and In-Hospital Mortality (OPTIMIZE-HF Registry)



From Gheorghiade M, et al. Relationship between admission serum sodium concentration and clinical outcomes in patients hospitalized for heart failure; an analysis from the OPTIMIZE-HF registry. *Eur Heart J.* 2007;28:980-988. Republished with permission.

Heart failure

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SERUM SODIUM

INCREASED (Hypernatremia)	DECREASED (Hyponatremia)
-Chronic renal dysfunction-look for elevated BUN and or creatinine	-Adrenal cortical hypofunction
-Dehydration	-Increase serum triglycerides - "pseudohyponatremia"
-Water softeners-many use sodium to soften the water	-Diabetes
-Adrenal cortical hyperfunction-consider if potassium is low	-Thyroid hypofunction
-Pyloric obstruction	-Anterior pituitary hypofunction
-Cushing's Syndrome	-Congestive heart failure
	-Peptic ulcer
	-Diarrhea
	-Addison's Disease

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SERUM SODIUM

INCREASED	DECREASED-
-Kidney extract	-Adrenal glandular
-Ascorbates	-Celery and/or celery juice
-L-arginine	-Talk to prescribing medical provider about eliminating diuretic
-Restrict sodium intake	
✓ ADHS	✓ADBS-Plus ™
✓ Cytozyme AD	✓Celtic Sea Salt in a glass of tepid water
✓ Celtic Sea Salt in a glass of tepid water	✓Cytozyme-AD ™
✓ Bio-GGG-B	✓Bio-Glycozyme Forte ™
✓ Phophatidylserine	✓Bio-3B-G ™
✓ Bio-Ashwaganda	✓DHEA ™
	✓Bio-Ashwaganda™

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SERUM POTASSIUM

Laboratory Range: 3.5 - 5.2mmol/L. **Optimal Range: 4.1 - 4.6**
WR range – < 3.0mmol/L or > 5.5. When serum potassium is outside of optimal ranges an EKG should be performed.

Clinical Discussion:
Potassium is one of the chief electrolytes, dissolved in the body's fluids, both intra and extracellularly. In the case of potassium, it is the chief intracellular ion, and its concentration inside the RBC is at least 15-20 times greater than that found in the serum/plasma.

Electrolytes play several important physiological jobs, but one of the most important is their role in sending electrical signals via the nervous system. So, it's not surprising that abnormalities in potassium lead to signaling issues in the electrical systems of the heart and in the nervous system. The concentration of electrolytes is monitored closely by the body's homeostatic mechanisms. Levels that are too high or too low can cause problems and even death. However, even with complex regulatory mechanisms, sometimes the concentration of potassium in the blood gets out of optimal ranges. Potassium serves as the primary oxidizing mineral the body is essential to maintenance of pH for blood and urine and maintenance of osmotic pressure.

Hypokalemia: Decreased serum potassium causes weak muscles, including the heart.

Hyperkalemia: Excess potassium ions in the extracellular fluids causes the heart muscle to become extremely dilated and flaccid and slows the heart rate (congestive heart failure).

CPT 84132

121

SERUM POTASSIUM

Subclinical hypo or hyperkalemia generally do not cause discernable symptoms, especially if otherwise healthy. However, hypo or hyperkalemia *can* cause serious symptoms and problems.

This is particularly likely if outside optimum ranges and symptoms are more likely if the level of potassium falls rapidly for some reason.

The nervous system, gastrointestinal system, the kidneys, and the heart can be affected. This can lead to symptoms like:

- **Muscle cramps and pain**
- **Weakness**
- **Fatigue**
- **Paralysis**
- **Constipation or complete intestinal paralysis**
- **Respiratory failure**

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SERUM POTASSIUM

INCREASED (Hyperkalemia)	**DECREASED (Hypokalemia)**
Adrenal cortical hypofunction	**Diarrhea**
Advanced chronic renal failure	**Adrenal cortical hyperfunction**
Acidosis	**Drug diuretics**
Pneumonia	**Chronic nephrosis**
Beta blocking drugs	**Testosterone overdose**
Potassium sparing diuretics	**Diet high in refined carbohydrates**
Uremia	**Diabetes and hyperinsulinism**
Acute bronchitis	
Fluoride intoxication	
Exercise with heavy sweating	

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SERUM POTASSIUM

INCREASED	DECREASED
Vitamin E	Adrenal extract
L-carnitine	L-carnitine
Posterior pituitary extract	Posterior pituitary extract
Co-Q10	Choline
DHEA	

- ✓ DHEA
- ✓ ADB5
- ✓ Cytozyme AD
- ✓ Celtic Sea Salt in a glass of tepid water
- ✓ Bio- 3B-G
- ✓ Phophatidylserine
- ✓ Bio-Ashwaganda

- ✓ Potassium HP – 1 scoop bid
- ✓ ADHS
- ✓ Cytozyme AD
- ✓ Cytozyme PY/HPT
- ✓ Celtic Sea Salt in a glass of tepid water
- ✓ Bio-GGG-B
- ✓ Phophatidylserine
- ✓ Bio-Ashwaganda

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SERUM CHLORIDE

Laboratory Range: 96 - 106mmol/L **Optimal Range: 100 - 105**
WR range – below 90 mmol/L or above 115 mmol/L

Clinical Discussion:
Chloride is the primary anion in the serum. If the patient exhibits a disturbed chloride value, this indicates an imbalance of the water shifting mechanism. A chloride level along with sodium, potassium and CO2 are important evaluating acid-base relationships, state of hydration, as well as adrenal and renal function.

Decreased chloride value along with decreased albumin (marked edema if the albumin is below 3.5)means that there is deficient water crossing the membranes and will yield a pitting edema. Chloride concentrations usually vary inversely with CO_2; hence, increase chloride is commonly associated with renal or systemic acidosis and decreased chief chloride with systemic alkalosis. Chloride is required for the production of HCl by the chief or peptic cells in the stomach.

If chloride is reduced below 100 with a total serum globulin below 2.4 or greater than 2.7, a serum phosphorus level below 3.0 and/or the BUN above 15, the probability of hypochlorhydria is extremely high.

CPT 82435

125

SERUM CHLORIDE

INCREASED (hyperchloremia)	DECREASED (hypochloremia)
Dehydration	Renal dysfunction
Renal dysfunction	Tetany
Primary CO_2 deficit	Primary CO_2 excess
Salicylate poisoning	Hypochlorhydria
Excessive salt intake	Pyloric spasm
Adrenal hyperfunction	Diabetes
Parathyroid hyperfunction	Adrenal cortical hypofunction
Nephritis	Respiratory distress
Nephrosis	Vomiting
Prostatic and urinary obstruction	Addison's disease

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SERUM CHLORIDE

With a low chloride you may want to consider the following:

- ➢If CO2 was increased, then metabolic alkalosis is probable
- ➢If BUN or creatinine are increased and other electrolytes are imbalanced, renal dysfunction is probable
- ➢If sodium is low been adrenal hypofunction is quite possible
- ➢His sodium is low with high potassium, bowel dysfunction/constipation is possible
- ➢If potassium is high, then hypochlorhydria is possible

With elevated chloride you may want to consider the following:

- ➢If CO2 is low then metabolic acidosis is probable (along with an elevated anion gap, source of acidosis is from renal dysfunction, diabetic ketoacidosis, lactic acidosis, or exogenous poisons such as ethylene glycol, salicylates, methanol, paraldehydel) or (with a normal anion gap, the cause is GI alkaline laws do to diarrhea, ileostomy or colostomy, renal tubular acidosis, selective hyperaldosteronism, ingestion of acetazolamide or ammonia chloride)
- ➢If BUN and creatinine are increased and other electrolytes are imbalanced, renal dysfunction possibly nephritis is probable
- ➢Rule out excess use of salicylates or table salt

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SERUM CHLORIDE

INCREASED	DECREASED
Ribloflavin	Celtic sea salt
Vitamin B6	Choline
Kidney gland extra	Adrenal gland extra
Adrenal glandular extract	Kidney glandular extract
L-arginine	L-arginine
✓ ADHS	✓ ADB5
✓ Cytozyme AD	✓ Cytozyme AD
✓ Cytozyme KD	✓ Renal Plus – 1 – 2 tid
✓ Renal Plus – 1 – 2 tid	✓ Celtic Sea Salt in a glass of tepid water
➢ Hydrozyme	➢ Hydrozyme
➢ Betaine Plus HP	➢ Betaine Plus HP

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CARBON DIOXIDE (CO2)

Laboratory Range: 20 - 29 mmol/L. **Optimal Range: 26 - 28**
WR range – below 17 mmol/L or above 35 mmol/L.

Clinical Discussion
Generally speaking, if the patient's CO2 level is elevated, the patient is considered to be in a state of alkalosis (anything above 32 mEq/L always order a pulmonary function test). CO2 represents the reserve of alkali readily available for the neutralization of acids.

Conditions involving primary CO2 excess and deficit cannot be determined by CO2 alone, serum chloride must be checked for inverse values and metabolic acidosis or metabolic alkalosis is suspected, however if the chloride value is 25 or less it is most likely due to systemic acidosis. Moderate acidosis is considered to run between 14-18, severe acidosis is less than 14. The patient may be in a state of metabolic acidosis and to a lactic acid or pyruvic acid and possibly a toxic buildup

If CO2 is high with low chloride, then metabolic alkalosis is probable. However, if CO2 is elevated along with high LDH, and basophils, then asthma (uric acid ↑) or some other obstructive lung condition may be likely. Alkalosis is a common finding in patients with food and environmental sensitivities.

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CARBON DIOXIDE (CO2)

INCREASED (alkalosis)	DECREASED (acidosis)
Metabolic alkalosis	Metabolic acidosis
Hyperventilation	Diabetes
Adrenal cortical hyperfunction	Thiamine deficiency
Respiratory distress	COPD
Oxygen therapy	Renal dysfunction
Loss of HCl from vomiting	Dehydration
Fever	Excessive exercise
	Renal dysfunction

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CARBON DIOXIDE (CO2)

INCREASED	***DECREASED***
Kidney glandular extract	Beta carotene
HCl	Thiamine
Pyridoxine	Adrenal glandular support
Beta carotene	Alkalizing green drink
Vitamin E	Alkalizing minerals
Germanium	Check essential fatty acid status
✓ Phosphatidylcholine – 1 – 2 tid	✓ Thiamine 50
✓ ~~Zn Zyme Forte~~	✓ Bio 3B-G
➢ Hydrozyme	✓ ADB5
➢ Betaine Plus HP	✓ Nitro Greens
	✓ Potassium HP
	✓ Optimal EFAs

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ANION GAP

The Anion Gap is an approximate measurement of ions, that is molecules with a charge, either negative or positive. Sodium and potassium are positively charged and therefore called cations; this is why they are often represented as Na and K respectively. These two are the main cations measured in the blood.

Negatively charged molecules are called anions, and the major anions measured in the blood are chloride (Cl) and bicarbonate (HCO). You can tell those electrolytes in the blood because they are measured as mEq/L rather than in milligrams/dL.

Since the body must remain neutral, or in other words have the same amount of positive ions as negative ions, the equation (Na + K + unmeasured cations) must = (Cl + HCO + unmeasured anions). Some of the unmeasured cations (~7Mmol/L) include calcium, magnesium, and most other minerals. Unmeasured anions (~24 Mmol/L) include proteins like albumin, and phosphates, sulfates, etc. There are always more unmeasured anions than cations, and thus the "anion gap" equation, (Na + K) – (Cl + HCO), is always greater than zero.

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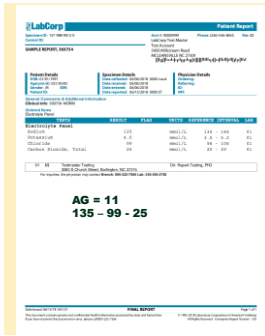
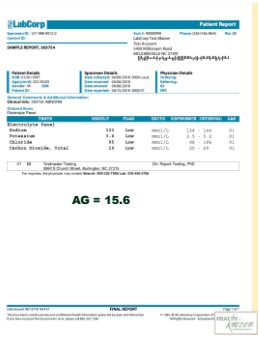


AG = 11
135 – 99 - 25



AG = 15.6

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ANION GAP

The Anion Gap is increased when there are excessive anions/acids in the blood. This is either from too much acid production or insufficient removal of acids (either through the lungs, stomach, or kidneys). Excess acids lead to a rapid respiratory rate (the body wants to blow off the extra CO), an inability to hold your breath (the acid build up forces you to exhale), low blood pressure (due to vasodilation), fatigue, poor appetite, etc.
The high anion gap indicates that the electrical charge of the fluids are too negative compared to the inside of the cell. Because the charge across cell membranes is required for many enzymes and energy production, a reduced charge may result in less energy production (oxidative phosphorylation and ATP). A high anion gap may also indicate a functional need for alkaline minerals.
The electrical potential between the inside of the cell and the outside of the cell is basis for nearly all transactions that occur with in the cell. Within the cell the chief cation is potassium and the chief anion is phosphorus. Outside the cell the sodium is balanced by chloride. The balance between the inside and the outside of the cell is maintained by a pump that sends potassium in and sends sodium out. When there is an insufficiency of these electrolytes, electricity can't be generated – as a result energy production and cellular function is compromised.

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ANION GAP

Anion gap (AG) = [Na+] - [Cl-] - [HCO3-](CO2) or alternative formula:
AG = [Na+] + [K+] - [Cl-] - [HCO3-](CO2)

A healthy anion gap is typically 4 - 12 mEq/L. But this may vary depending on the lab testing. It is especially useful in helping to differentiate the cause of a metabolic acidosis, as well as following the response to therapy.

Signs of acidosis (high blood acid) may include: increased anion gap
- **Shortness of breath**
- **Nausea or vomiting**
- **Abnormal heartbeat**
- **Confusion or fatigue**

Signs of alkalosis (too basic blood) may include: decreased anion gap
- **Nausea or vomiting**
- **Confusion or lightheadedness**
- **Hand tremors**
- **Numbness or tingling in the face, hands, or feet**
- **Muscle spasms**

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SERUM CALCIUM

Laboratory Range: 8.7 - 10.3 mg/dL (F) 8.6 – 10.2 (M) Optimal Range: 9.7-10.1

WR range – below 7.4 mg/dL or above 12.0 mg/dL

Clinical Discussion:

99% of the body's calcium is stored in our bones. It is the most abundant macro-mineral. Calcium is absorbed from the upper small intestine and the amount of absorption depends upon the acidity of the stomach as well as the amount of phosphate present. Calcium levels reflect bone metabolism, the absorption of fats in the intestine, and protein absorption. Protein levels affects the calcium level. Calcium exists in the ionized form (approximately 55%) and the non-diffusible form (approximately 45%), which is bound of protein, primarily albumin.

The practitioner needs to make sure that the patient's calcium level does not exceed 12.0, which indicates an extremely morbid clinical condition. Acidity of the intestinal tract, lactose and vitamin D enhances calcium absorption. Vitamin D and parathyroid hormone provide long-term control of calcium ion concentration by controlling calcium absorption from the gut. High fiber diets, phytates, cellulose, oxalates, hyaluronic acid, and low HCl will hinder calcium absorption.

For the diagnosis of hypercalcemia, serum calcium should be measured on at least 3 different occasions because serum calcium can change significantly when the albumin is increased or decreased.

CPT 82310

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SERUM CALCIUM

INCREASED (hypercalcemia)
Hyperparathyroidism
Hyperplasia or tumor of the thyroid
Hypervitaminosis D
Multiple myeloma
Bone metastasis
Hypothyroidism
Adrenal cortical hypofunction
Some cases of osteoporosis
Ovarian hypofunction

- ✓ **Mg-Zyme**
- ✓ **Super Phosphozyme liquid**

DECREASED (hypocalcemia)
Hypoparathyroidism
Pregnancy
Rickets
Osteomalacia
Hypochlorhydria
Metabolic acidosis
Protein malnutrition

- ✓ **Ca/Mg Zyme**
- ✓ **Ca/Mg Plosteous**
- ✓ **Osteo-B Plus**
- ✓ **Optimal EFAs**
- ✓ **Ca/Mg Plus**

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CALCIUM THERAPIES

Urine pH	Nutrients indicated
> 7.5	HCl, vitamin C, calcium lactate, calcium phytate, ammonium chloride
7.5-6.8	Calcium lactate, vitamin C, (children under 10-calcium gluconate)
6.8-6.4	Calcium lactate, vitamin C
6.4-6.0	Calcium citrate, calcium gluconate, calcium carbonate
6.0-5.6	Calcium citrate, calcium gluconate, calcium carbonate, vitamin D
5.6-5.1	Calcium citrate, calcium gluconate, calcium carbonate
<5.1	Calcium citrate, calcium gluconate, no vitamin C

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SERUM CALCIUM

Considerations:

- ✓When both calcium and phosphorus are elevated, consider hypervitaminosis D or hydrochloric acid deficiency.
- ✓With decreased calcium and elevated phosphorus, consider gallbladder dysfunction.
- ✓When calcium is decreased and phosphorus and alkaline phosphatase are elevated, consider vitamin D deficiency.
- ✓Decreased calcium along with decreased protein indicates a protein deficiency
- ✓When calcium, bilirubin and phosphorus are decreased, consider fat absorption from the intestines as being deficient.
- ✓A decrease calcium with a decrease triglyceride and elevated LDH indicates pancreatic insufficiency.
- ✓A classic finding of low calcium, low phosphorus and a high alkaline phosphatase also suggests pancreatic insufficiency.

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SERUM PHOSPHOROUS*

Laboratory Range: 3.0 - 4.3 mg/dL(F) 2.8 – 4.1(M) **Optimal Range: 3.6 - 4.1**
WR range – below 2.3 mg/dL or above 5.0 mg/dL

Clinical Discussion:

Calcium and phosphorus ions undergo continuous turnover in bone which provides the major reservoir. Most of the body's phosphorus is combined with calcium in the bones, but about 15% exists -- as phosphate (PO_4) ions -- in the blood and other soft tissues and body fluids.

Phosphorus plays a role in a number of important different areas including bone physiology, as well as the formation of ADP, ATP, phospholipid membranes, nucleic acids, creatine phosphate, and is necessary for proper glucose utilization. Phosphorus is an indicator of digestive function and is a good indicator of intestinal pH. If low intestinal tract is generally acid, and if elevated the gut is alkaline. If phosphorus is decreased below 3.0, hypochlorhydria is quite probable.

Calcium and phosphorus have a reciprocal relationship in the serum; if one rises, the other tends to fall. Once renal failure causes a chronically elevated serum phosphorus level, serum calcium falls reciprocally. Several factors are important in the regulation of serum phosphorus including: Parathyroid hormone, and the functional status the kidneys.

CPT 84100

140

SERUM PHOSPHOROUS

INCREASED	***DECREASED***
Hypoparathyroidism	Hyperparathyroidism
Acute and chronic renal dysfunction	Hypochlorhydria
Hypervitaminosis D	Vitamin D deficiency-common
Normally found elevated in children and during bone repair	Diabetes
	Liver dysfunction
Bone metastasis	Hyperinsulinism
Ovarian hyperfunction	Diet high in refined carbohydrates
Edema	Protein malnutrition
Diabetes	Osteomalacia
Cirrhosis	Asthma

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SERUM PHOSPHOROUS

INCREASED	***DECREASED***
HCl	Vitamin D
Folic acid/B12	HCl
Bile salts	Reduce refined carbohydrates
Kidney glandular extract	Lipase
Decrease vitamin D supplementation	Treat the underlying disease
Treat the underlying disease	
Think parathyroid	

- ✓ Check parathyroid hormone (PTH)
- ✓ B12-2000 lozenges

- ✓ Super Phosphozyme liquid
- ✓ Hydrozyme
- ✓ Mg-Zyme

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SERUM MAGNESIUM*

Laboratory Range: 1.6 - 2.3 mg/dL **Optimal Range: 2.2 - 2.8**
WR range – < 1.3 mg/dL

Clinical Discussion

Magnesium is the fourth most common cation the body following calcium, potassium and sodium. 60% of the body's stores are found in bone with another 20% found in the muscle tissue. Magnesium is absorbed in the small intestine and vitamin D enhances its absorption. It is an essential cofactor entrance for transphosphorylation reactions involving ATP and in the regulation of electrical potentials across nerve and muscle membranes. Only potassium occurs higher inside the cell; hence the value of measuring intracellular (see RBC) magnesium versus extracellular (serum) magnesium to determine magnesium needs.

Magnesium plays an important role in numerous enzyme reactions. Magnesium, like calcium, is partially protein-bound and is therefore slightly decreased total serum protein or serum albumin are decreased. Conversely, if the total protein or serum albumin is increased, the serum magnesium may also be increased.

It is well documented that MI patients who are deficient and magnesium have a greater fatality rate than those who have normal or slightly elevated levels. Hypomagnesemia is far more frequent than hypermagnesemia. Magnesium deficiency may occur due to dietary deficiencies and malabsorption. In general, decreased absorption occurs much in the same manner as does decrease calcium absorption.

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SERUM MAGNESIUM

INCREASED (hypermagnesemia)	***DECREASED*** (hypomagnesemia)
*Renal dysfunction	Epilepsy
*Hypoparathyroidism	Malnutrition
Hypothyroidism	Adrenal cortical hyperfunction
Adrenal cortical hypofunction	Parathyroid hyperfunction
Excessive use of antacids containing magnesium	Digestive inflammation

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SERUM MAGNESIUM

INCREASED

- Renal glandular extract
- Beta carotene
- Treat the underlying disease

✓ Cytozyme KD

DECREASED

- Magnesium
- Renal glandular extract
- Vitamin C
- Treat the underlying disease

✓ Mg-Zyme

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nutrients

MDPI

Review

Magnesium and the Hallmarks of Aging

Magnesium deficiency is very common in old age. Age-related chronic diseases and the aging process itself are frequently associated with low-grade chronic inflammation, called '<u>inflammaging</u>'. Because chronic magnesium insufficiency has been linked to excessive generation of inflammatory markers and free radicals, inducing a chronic inflammatory state, we formerly hypothesized that magnesium inadequacy may be considered among the intermediaries helping us explain the link between inflammaging and aging-associated diseases. We show in this review evidence of the relationship of magnesium with all the hallmarks of aging (<u>genomic instability, telomere attrition, epigenetic alterations, loss of proteostasis, deregulated nutrient sensing, mitochondrial dysfunction, cellular senescence, stem cell exhaustion, altered intercellular communication, disabled autophagy, dysbiosis, and chronic inflammation</u>), which may positively affect the human healthspan It is feasible to hypothesize that maintaining an optimal balance of magnesium during one's life course may turn out to be a safe and economical strategy contributing to the promotion of healthy aging. Future well-designed studies are necessary to further explore this hypothesis.

Dominguez LJ, Veronese N, Barbagallo M. Magnesium and the Hallmarks of Aging. *Nutrients.* 2024; 16(4):496. https://doi.org/10.3390/nu16040496

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TOTAL PROTEIN

Laboratory Range: 6.0 - 8.5 g/dL **Optimal Range: 7.0 - 7.6**

WR range – below 5.8 g/dL, or above 8.7 g/dL

Clinical Discussion:

Albumin and globulin added together make up the total protein value. It is possible to have a normal total protein yet have abnormal indices of globulin and/or albumin. Thus, the total serum protein concentration can remain the same in acute phase reactions, get the composition of the albumin and globulin are altered.

Total protein closely approximates ionized calcium. If the total protein is elevated, serum calcium we'll also probably be elevated. Likewise, if total protein is decreased, calcium we'll also most likely be decreased, suggesting poor protein assimilation. Elevated total protein indicates poor utilization of protein and is found in serious pathological disorders or and states of dehydration.

<u>Be aware of the sign of 88</u>. This is where the BUN value falls to 8, and a serum protein value climbs to 8, thus making the sign of 88.This scenario creates a favorable environment for the future development of free radical pathology.**

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TOTAL PROTEIN

Clinical considerations:

- A decreased total protein with decreased BUN and altered ALT suggest hepatic dysfunction.
- A decreased total protein with decreased serum calcium indicates poor protein assimilation.
- A decreased protein with a decreased total cholesterol, and a decreased ALT indicates a poorly functioning liver and most likely NAFLD.
- A decreased total protein with a decreased A/G ratio is typical of protein malnutrition.
- An elevated total protein along with elevated serum uric acid and an altered serum calcium (too high or too low) suggests pancreatic enzyme deficiency.

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TOTAL PROTEIN

INCREASED	***DECREASED***
-Neoplasm	-Protein malnutrition/amino acid need
-Multiple myeloma	-Hyperthyroidism
-Poor enzymation	-Birth control pills
-Liver/biliary dysfunction	-Edema
-Dehydration	-Liver-functional fatty liver congestion
-Adrenal cortical hypofunction	-Digestive tract inflammation-leaky gut, Crohn's, IBS, colitis, gastritis, ileitis, etc.
-Rheumatoid arthritis	-Renal dysfunction-usually due to diabetes or hypertension
-Hypochlorhydria	
-Pneumonia	

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TOTAL PROTEIN

INCREASED	***DECREASED***
Protease enzymes	Choline-check ALT (fatty liver)
HCl	Inositol - check ALT (fatty liver)
Calcium	Methionine- check ALT (fatty liver)
Vitamin D	L-arginine
Iodine	Consider alternate forms of BC, if BCP
Treat underlying disease process	Treat underlying disease process
	HCl
➢ Protein	➢ Protein
➢ Hydrozyme or Betaine Plus HP	➢ Hydrozyme or Betaine Plus HP

150

SERUM ALBUMIN

Laboratory Range: 3.9 - 4.9 g/dL **Optimal Range: 4.2 - 4.8**
WR range – below 3.6 g/dL

Clinical Discussion:
The albumin in the body is almost exclusively produced by the liver. Albumin is responsible for the vast majority of osmotic pressure between blood and tissue fluids. Decreased serum albumin is always an indication of significant liver or immune dysfunction and in many cases; decreased albumin indicates frank or developing free radical pathology.

According to the peer-reviewed literature, patient's with a decreased serum albumin upon admission had a much greater chance of dying in the hospital then to the patients with normal serum albumin levels. With an albumin of 3.5 or below and an absolute lymphocyte count of 1500 or less the patient has a 4 times morbidity and 20 times increased mortality. Low albumin may result from 3 causes:

- **Lack of protein polarity in the liver-low serum phosphorus.**
- **Renal tubular loss-low sodium**
- **Increased cell permeability-edema and ascites**

CPT 82040

151

SERUM ALBUMIN

Clinical Discussion: ***The four ominous signs***

- ✓ **Albumin levels and ratios with other entities, plays a significant role in assessing the patient's morbidity risk. 3 of the 4 ominous signs include albumin in the equation. Perhaps the most ominous of the 4 ominous signs is an albumin that is 3.5 or below, with a total absolute lymphocyte count of less than 1500.**
- ✓ **A low (reversed or inverted) A/G. ratio less than 1.0 is another of the 4 ominous signs. These people may have a serious, developing, or currently manifesting free radical pathological process going on.**
- ✓ **The calcium/albumin ratio is elevated to greater than 2.7 is another of the for ominous signs. This is due to malnutrition or visceral protein loss secondary to a potential free radical pathological process.**
- ✓ **The fourth ominous sign is a decreased serum cholesterol value of less than 140 mg/dL, unless the cause is due to endurance training or is a child.**

Remember, the sign of 88. This is where the BUN value falls to 8 and a serum protein value climbs to 8 thus making the sign of 88. This scenario rates a favorable environment for the future development of a free radical pathology.

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Serum Albumin

INCREASED	DECREASED
-Dehydration-an elevated albumin indicates dehydration therefore check the BUN/creatinine ratio as it elevates with dehydration as well.	-Liver-biliary dysfunction-see ALT and GGT
-Hypothyroidism-uncommon	-Protein malnutrition
-Adrenal cortical hypofunction-uncommon	-Malnutrition
	-Digestive inflammatory diseases-usually secondary to HCl need
	-Hyperthyroidism
	-Pregnancy

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Serum Albumin

INCREASED	DECREASED
Increase hydration	*Address liver conditions appropriately: Methionine Choline Inositol Ascorbates L-arginine Renal glandular extract Colostrum HCl

- Protein
- Hydrozyme or Betaine Plus HP

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SERUM GLOBULIN

Laboratory Range: 1.5 - 4.5g/dL **Optimal Range: 2.4 – 2.8**
WR range – below 2.0 g/dL or above 3.5 g/dL

Clinical Discussion:

There are several fractions to the globulin serum level these include: alpha-I, alpha-2, beta and gamma fractions. Therefore, of varying levels of any of these fractions can influence total globulin levels. Globulin is a sophisticated form of protein. It indicates the amount of circulating coital protein that is used to manufacture antibodies, blood cells and enzymes. Globulin will combine with phosphorus, copper, iodine, and iron to have IgG, IgA, IgM, and IgE immunoglobulins

Any increase or decrease in any one of the alpha-I, alpha-2, beta and gamma fractions will cause an increase or decrease in the total globulin. For this reason, the clinician must exercise care one making a diagnosis based upon the total globulin alone. Total globulin is useful utilized with other tests for assessing degenerative, inflammatory and infectious processes.

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SERUM GLOBULIN

INCREASED	DECREASED
Hypochlorhydria	Severe anemias
Infection	Hemorrhages
Neoplasm-early malignancy or multiple myeloma	Chronic viral or bacterial infection
Parasitic infections	Liver dysfunction
Infectious Hepatitis	Hypochlorhydria
Lymphogranuloma	

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SERUM GLOBULIN

INCREASED	***DECREASED***
HCl	CoQ10
Betaine hydrochloride	Molybdenum
Lipoic acid	Colostrum
Selenium	Ascorbates/vitamin C
Treat underlying pathological process as indicated	Treat underlying pathological processes indicated

3 mechanisms which primarily regulate globulin:

1. Thyroid (see check T3, T4, T7) if hyperthyroid use iodine and chlorophyll
2. Thymus (look for elevated bilirubin, RBC, Hgb, HCT) use copper and vitamin D.
3. Red blood cells (look for decreased bilirubin, RBC, Hgb, HCT) use iron and vitamin E (not at the same time)

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SERUM GLOBULIN

INCREASED	***DECREASED***
HCl	CoQ10
Betaine hydrochloride	Molybdenum
Lipoic acid	Colostrum
Selenium	Ascorbates/vitamin C
Treat underlying pathological process as indicated	Treat underlying pathological processes indicated
➢ Hydrozyme or Betaine Plus HP	➢ Hydrozyme or Betaine Plus HP

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ALBUMIN/GLOBULIN RATIO (A/G RATIO)

Laboratory Range: 1.2 - 2.2
WR range – below 1.0

Optimal Range: 1.2 - 1.6

Clinical Discussion:

And A/G. ratio of less than one is one of the for ominous signs suggest any serious free radical pathological process of some type. An elevated A./G. ratio, elevated protein, and elevated cholesterol suggests excessive protein in the diet.

INCREASED	DECREASED
-An elevated A/G ratio is not considered to be clinically significant	-Neoplasm, including multiple myeloma or metastatic disease -Infectious disease including AIDS -Intestinal disease -Liver disease -Renal disease -Congestive heart failure -The cachexic patient

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CALCIUM/ALBUMIN RATIO (Ca/A ratio)

Laboratory Range: 2.2 - 2.5 **Optimal Range: 2.03 - 2.71**
WR range – >2.7

Clinical Discussion:

A calcium/albumin ratio greater than 2.7 is considered one of the for ominous signs and indicates visceral protein loss from either disease or malnutrition. An elevated ratio should be caused to aggressively investigate and treat accordingly, consider referral for oncological studies.

A depressed Ca/A ratio is usually considered clinically insignificant. Some clinicians believe it represents possible subclinical dehydration.

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TOTAL or SERUM BILIRUBIN

Laboratory Range: 0.0 - 1.2 mg/dL **Optimal Range: 0.5 - 0.7**
WR range – > 2.0 mg/dL

Clinical Discussion:
Bilirubin is formed by the breakdown hemoglobin in the spleen, liver, and bone marrow. The liver forms a water-soluble molecule which is excreted through the kidneys or bile. When the value goes above 1.3 a protocol to dissolve gallstones is indicated.

Some labs report indirect bilirubin which will assist the in determination if the increased total bilirubin is pre-or post-hepatic. The values for serum bilirubin are obtained by adding the direct and indirect bilirubin values.

- **Direct bilirubin reference ranges should be 0-0.2 mg/dL with a panic range when values are greater than 0.8 mg/dL.**
- **Indirect bilirubin reference ranges should be 0.1-1.0 mg/dL with a panic range one values are greater than 1.8 mg/dL.**

161

TOTAL or SERUM BILIRUBIN

INCREASED	***DECREASED***
Biliary obstruction	Biliary stasis
Pernicious anemia	Secondary aplastic anemia
Chronic cholecystitis	
Hepatic injury	
Hemolytic anemia	

3 possible causes for increased bilirubin:

1. **Red blood cell destruction (pre—hepatic-excess production)**
2. **Hepatocellular damage (hepatic-dysfunction of liver cells)**
3. **Biliary tree obstruction (see post-hepatic-interference with removal)**

- ✓ **The total bilirubin is elevated with altered lymphocyte count suspect thymus involvement**
- ✓ **If total bilirubin is elevated with elevation in HCT, Hgb, and a decreased RBC, consider spleen hyperfunction.**
- ✓ **If total bilirubin is below 0.1, HCT below 12.5, and RBC below 4.0, with serum iron above 100 suspect spleen hypofunction.**

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TOTAL or SERUM BILIRUBIN

INCREASED	DECREASED
Biliary obstruction	Biliary stasis
Pernicious anemia	Secondary aplastic anemia
Chronic cholecystitis	
Hepatic injury	
Hemolytic anemia	

3 possible causes for increased bilirubin:

1. **Red blood cell destruction (pre—hepatic-excess production)**
2. **Hepatocellular damage (hepatic-dysfunction of liver cells)**
3. **Biliary tree obstruction (see post-hepatic-interference with removal)**

- ✓ **The total bilirubin is elevated with altered lymphocyte count suspect thymus involvement**
- ✓ **If total bilirubin is elevated with elevation in HCT, Hgb, and a decreased RBC, consider spleen hyperfunction.**
- ✓ **If total bilirubin is below 0.1, HCT below 12.5, and RBC below 4.0, with serum iron above 100 suspect spleen hypofunction.**

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TOTAL or SERUM BILIRUBIN

INCREASED	DECREASED
Thymus glandular extract	Spleen glandular extract
Spleen glandular extract	Iron

If due to gallstones consider abdominal ultrasound to determine size. If less than 1.5 cm in diameter natural therapies will frequently work. If not calcified, begin with bile viscous thinning agents such as beat extracts and apple cider vinegar

There is virtually no significance with a lower total bilirubin with the exception of possible secondary aplastic anemia.

Bilirubin in the urine indicates the presence of hepatocellular disease or intra- or extrahepatic biliary obstruction. **It is an early sign of these disorders and is therefore an extremely useful diagnostic tool.**

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TOTAL or SERUM BILIRUBIN

INCREASED	DECREASED
Thymus glandular extract	Spleen glandular extract
Spleen glandular extract	Iron

- **Beta TCP**
- **Cytozyme THY**
- **Cytozyme SP**

- **Beta Plus**
- **Cytozyme SP**

165

ALKALINE PHOSPHATASE

Laboratory Range: 44 - 121 IU/L **Optimal Range: 60 - 80**
WR range – If less than 25% above or below the reference range. Consider an isoenzyme study if it is.

Clinical Discussion:

Alkaline phosphatase a zinc metalloproteinase enzyme, therefore, it is a zinc dependent enzyme. Alkaline phosphatase is found in several different tissues but particularly bone, liver and intestines. ALP is normally increased with children due to rapid bone growth and following fractures because of bone repair. A fatty meal will also increase alkaline phosphatase for 2 - 4 hours. An isoenzyme study will help to discern the origin of tissue breakdown.

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ALKALINE PHOSPHATASE Isoenzymes

The Alkaline phosphatase isoenzymes are as follows:

·Liver isoenzyme a1—also called the "fast liver isoenzyme". It is associated with metastatic cancer to the liver, viral hepatitis, alcoholic cirrhosis, NAFLD and other hepatic conditions.

·Liver isoenzyme a2 – this is the isoenzyme generally increased when total serum alkaline phosphatase is elevated. A number of conditions elevate this isoenzyme including: cirrhosis, hepatitis, NAFLD, hepatic toxicity associated with drugs, biliary obstruction, as well as hepatic carcinoma.

·Bone isoenzyme - associated with an increase in osteoblastic activity.

·Intestinal isoenzyme - generally increased with perforation of the bowel, ulcerative diseases of the intestines and sometimes with liver cirrhosis. Can be a normal finding in Type O or B blood types.

·Placental isoenzyme - generally increased during pregnancy.

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ALKALINE PHOSPHATASE

INCREASED	DECREASED
Hepatic dysfunction	Almost always a zinc deficiency
Hepatitis-toxic and infectious	Hypothyroidism
Obstructive jaundice	Osteolytic sarcoma
Hyperparathyroidism	Multiple myeloma
Cancer metastasis to bone	Severe chronic nephritis
Neurofibromatosis	Anemia
Liver abscesses	Cretinism
Rickets	Estrogen therapy
Osteomalacia	Hypothyroidism-occasionally
Paget's disease	Celiac disease

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ALKALINE PHOSPHATASE

INCREASED

Hepatic glandular extract
Silymarin
Beat extract is a potent bile viscosity thinning agent
Ascorbates
Treat the underlying disease process

- Run Isoenzymes

DECREASED

Zinc - may take up to 18 months
Discuss HRT removal
Treat underlying disease process

- Zn Zyme & Zn Zyme Forte

169

SERUM LACTIC DEHYDROGENASE (LDH)*

Laboratory Range: 100 - 250 IU/L **Optimum Range: 130 - 190**
WR range – > 25% above or below the reference range.

Clinical Discussion:
As an enzyme, LDH is a catalyst for the conversion of pyruvic acid to lactic acid during normal cellular energy production, or carbohydrate metabolism. Total LDH is generally elevated in any distracted process or trauma within the body. It is widely distributed in the heart, skeletal muscle, liver, kidney, and red blood cells. When ever an elevated total LDH is discovered, it is clinically prudent to order an LDH isoenzymes study. there are 5 isoenzymes with some cross-over noted between them. By ordering an LDH isoenzyme study it is possible to narrow a developing disease process by organ system early on in its development. If the patient exhibits an elevated total LDH, the isoenzymes study will aid in the identification and treatment of the afflicted organ/tissue accordingly.

- Run Isoenzymes

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SERUM LACTIC DEHYDROGENASE (LDH)

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LDH isoenzyme #1 - is found in heart and RBCs
LDH isoenzyme #2 - is found in heart, lymph, and RBCs
LDH isoenzyme #3 - is found in pulmonary, spleen, adrenal and kidney
LDH isoenzyme #4 - is found and liver, skeletal muscle, prostate/uterus
LDH isoenzyme #5 - is found in liver and skeletal muscle

A decrease in LDH isoenzyme #5 often occurs in patients who have experienced long-term, insidious exposure to noxious gases like carbon monoxide. Be aware if your patients complains of unexplained illness, fatigue, loss of memory, etc. If this isoenzyme is decreased, it may indicate a heavy metal burden.

By ordering LDH isoenzymes studies, it is possible to narrow a developing disease process by organ systems early on in this development.

A low LDH may be Reactive hypoglycemia.

171

ASPARTATE AMINOTRANSFERASE (AST)
SERUM GLUTAMIC OXAOCETIC TRANSAMINASE (SGOT)

Laboratory Range): 0 - 40 IU/L **Optimal Range: 18 – 26**
WR range – > 90 IUL.

Clinical Discussion:

AST is one of the 2 enzymes most often associated with hepatocellular damage. AST enzymes are found in larger quantities in the heart and liver but are also found and skeletal muscle, kidneys and brain. AST generally elevates when destructive processes are affecting these organs. History is important for differentiating the cause an elevated AST. With liver disease, serum levels of AST and ALT closely parallel and elevate roughly in proportion to the extent of the hepatocellular damage. Non-hepatic diseases may also cause the AST to elevate, including skeletal muscle damage, congestive heart failure, myocardial infarction, and circulatory collapse. In cardiac related conditions, AST will not return to normal as quickly as ALT. Pyridoxine (P-5-P) (B6) is essential in the formation of AST, ALT women taking BCP are deficient in this nutrient in addition to vitamins B12 and vitamin C.

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ASPARTATE AMINOTRANSFERASE (AST)
SERUM GLUTAMIC OXAOCETIC TRANSAMINASE (SGOT)

INCREASED	***DECREASED***
Congestive heart failure	Vitamin B6 deficiency
Coronary artery insufficiency	
Myocardial infarction (confirm with troponin)	
Hepatocellular damage	
Pancreatitis	
Pulmonary embolism	
Myositis/skeletal muscle damage	
Alcoholism	
Neoplasms	
Essential hypertension	

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ASPARTATE AMINOTRANSFERASE (AST)
SERUM GLUTAMIC OXAOCETIC TRANSAMINASE (SGOT)

INCREASED	**DECREASED**
Broad-spectrum pancreatic enzymes	Vitamin B6
L-carnitine	
Magnesium	
Glutathione	
Utilize nutritional therapy consistent with the findings from additional tests and history	

If AST > ALT and both are out of clinical range – think hepatocellular carcinoma.

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ASPARTATE AMINOTRANSFERASE (AST)

SERUM GLUTAMIC OXAOCETIC TRANSAMINASE (SGOT)

INCREASED	DECREASED
Broad-spectrum pancreatic enzymes	Vitamin B6
L-carnitine	
Magnesium	
Glutathione	
Utilize nutritional therapy consistent with the findings from additional tests and history	

- Beta TCP
- Beta Plus
- Cytozyme LV
- Livotrit Plus

- B6 Phosphate

175

ALANINE AMINOTRANSFERASE (ALT)

SERUM GLUTAMIC PYRUVIC TRANSAMINASE (SGPT)

Laboratory Range: 0 – 44 IU/L **Optimal Range: 18 - 26**
WR range – > 90 IU/L.

ALT is functionally similar to AST. However, it is not increased as much as AST with cardiovascular issues. It does not return to normal as quickly as AST with hepatic dysfunction. It is more specific than AST for liver disease and injury. ALT is found primarily in the liver and lesser amounts and heart, muscle and kidney tissue. An elevation in ALT indicates an over oxidized, swollen liver. Decreased ALT indicates a hypometabolic, underactive, fatty, congested liver.

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ALANINE AMINOTRANSFERASE (ALT)

SERUM GLUTAMIC PYRUVIC TRANSAMINASE (SGPT)

INCREASED	DECREASED
Cirrhosis	B6 anemia
Acute and chronic liver necrosis	Fatty liver congestion (ALT less than 10 in conjunction with increased total cholesterol, greater than 220)
Alcoholism	
Myocardial infarction	
Hepatitis	
Mononucleosis Epstein-Barr virus	
Cytomegalovirus	
Congestive heart failure	
Hypertension	

When ALT is greater than the AST (see laboratory reference ranges) this typically indicates an extra-hepatic conditions such as hepatitis, extra-hepatic obstruction (GI gallstones) and toxic hepatitis. When AST is greater than ALT see laboratory reference ranges) this is typically at any traumatic hepatic condition such as primary liver cancer, cirrhosis, primary sclerosing cholangitis. Clearly, the latter scenario is associated with increased risk for mortality.

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ALANINE AMINOTRANSFERASE (ALT)

SERUM GLUTAMIC PYRUVIC TRANSAMINASE (SGPT)

INCREASED	***DECREASED***
Methionine	Pyridoxine
Beta carotene	Methionine
Liver glandular extract	B alkaline vitamins
Iodine	Choline
Lithium	Inositol
Alpha lipoic acid	Iron
Milk thistle	Copper

- Beta TCP
- Beta Plus
- Cytozyme LV
- Livotrit Plus
- B6 Phosphate

178

SERUM GAMMA GLUTAMYL TRANSFERASE (GGT)*

Laboratory Range: 0-65 IU/L **Optimal Range: 10 - 35**
WR range – > 100 UL.

Clinical Discussion:

GGT enzymes are found in large amounts in the renal tubular epithelial cells and relatively abundant in the liver and pancreas. GGT is considered to be more specific and sensitive for hepatic dysfunction. It will be increased in all liver/biliary dysfunction and generally it will be greater than ALT or AST.

When the GGT is elevated approximately 5 times the normal, suspect pancreatic involvement. Viral hepatitis will cause a combination of hepatocellular damage and intrahepatic cholestasis leading to an increase in indirect and direct bilirubin. An elevated GGT has the same significance as an elevated alkaline phosphatase with moderate increases indicating moderate hepatocellular degeneration and pronounced elevation showing obstructive disease or hepatocellular carcinoma.

179

SERUM GAMMA GLUTAMYL TRANSFERASE (GGT)

INCREASED	***DECREASED***
Hepatic disease	None
Pancreatic disease especially if > 300	
Cardiovascular disease	
Diabetes	
Epilepsy	
Severe trauma	
Post radiation	
Hepatobiliary cancers	
Alcoholism	

180

SERUM GAMMA GLUTAMYL TRANSFERASE (GGT)

INCREASED	DECREASED
Methionine	
Yakriton	
Liver glandular extract	
Beta carotene	
Phosphorus	
B6	
Treat the underlying pathology appropriately	

If due to biliary tree obstruction, follow gallbladder protocol.

If due to pancreatitis, no alcohol, digestive enzymes, no allergy/sensitivity foods.

181

SERUM GAMMA GLUTAMYL TRANSFERASE (GGT)

INCREASED	DECREASED
Methionine	
Yakriton	
Liver glandular extract	
Beta carotene	
Phosphorus	
B6	
Treat the underlying pathology appropriately	

- Beta TCP
- Beta Plus
- Cytozyme LV
- Livotrit Plus

- B6 Phosphate

182

SERUM IRON*

Laboratory Range: 27 - 139ug/dL(F) 38 – 169 (M) Optimal Range: 85 - 110
WR range – < 20 ug/dL or above 200 ug/dL.

Clinical Discussion:
Iron is by far the most abundant heavy-metal in the body. It is essential for hemoglobin synthesis and red blood cell formation. Excess iron in the blood is deposited in all cells of body, but especially macrophages in the liver were about 60% of iron a store. Surplus iron is stored in the body as ferritin and also as its denatured counterpart, hemosiderin. As iron as needed to his return from storage deposits and transported back to the erythroid precursors. This transportation requires a highly specialized plasma protein, transferrin. Transfer molecule simply deliver iron to be erythroid precursors then return to the macrophages for another load.

.

183

SERUM IRON*

INCREASED	DECREASED
Hemochromatosis	Insulin Resistance
	Iron deficiency anemia
Hepatic dysfunction	Menses
Iron therapy	Vitamin C anemia
Thalassemia	Hepatic dysfunction
Sideroblastic anemia	Intestinal parasites
Hemolytic anemia	Crohn's disease
Cofactor deficiency-B12, 6, folic acid, copper and/ or molybdenum deficiency	Intestinal inflammation
	Malabsorption

184

SERUM IRON*

INCREASED	DECREASED
Liver glandular extract	Iron
Spleen glandular extract	Spleen glandular extract
	Cofactors

Iron is one of a few nutrients that can be fatal overdose. Acute iron poisoning is by far the most common in children who may confuse the tablets for candy and accidentally swallowed overdose. Nausea, vomiting, intestinal bleeding, shock, and a high likelihood of death are common findings.

185

SERUM IRON*

INCREASED	DECREASED
Liver glandular extract	Iron
Spleen glandular extract	Spleen glandular extract
	Cofactors

- Zn Zyme
- Zn Zyme Forte
- Phlebotomy

- Fe Zyme

186

SERUM FERRITIN*

Laboratory Range: 15 – 150 (F) 39 – 400 (M) ng/mL. Optimal Range: 25 - 200
WR Range – < 10 ng/mL or above 300 ng/mL.

Clinical Discussion:
Serum ferritin is generally considered the most accurate test for elevation of the body's iron storage pool. Serum iron can only evaluate the functional iron and hemoglobin of circulated red blood cells and does not address the more essential concern of overall iron storage. Iron-storage depletion can occur over the course of your as well hemoglobin serum iron remains intact. The serum ferritin relates closely to iron stores and is significantly reduced in iron deficiency anemia and conversely increasing in disorders associated with iron overload. There is certain other factors which will result in elevations of ferritin, the most important is inflammation.

In addition to hemochromatosis, elevated ferritin is also followed and several other conditions including hepatic disease, chronic inflammatory neoplasms, hyperthyroidism, infections, inflammatory bowel disease, rheumatoid arthritis, myxedema and other inflammatory states. Elevated serum ferritin is commonly found in many malignancies. Height values generally forecasted poor prognosis, a return to normal equated with remission

187

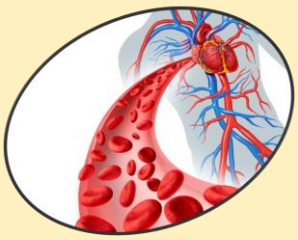
SERUM FERRITIN*

INCREASED	***DECREASED***
Hemochromatosis	Iron deficiency anemia
Neoplasms	Intestinal inflammation/ulceration
Inflammation	
HIV infection	
Hepatitis	
Several inherited anemias-LC, sickle cell, etc.	
Rheumatoid arthritis	
Hepatic disease	

- **Fe Zyme**

- **Zn Zyme**
- **Zn Zyme Forte**
- **Phlebotomy**

188



Lipid Panel:
- Total Cholesterol
- Triglycerides
- HDL Cholesterol
- LDL Cholesterol
- Cholesterol/HDL Ratio

189


WHAT IS CHOLESTEROL?
Where does cholesterol come from?
Cholesterol comes from two different places.
1 Blood cholesterol comes from your liver and it helps your body build cells and make vitamins and certain hormones. Your body produces all of the cholesterol it needs through this process.
2 Dietary cholesterol comes from foods you eat, primarily animal products like meat, eggs, cheese and milk. Dietary cholesterol can lead to health problems if it gets too high.
The bad kind of cholesterol
The good kind of cholesterol
Triglycerides contribute to high cholesterol
Check your cholesterol to avoid a heart attack or stroke
Learn more at heart.org/cholesterol
HEALTH Kaizen

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Circulation Research
REVIEW
Gut Microbiota and Cardiovascular Disease
Journal of Human Hypertension
REVIEW ARTICLE
Recent advances in modulation of cardiovascular diseases by the gut microbiota
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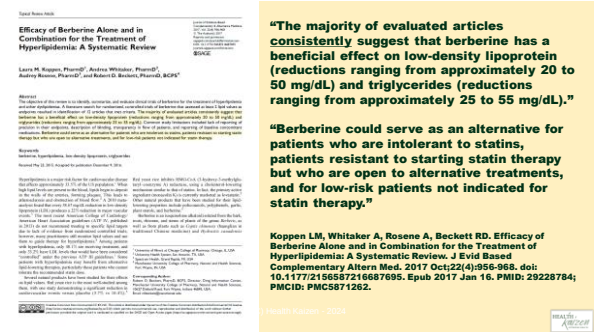
191


Efficacy of Berberine Alone and in Combination for the Treatment of Hyperlipidemia: A Systematic Review
"The majority of evaluated articles consistently suggest that berberine has a beneficial effect on low-density lipoprotein (reductions ranging from approximately 20 to 50 mg/dL) and triglycerides (reductions ranging from approximately 25 to 55 mg/dL)."
"Berberine could serve as an alternative for patients who are intolerant to statins, patients resistant to starting statin therapy but who are open to alternative treatments, and for low-risk patients not indicated for statin therapy."
Koppen LM, Whitaker A, Rosene A, Beckett RD. Efficacy of Berberine Alone and in Combination for the Treatment of Hyperlipidemia: A Systematic Review. J Evid Based Complementary Altern Med. 2017 Oct;22(4):956-968. doi: 10.1177/2156587216687695. Epub 2017 Jan 16. PMID: 29228784; PMCID: PMC5871262.
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192

Total Cholesterol

Laboratory Range: 100 – 199mg/dL **Optimum range: 185 - 200**
WR range: >250

Clinical discussion:
Cholesterol circulates as different fractions or particles referred to as lipoproteins; HDL, LDL and VLDL. The sum total of HDL, LDL, and VLDL equal the Total Cholesterol. Cholesterol is often communicated as a bad thing, and we are given the impression that we always need to get Cholesterol to a lower number to be healthy. The reality is that Cholesterol is needed to be healthy, and it is essential for life. What most don't know is that in the original research on Cholesterol completed decades ago the researchers found that not only does high Cholesterol have a negative impact on health . . . primarily to the heart and the whole cardiovascular system. They also found that having low Cholesterol levels has its own unique set of consequences. Specifically, those people with low Cholesterol levels have an increased risk of developing dementia, cancer, and other serious health problems over time.

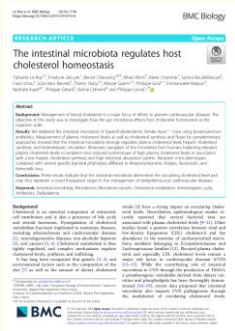
193

Total Cholesterol

Laboratory Range: 100 – 199mg/dL **Optimum range: 185 - 200**
WR range: >250

Clinical discussion: TC = HDL + LDL + VLDL
Cholesterol circulates as different fractions or particles referred to as lipoproteins; HDL, LDL and VLDL. The sum total of HDL, LDL, and VLDL equal the Total Cholesterol. Cholesterol is often communicated as a bad thing, and we are given the impression that we always need to get Cholesterol to a lower number to be healthy. The reality is that Cholesterol is needed to be healthy, and it is essential for life. What most don't know is that in the original research on Cholesterol completed decades ago the researchers found that not only does high Cholesterol have a negative impact on health . . . primarily to the heart and the whole cardiovascular system. They also found that having low Cholesterol levels has its own unique set of consequences. Specifically, those people with low Cholesterol levels have an increased risk of developing dementia, cancer, and other serious health problems over time.

194


BMC Biology

RESEARCH ARTICLE Open Access

The intestinal microbiota regulates host cholesterol homeostasis

BMC

"Management of blood cholesterol is a major focus of efforts to prevent cardiovascular diseases. The objective of this study was to investigate how the gut microbiota affects host cholesterol homeostasis at the organism scale."

"Conclusions: These results indicate that the intestinal microbiota determines the circulating cholesterol level and may thus represent a novel therapeutic target in the management of dyslipidemia and cardiovascular diseases.

Le Roy et al. BMC Biology (2019) 17:94
https://doi.org/10.1186/s12915-019-0715-8

195

Ancel Keys – villian or hero?

His theory, often referred to as the lipid theory or diet-heart theory, has become so widely accepted that most people today take for granted that it is absolutely true.

It led to widespread fear of saturated fats, to the point where the many health benefits of saturated fats get totally ignored and forgotten. To most people today, doctors, nutritionists and lay people alike, still believe saturated fats are bad, bad, bad.

Ancel Keys | Jan. 13, 1961

196

Ancel Keys – villian or hero?

However, a major criticism is that Ancel Keys had chosen to study only those countries where both saturated fats consumption and heart disease were high. He ignored other countries that ate similar diet but had low rates of heart disease.

Ancel Keys | Jan. 13, 1961

197

Ancel Keys – villian or hero?

"The dietary assessment methodology was highly inconsistent across cohorts and thoroughly suspect. In addition, careful examination of the death rates and associations between diet and death rates reveal a massive set of inconsistencies and contradictions. . .

It is almost inconceivable that the Seven Countries study was performed with such scientific abandon. It is also dumbfounding how the NHLBI/AHA alliance ignored such sloppiness in their many "rave reviews" of the study. . .

In summary, the diet-CHD relationship reported for the Seven Countries study cannot be taken seriously by the objective and critical scientist."

– Diet, Blood Cholesterol and Coronary Heart Disease:
A Critical Review of the Literature, Volume 2, November 1991

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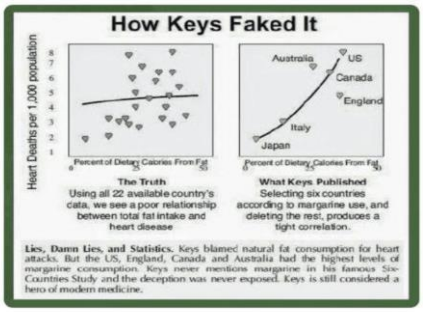

Source: Deep Nutrition, Cate Shanahan

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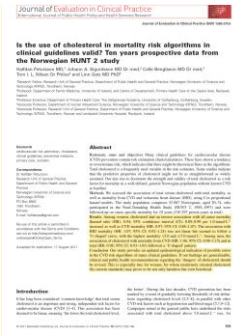

Is the use of cholesterol in mortality risk algorithms in clinical guidelines valid? Ten years prospective data from the Norwegian HUNT 2 study

Results Among women, cholesterol had an inverse association with all-cause mortality [hazard ratio (HR): 0.94; 95% confidence interval (CI): 0.89–0.99 per 1.0 mmol L−1 increase] as well as CVD mortality (HR: 0.97; 95% CI: 0.88–1.07). The association with IHD mortality (HR: 1.07; 95% CI: 0.92–1.24) was not linear but seemed to follow a 'U-shaped' curve, with the highest mortality <5.0 and 7.0 mmol L−1. Among men, the association of cholesterol with mortality from CVD (HR: 1.06; 95% CI: 0.98–1.15) and in total (HR: 0.98; 95% CI: 0.93–1.03) followed a 'U-shaped' pattern.

Conclusion Our study provides an updated epidemiological indication of possible errors in the CVD risk algorithms of many clinical guidelines. If our findings are generalizable, clinical and public health recommendations regarding the 'dangers' of cholesterol should be revised. This is especially true for women, for whom moderately elevated cholesterol (by current standards) may prove to be not only harmless but even beneficial.

Journal of Evaluation in Clinical Practice 18 (2012) 159–168

200

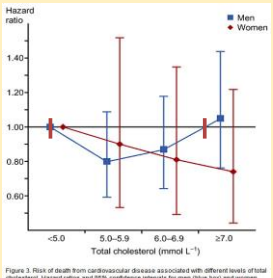

Figure 3. Risk of death from cardiovascular disease associated with different levels of total cholesterol. Hazard ratios and 95% confidence intervals for men (blue box) and women (red diamond). Adjusted for age, smoking and systolic blood pressure.

It found higher mortality in men with low cholesterol (less than ~193 mg/dl) and high cholesterol (greater than ~270 mg/dl) compared to men with levels in between (193 to 270).

Here's one graph from the study. The U-shape in the men's curve is evident. (convert mmol/L to mg/dl by dividing by 0.0259, so 5 mmol/L divided by 0.0259 = 193 mg/dl.)

Journal of Evaluation in Clinical Practice 18 (2012) 159–168

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Nutrition & Metabolism

RESEARCH Open Access

A nonlinear association of total cholesterol with all-cause and cause-specific mortality

BMC

All-cause, cardiovascular, and cancer mortality showed U-curve associations after adjusting for confounding variables in the restricted cubic spline analysis. Hazard ratios (HRs) of all-cause and cancer mortality were particularly negatively related to TC levels in the lower range < 200 mg/dL, especially in the range < 120 mg/dL (HR 1.97; 95% CI 1.38, 2.83, HR 2.39; 95% CI 1.21, 4.71, respectively). However, the HRs of cardiovascular disease mortality in the range < 120 mg/dL were the lowest (HR 0.60; 95% CI 0.15, 2.42). In the upper range, a TC range of ≥ 280 mg/dL was correlated with mortality as a result of CVD and cancer (HR 1.31; 95% CI 0.87, 1.97 and HR 1.22; 95% CI 0.82, 1.79)

Conclusions: A nonlinear association of TC level with all-cause, cancer, and CVD mortality in the American population was observed, suggesting that too low or too high serum total cholesterol levels might correlate with adverse outcomes.

He *et al. Nutr Metab (Lond) (2021) 18:25*
https://doi.org/10.1186/s12986-021-00548-1

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RESEARCH ARTICLE

The Association Between Low Serum Cholesterol and Non-Cardiovascular Mortality among Italian Males and Females: A Nine- Year Prospective Cohort Study

Conclusion: Among males, there were significant inverse hazard associations between the lowest cholesterol decile and all-cause and non-CVD deaths. Among females, there were significant inverse hazard associations of lowest and fourth cholesterol decile for all-cause and also risk first and fourth deciles for non-CVD mortality.

***Asian Pac J Cancer Prev,* 20 (5), 1361-1368**

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Open Access Research

BMJ Open Lack of an association or an inverse association between low-density-lipoprotein cholesterol and mortality in the elderly: a systematic review

"For decades, the mainstream view has been that an elevated level of total cholesterol (TC) is a primary cause of atherosclerosis and cardiovascular disease (CVD). There are several contradictions to this view, however. No study of unselected people has found an association between TC and degree of atherosclerosis.

Moreover, in most of the Japanese epidemiological studies, high TC is not a risk factor for stroke, and further, there is an inverse association between TC and all cause mortality, irrespective of age and sex."

Ravnskov U, et al. BMJ Open 2016;6:e010401. doi:10.1136/bmjopen-2015-010401

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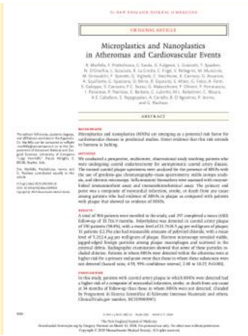

ORIGINAL ARTICLE

Microplastics and Nanoplastics in Atheromas and Cardiovascular Events

"**CONCLUSIONS** In this study, patients with carotid artery plaque in which MNPs were detected had a higher risk of a composite of myocardial infarction, stroke, or death from any cause at 34 months of follow-up than those in whom MNPs were not detected"

N Engl J Med 2024;390:900-10. DOI: 10.1056/NEJMoa2309822

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Cholesterol Functions

It will help to understand the importance of cholesterol by reviewing some of cholesterol's functions:

- Cholesterol is part of the cell membrane (the outer layer of the cell) for all the cells in your body, so Cholesterol is necessary for healthy cells.
- About 60 - 65% of your brain is made up of fat and Cholesterol, so having enough Cholesterol is needed for a healthy brain and nervous system.
- Bile salts are derived from cholesterol.
- Cholesterol is a hormone precursor . . . including male and female hormones and adrenal hormones, so Cholesterol is needed for healthy hormone levels.
- Cholesterol is even a pretty good antioxidant . . . which means that it has the ability to protect the cells from being damaged, and when your cells do get damaged healthy cholesterol comes to the rescue and help repair the cell damage.

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Cholesterol

The liver, adrenals, sex glands, intestines, and even the placenta manufacture cholesterol. Cholesterol is best used as an indication of metabolic dysfunction. In and of itself it is not a disease and is indicative of other health issues:

- Hypercholesterolemia –
  - Dysbiosis
  - Hypothyroidism
  - Excess carbohydrate intake
  - Blood sugar dysfunction
  - Hepatobiliary dysfunction dysfunction
  - Pancreatic dysfunction
  - Food sensitivities
  - Renal dysfunction
- Hypocholesterolemia
  - Medication issues
  - Dysbiosis
  - Free radical pathology
  - Inflammatory condition
  - Hyperthyroidism
  - Hepatic dysfunction
  - Poor nutrition and low fat intake
  - Vegetarian or vegan diet
  - Malabsorption in intestinal tract

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✓**The fourth ominous sign is a decreased serum cholesterol value of less than 140 mg/dL, unless the cause is due to endurance training or is a child.**

208

SERUM ALBUMIN

Clinical Discussion: ***The four ominous signs***

- ✓ **Albumin levels and ratios with other entities, plays a significant role in assessing the patient's morbidity risk. 3 of the 4 ominous signs include albumin in the equation. Perhaps the most ominous of the 4 ominous signs is an albumin that is 3.5 or below, with a total absolute lymphocyte count of less than 1500.**
- ✓ **A low (reversed or inverted) A/G. ratio less than 1.0 is another of the 4 ominous signs. These people may have a serious, developing, or currently manifesting free radical pathological process going on.**
- ✓ **The calcium/albumin ratio is elevated to greater than 2.7 is another of the for ominous signs. This is due to malnutrition or visceral protein loss secondary to a potential free radical pathological process.**
- ✓ **The fourth ominous sign is a decreased serum cholesterol value of less than 140 mg/dL, unless the cause is due to endurance training or is a child.**

Remember, the sign of 88. This is where the BUN value falls to 8 and a serum protein value climbs to 8 thus making the sign of 88. This scenario rates a favorable environment for the future development of a free radical pathology.

209

Triglycerides

Laboratory Range: 0 – 149mg/dL **Optimum range: 75 - 100**
WR range: >250

Clinical discussion:
Triglycerides are esters of glycerol combined with 3 chains of fatty acids. It in essence is 90% sugar and 10% fat. An otherwise healthy individual will have a triglyceride level approximately 50% of total cholesterol. Elevated triglycerides indicate poor utilization or overproduction. Low levels represent poor release of fatty acids. Most cases of low or high values represent compromised hepatic, endocrine, or over consumption refined carbohydrates.

210

HDL Cholesterol

Laboratory Range: >39mg/dL **Optimum range: 55 - 120**
WR range: NA unless TC/HDL ratio is >4.5

Clinical discussion:

HDL refers to a form of cholesterol called High Density Lipoprotein. For cholesterol to be carried through your bloodstream it needs to be carried and transported by a particle called a lipoprotein, and HDL is one of these lipoprotein particles. It is oftened referred to as the "good cholesterol", because these HDL particles have the ability to clean out deposits that can build-up in your arteries and HDL may prevent the build-up of plaque that can damage your blood vessels. Having your HDL levels high enough will help to protect and improve the health of your blood vessels and can be a positive factor in preventing cardiovascular problems including heart attack and stroke. The best ways we know of to naturally improve or maintain healthy levels of HDL is through regular exercise, consuming enough Omega 3 Essential Fatty Acids (EFA), maintaining healthy blood sugar levels, and keeping your body at a healthy weight.

211

LDL Cholesterol

Laboratory Range: 0.0 - 99mg/dL **Optimum range: 60 - 115**
WR range: NA unless TC/HDL ratio is >4.5

Clinical discussion:

LDL - Low Density Lipoprotein. Fat and water would normally repel each other, therefore a method of transporting fats through the blood is needed A lipoprotein is a particle that helps to transport fats such as cholesterol and triglycerides through your bloodstream. LDL carries mostly cholesterol in the bloodstream bringing it to the cells and tissues to fulfill their duties and functions. LDL is often called the "bad cholesterol" because excess amounts can result in cholesterol getting deposited in the walls of your blood vessels leading to hardening of the arteries and cardiovascular problems including heart attack and stroke. LDL (the bad cholesterol) has an inverse relationship with HDL (the good cholesterol) . . . meaning that as LDL increases HDL will often decrease. Many of the same things that will raise the good cholesterol (HDL) will also lower the bad cholesterol (LDL).

212

VLDL Cholesterol
Very Low Density Lipoprotein

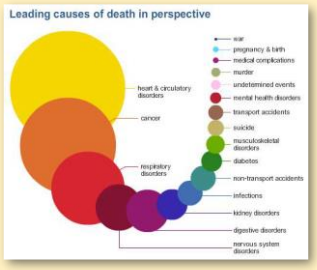
Laboratory Range: 5 - 40mg/dL **Optimum range: lower is better**
WR range: NA

Clinical discussion:

TC – HDL – LDL = VLDL

Fat and water would normally repel each other, therefore a method of transporting fats through the blood is needed: VLDL is that solution ☺. A lipoprotein is a particle that helps to transport fats such as cholesterol and triglycerides through the bloodstream. VLDL carries primarily triglycerides and is converted to LDL after losing its triglyceride. Many of the same things that affect LDL levels will also affect VLDL levels. The consequences of higher levels of VLDL are similar to having higher levels of LDL, and are associated with an increased risk for hardening of the arteries, and cardiovascular problems including heart attack and stroke.

213



214

When it comes to the size of cholesterol particles, the phrase "bigger is better" certainly applies. Believe it or not, even "bad" cholesterol may not carry all the same health risks if the particles are larger.

215

Homocysteine

Laboratory Range: 0 – 17.2 umol/L. **Optimum range: 6 - 7umol/L.**
WR range: > 29 umol/L.

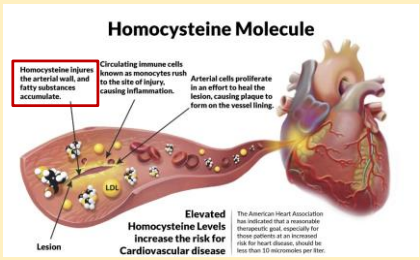
Clinical discussion:
Homocysteine is an intermediate amino-acid metabolite which is at the crossroads of two critical pathways in the body, including methylation reactions and trans-sulferation reactions. It is an intermediate in the biosynthesis of cysteine from methionine, via cystathione. Deficiencies of B12, folate, and or vitamin B6 can affect enzyme pathways involved in cysteine formation, resulting in increased circulating homocystiene levels in the blood.

Because homocystiene is located at a key metabolic pathway, it affects methyl and sulfur group metabolism throughout the body, and may serve as a critical functional marker for assessing the status of the methylation, skeletal and nervous systems as well.

Homocysteine is considered to be an independent risk factor for the development of cardiovascular disease. Patients with cardiovascular disease, including heart disease, stroke, peripheral vascular disease, and thromboembolic disease generally have higher homocystiene levels than matched controls.

Once homocystiene is increased, vascular inflammation is all but certain, as is generalized systemic inflammation!!!!

216



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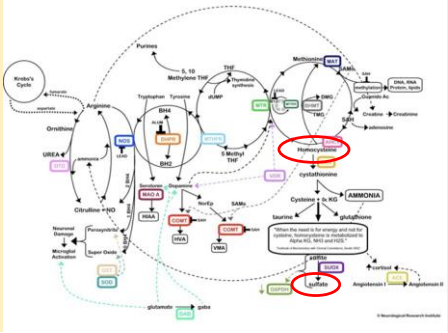

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Generally accepted Homocysteine levels:

- Desirable - ≤ 10 µmol/L
- Intermediate – 11 – 14 µmol/L
- High – 15 – 29 µmol/L
- Very High - > 29 µmol/L

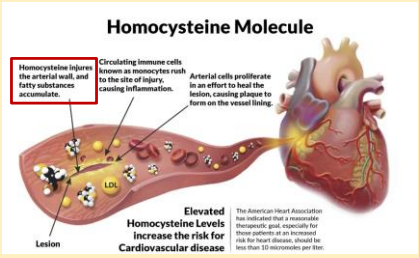
My range – desirable 6 – 7 µmol/L

219

Mechanisms of vascular injury Homocysteine

- Promotes leukocyte recruitment & activation.
- Metabolite of homocysteine aggregates with LDL and is taken by macrophages.
- Increases smooth muscle proliferation & collagen.
- Free radicals (during the oxidation of homocysteine) directly injure endothelium.
- Platelet accumulation: pro-aggregatory effects of homocysteine + endothelial impairment.
- Prolonged exposure of endothelial cells to homocysteine impairs the production of NO.

220



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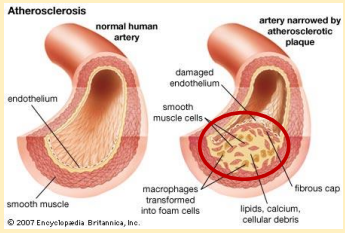

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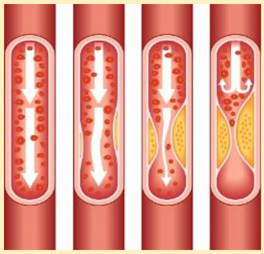

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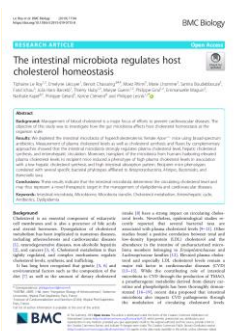
Le Roy et al. BMC Biology

BMC Biology

RESEARCH ARTICLE Open Access

The intestinal microbiota regulates host cholesterol homeostasis

BMC

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"<u>Conclusions: These results indicate that the intestinal microbiota determines the circulating cholesterol level</u> and may thus represent a novel therapeutic target in the management of dyslipidemia and cardiovascular diseases.

Le Roy et al. BMC Biology (2019) 17:94
https://doi.org/10.1186/s12915-019-0715-8

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Signal Transduction and Targeted Therapy

ARTICLE OPEN

Berberine treats atherosclerosis via a vitamine-like effect down-regulating Choline-TMA-TMAO production pathway in gut microbiota

Trimethylamine-N-oxide (TMAO) derived from the gut microbiota is an atherogenic metabolite

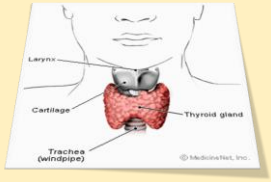
Oral BBR decreased TMAO production in animal intestine, lowered blood TMAO and interrupted plaque formation in blood vessels in the HFD-fed hamsters. <u>Moreover, 21 patients with atherosclerosis exhibited the average decrease of plaque score by 3.2% after oral BBR (0.5 g, bid) for 4 months (*P < 0.05, n = 21); whereas the plaque score in patients treated with rosuvastatin plus aspirin, or clopidogrel sulfate or ticagrelor (4 months, n = 12) increased by 1.9%.</u> TMA and TMAO in patients decreased by 38 and 29% in faeces (*P < 0.05; *P < 0.05), and 37 and 35% in plasma (*P < 0.001; *P < 0.05), after 4 months on BBR. <u>BBR might treat atherosclerotic plaque at least partially through decreasing TMAO in a mode of action similar to that of vitamins</u>**

(C) Health Kaizen - 2024

Signal Transduction and Targeted Therapy (2022) 7:207 ;

225

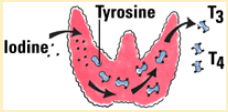
Thyroid Disease
Putting it Together



Every cell in the body depends upon thyroid hormones for regulation of their metabolism.

226

Thyroid Function

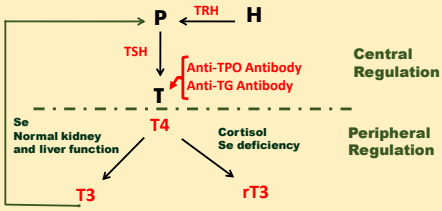


The thyroid gland takes Iodine, found in the diet, and converts it into thyroid hormones

The normal thyroid gland produces about 80% T4 and about 20% T3. The other 80% of T3 comes from the "deiodination" of T4. T3 possesses about four times the hormone "strength" as T4.

227

Thyroid Physiology



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Thyroid Disorders

- Hyperthyroidism
- Hypothyroidism
- Autoimmune Disorders
  - Grave's Disease
  - Hashimoto's
- Poor conversion of T4 to T3
- Goiter
- Nodules
- Cancer

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Characteristics	Adrenal Fatigue	Hypothyroidism
Body Measurements		
Weight	Early: gain weight; severe - unsure gain weight	Generalized weight gain
Body Temp	97.8 or lower	Low 90s to 98.6
Temp regulation	Hacketing and exaggerated	Steady
Physical Looks		
Eyebrows	Full	sparse some 1/3
Hair	Thin, sparse on extremities	Coarse and sparse
Hair loss	Sometimes	Common
Nails	Thin, brittle	Normal to flask
Peri-orbital Tissue	Sunken	Puffy
Skin	Thin	Normal
Skin tone	Dry	Oily or moist
Internal feeling		
Ligaments Flexibility	Good	Poor
Fluid retention	No	Yes
Pain	Headache, muscular, migraines	Joints, muscles
Reactivity	Heightened and hyper-reactive	Hypo-reactive
Concomitant condition		
History of Infections	Common	Occasional
Chronic Fatigue	Yes	Yes
Orthostatic Hypotension	Frequent	No
Blood Sugar	Tendency toward hypoglycemia	Normal to hyperglycemia
Heart Palpitation	Frequent	No
GI Inaction	Irritable or hyperactive	Constipation and hypoactive
Personality Traits		
Personality Type	Type A	Type A or B
Obsessive Compulsive	Frequent	Mixed
Habits		
Sleep Pattern	Wake up 2-4 am	Sleepy
Temperature Tolerance	Intolerance to Cold	Intolerance to Heat
Food Craving	Craving for sweet and salty	Craving for Fats

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"Well, just to be clear, your thyroid problems aren't the usual thyroid problems. And by that, I mean although the ailment itself is common, there's two issues that can happen with your thyroid. It can underperform – that's hypothyroidism – or it can overperform – hyperthyroidism. But your issue, Oprah, and you're so unique, is that you were having a frat party in your thyroid. You were having a bunch of different things happen at once. And so you have these two ailments: One was stimulating the thyroid with antibodies; the other one was actually waging war on the thyroid. And so when these two level out, they actually bring you to a place of peace – which interestingly is where you are right now."
Dr. Oz

232

"40% of the American people – four of every 10 children and adults – today are suffering needlessly and many are dying for lack of an ingredient vital for health. Is this ingredient unknown? No. Or unavailable? No. For years, medicine has recognized the role of deficiency in some areas of health and disease and has had clues to its great importance in many other areas. But the knowledge too often has not been used – and still is not being used – because of unreliability of laboratory tests that have failed to show the deficiency even when doctors could see its manifestations clearly enough in patients before them. And while laboratory tests have erred and have misled both doctors and patients, patients have suffered."

Broda O. Barnes, MD, *Introduction to Hypothyroidism, The Unsuspected Illness.* 1976

233

The **American Thyroid Association (ATA)** is the world's leading professional association of medical specialists dedicated to education and research to improve thyroid disease prevention, diagnosis and treatment; improving thyroid patient care; and educating the public about thyroid health and diseases.

Prevalence and Impact of Thyroid Disease

More than 12 percent of the U.S. population will develop a thyroid condition during their lifetime.
·An estimated 20 million Americans have some form of thyroid disease.
·Up to 60 percent of those with thyroid disease are unaware of their condition.
·Women are five to eight times more likely than men to have thyroid problems.
·One woman in eight will develop a thyroid disorder during her lifetime.
·Most thyroid cancers respond to treatment, although a small percentage can be very aggressive.
·The causes of thyroid problems are largely unknown.
·Undiagnosed thyroid disease may put patients at risk for certain serious conditions, such as cardiovascular diseases, osteoporosis and infertility.

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The American Thyroid Association (ATA)

·Pregnant women with undiagnosed or inadequately treated hypothyroidism have an increased risk of miscarriage, preterm delivery, and severe developmental problems in their children.
·Most thyroid diseases are life-long conditions that can be managed with medical attention.
Association over the past 40 years has accomplished:
·Mandatory screening of newborns for congenital hypothyroidism, and early treatment that has prevented mental retardation.
·Cost-effective methods to detect thyroid cancer by screening the 250,000 thyroid nodules developed in Americans each year.
·Groundbreaking work in brain development and thyroid hormone function.
·Promising Graves' disease genetic research that may lead to improved prognosis and new preventive treatments.
·An experimental drug that may prove useful for treatment and prevention of eye problems associated with Graves' disease

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Thyroid Hormones

- Affect every cell in the body.
- A patient cannot obtain 'Optimal Health' without a properly functioning thyroid.
- It is estimated that hypothyroid may be one of the most commonly missed diagnosis.
- It is estimated that 40% of the population may be hypothyroid.

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Hormone

A Greek word - "setting in motion". A signaling molecule produced by glands which are transported by the circulatory system to a "Distant" target organ to regulate physiology and behavior. When a hormone binds to the target receptor, it results in the activation of a signal transduction pathway resulting in a change in cell function

Diverse chemical structures, mainly of three classes:

- **eicosanoids,**
- **steroids, and**
- **amino acid/protein derivatives (amines, peptides, and proteins).**

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Hormone

The glands that secrete hormones comprise the endocrine system. The term hormone is sometimes extended to include chemicals produced by cells that affect the same cell (autocrine or intracrine signaling) or nearby cells (paracrine signaling).

Used to communicate between organs and tissues for physiological regulation and behavioral activities, such as:

- **digestion**
- **metabolism**
- **respiration**
- **tissue function**
- **sensory perception**
- **sleep**
- **excretion**
- **lactation**
- **stress**
- **growth and**
- **development**
- **movement**
- **reproduction, and**
- **mood.**

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The Thyroid Gland

Hormones Produced:

Thyroxine (T_4) - 80% ***made in follicle***
Triiodotyronine (T_3) - 20% ***made in follicle***
} **hormones that affect tissue metabolic rates**

Calcitonin ***made by C cells*** **- a hormone that usually plays a minor role in calcium ion homeostasis by opposing the action of parathyroid hormone**

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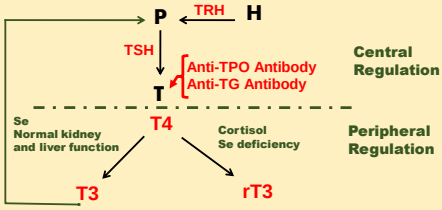
Thyroid Physiology



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Thyroid Profile with TSH:

- ✓TSH - Thyroid Stimulating Hormone
- ✓Thyroxine (Total T4)
- ✓T3 Uptake
- ✓Free Thyroxine Index

CPT 84443

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Blood Chemistry to consider:

At a minimum
- **TSH – Thyroid Stimulating Hormone**
- **Thyroxine (T4)**
- **T3 Uptake**
- **Free Thyroxine Index**

Really need to consider:
- **Free T4**
- **Free T3**
- **rT3**

Autoimmunity considerations:
- **Thyroglobulin Ab**
- **Anti-TPO**

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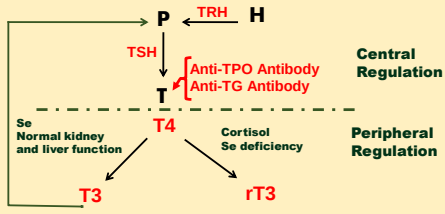
Thyroid Physiology



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Thyroid Disorders

- Hyperthyroidism
- Hypothyroidism
- Autoimmune Disorders
  - Grave's Disease
  - Hashimoto's
- Poor conversion of T4 to T3
- Goiter
- Nodules
- Cancer

245

Thyroid Dysfunction

Negative influences on thyroid function:

- Stress
- Microbiome disturbances particularly candidiasis
- Inflammation
- Endocrine Disrupting Chemicals
- Iodine deficiency
- Medications
- Tap Water (halogens – fluoride, chlorine, bromide)
- Liver dysfunction
- Fatty acid or protein deficiency
- Hydrogenated oils
- Estrogen
- Dieting
- Mercury amalgams and other heavy metals (Al)
- High carbohydrate diets
- Lack of sleep

246

Thyroid Dysfunction

What can go wrong?

- **Primary thyroid dysfunction**
- **Secondary or peripheral thyroid dysfunction**
  - **Hypothalamic – pituitary (TRH)**
  - **Pituitary – thyroid (TSH)**
  - **T4 – T3 conversion**
    - ✓ **Reverse T3**
    - ✓ **Conversion issue in peripheral** - kidneys, liver, muscle, brain, skin, and, when applicable, the placenta.
- **Autoimmune disease**

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Thyroid Stimulating Hormone (TSH)

Laboratory range: 0.450 – 4.50 **Optimal range: 1 – 2.5**
Will Robinson (WR) range: <0.350 and >15.0

Clinical Discussion:
TSH is the most common lab test performed to measure and monitor thyroid function. However, too many health providers rely on this test as the only measure of thyroid function, and this can be very misleading. The TSH lab result can be in the labs normal range and a person can still have altered thyroid function as determined by the other thyroid lab tests. This overreliance on TSH as a primary indicator of thyroid function has resulted in millions of people not getting properly diagnosed with a real thyroid problem.

TSH is secreted from the anterior pituitary in response to thyrotropin-releasing hormone (TRH) from the hypothalamus.

Cholesterol levels often inversely correlate with thyroid function. Proper liver function is a must, generally cholesterol will increase with hypothyroid function. However, if hyperthyroid with decreased cholesterol, pituitary is probably primary problem.

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Complete Thyroid Panel:

- ✓**TSH - Thyroid Stimulating Hormone**
- ✓**T3 Uptake**
- ✓**Free Thyroxine Index**
- ✓**Thyroxine (Total T4)**

- **Triiodothyronine, Free (Free T3)**
- **Thyroxine (Free T4), Direct**
- **Reverse T3**
- **Thyroid Peroxidase (TPO) Antibody**
- **Thyroglobulin Antibody**

249

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  - **Pituitary – thyroid (TSH)**
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250

Thyroid Disorders

- **Hyperthyroidism**
- **Hypothyroidism**
- **Autoimmune Disorders**
  - **Grave's Disease**
  - **Hashimoto's**
- **Poor conversion of T4 to T3**
- **Goiter**
- **Nodules**
- **Cancer**

251

Findings Associated With Hyperthyroidism

- **Difficulty gaining weight**
- **Easily flushed**
- **Fast pulse (at rest)**
- **Heart palpitations**
- **Insomnia**
- **Inward trembling**
- **Intolerant to higher temperatures**
- **Nervous – emotionally, unable to work under pressure**
- **Night sweats**
- **Reflexes brisk**

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Classic signs of Hyperthyroidism:

- Adults
  - Insomnia
  - Hand tremors
  - Nervousness
  - Feeling excessively hot in cool to normal temperatures
  - Frequent bowel movements
  - Losing weight despite normal to increased appetite
  - Excessive sweating
  - Menstrual period becomes scant, or stops altogether
  - Joint pains
  - Difficulty concentrating
  - Eyes seem to be enlarging

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Classic signs of Hyperthyroidism:

- Elderly
  - Worsening angina (chest pain) in those with heart disease
  - Worsening of shortness of breath in those with heart failure
  - Muscle weakness, especially in the shoulders and thighs

254

Classic signs of Hyperthyroidism:

- Children
  - Similar to adult symptoms
  - Declining school performance
  - Behavior problems

255

Findings Associated With Hypothyroidism

- Acne
- Anemia
- Arthritis
- Arteriosclerosis
- Constipation
- Cold extremities
- Dry skin
- Eczema
- Edema (pretibial & periorbital)
- Fatigue in the A.M.
- Goiter
- Hair loss
- Hypertension
- Headaches
- Hypercholesterolemia
- Hypertension
- Infertility
- Increased sleepiness
- Menstrual Disorders
- Ovarian Cysts
- PMS
- Poor eyebrow growth
- Poor memory
- Psoriasis
- Recurrent infections
- Sleep apnea
- Sluggish reflexes

256

Classic signs of Hypothyroidism:

- Early symptoms
  - Fatigue easily
  - Loss of the lateral 1/3 of eyebrows
  - Intolerance of cold temperatures
  - Elevated cholesterol
  - Constipation
  - Carpal tunnel syndrome
  - Loss of libido

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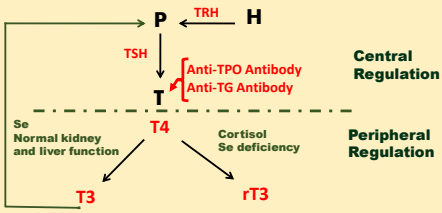
Thyroid Physiology



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THYROID PROTOCOLS HYPERFUNCTION CONSIDERATIONS

- ✓ **Bio-AE Mulsion Forte-5 drops twice a day for one week, then 2 drops twice a day**
- ✓ **Cytozyme THY - 5 tablets tid**
- ✓ **Li-Zyme Forte - 2 tablets per waking hour for 10 days, then 3 tablets tid**
- ✓ **L-Carnitine -1000 mg tid**
- ✓ **Se-Zyme Forte - 2 tabs/day if antibodies are increased or Aqueous Selenium**
- ✓ **Support adrenals**

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THYROID PROTOCOLS HYPOFUNCTION CONSIDRATIONS

- ✓**Thyrostim – 1-2 bid**
- ✓**Meda-Stim -1-2 per day**
- ✓**GTA/ GTA Forte II**
- ✓**Iodizyme HP – check if use >1/day**
- ✓**L-Tyrosine - 2bid - if the T4 (total or free) is decreased below the midline of the laboratory range**
- ✓**SE-Zyme Forte if antibodies are increased - 2 per day or Aqueous Selenium**
- ✓**Support adrenals**

260

T3 Uptake

Laboratory range: 24 – 39% **Optimal range: 27 – 35**
Will Robinson (WR) range: NA

Clinical Discussion:
T3 Uptake measures the number of binding sites that are available on proteins that would bind to Thyroxine (T4). It is usually measured as a percentage, and this number is needed to determine the result of another lab test called the Free Thyroxine Index. This lab test is normally done with other thyroid lab tests as it provides limited information on its own. It is used as a way to rule out an error in the labs reporting of increased T4 levels.

If T4 and T3 Uptake are both increased . . . then it helps to confirm a true increase in T4 levels.

1) hypo-thyroid function, 2) a pituitary problem, 3) a nutrient deficiency in iodine or selenium, 4) elevated estrogen levels in the body, 4) a liver problem, 5) the effect of some medications.

261

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Will Robinson (WR) range: NA

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262

Free Thyroxine Index (FTI) or T7

Laboratory range: 1.2 – 4.9 **Optimal range: 2.6 – 3.6**
Will Robinson (WR) range: NA

Clinical Discussion:
The Free Thyroxine Index (FTI) is FTI = T3/100 X T4, it is an indirect way to determine Free T4 levels by using this calculation. This calculation has been found to be a less reliable way to measure Free T4 compared to simply testing Free T4 directly in blood testing. it is possible to have a normal FTI with an abnormal T-3 Uptake or Total T-4.

263

Thyroxine - Total T4

Laboratory range: 7.0 – 9.00 **Optimal range: 4.5 – 12.0**
Will Robinson (WR) range: <0.350 and >15.0

Clinical Discussion:
Thyroxine (also called T4) exists as either the active form, Free T4, or in the inactive form where T4 is bound to a protein. This test measures the total amount of T4 in your body in both the active and inactive forms. When stimulated by TSH the thyroid produces thyroid hormone primarily in this form of T4, which is 4 iodine molecules attached to tyrosine. It is transported in the blood bound to thyroid binding globulin (TBG), It has little biological activity or effect on the cells. It's not until T4 gets converted to T3 by deiodination in other areas of the body that the thyroid hormone will have its primary effect on the metabolism and function of the cells.

264

Thyroid Dysfunction

Negative influences on thyroid function:

- Stress
- Microbiome disturbances particularly candidiasis
- Inflammation
- Endocrine Disrupting Chemicals
- Iodine deficiency
- Medications
- Tap Water (halogens – fluoride, chlorine, bromide)
- Liver dysfunction
- Fatty acid or protein deficiency
- Hydrogenated oils
- Estrogen
- Dieting
- Mercury amalgams and other heavy metals (Al)
- High carbohydrate diets
- Lack of sleep

265

Thyroid Dysfunction

Mitigating thyroid dysfunction:

- Avoid gluten (mimics thyroid antibodies)
- Stress – support adrenals
- Microbiome disturbances particularly candidiasis
- Inflammation
- Iodine excess or deficiency
- Medications
- Tap Water (halogens – fluoride, chlorine, bromide)
- Liver dysfunction
- Fatty acid or protein deficiency
- Hydrogenated oils
- Estrogen
- Dieting
- Mercury amalgams
- High carbohydrate diets
- Lack of sleep

266

C–reactive protein (CRP)

Laboratory Range: 0 – 4.9 mg/L **Optimum Range: < 2**
WR Range – ≥ 10

Clinical discussion:
C-Reactive protein is a specific type of protein produced by the liver. It is only present during episodes of acute inflammation.CRP is traditionally used as a marker for various inflammations.

hsCRP (cardiac), also referred to as high sensitivity CRP, is a more sensitive test for the same substance. Both measure the same substance, but the cardiac test is like looking through a high-powered microscope.

CRP is an acute phase reactant, which can be used as a test for inflammatory diseases, infections, and neoplastic diseases. Progressive increases correlate with increases of inflammation/injury. CRP is more sensitive, response more quickly than ESR.

267

C-Reactive protein(CRP)

INCREASED	***DECREASED***
Any acute phase inflammatory process	Not clinically relevant
Cardiovascular and peripheral vascular issues	
Rheumatoid arthritis	
Acute bacterial infections	
Viral hepatitis	
Rheumatic fever	
Free radical pathology	
Cirrhosis	
Burns	

268

CBC with Differential

Test Includes:
White Blood Cell count (WBC), Red Blood Cell count (RBC), Hemoglobin, Hematocrit, Mean Corpuscular Volume (MCV), Mean Corpuscular Hemoglobin (MCH), Mean Corpuscular Hemoglobin Concentration (MCHC), Red Cell Distribution Width (RDW), Platelets, Percentage and Absolute differential WBC counts, Percentage and Absolute Immature Granulocytes, and Sedimentation Rate.;

CPT - 85025

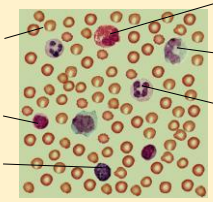
269

Complete Blood Count (CBC)

- Red blood cells
- Hemoglobin concentration
- Hematocrit
- Mean cell volume (MCV)
- Mean cell hemoglobin (MCH)
- Mean cell hemoglobin concentration (MCHC)
- White blood cell count (WBC)
- Differential: indicates percentages of different kinds of WBC

270

The Cells of the Immune System



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White Blood Cell (WBC)

Laboratory Range: 3.4 - 10.8 x 10E3 /uL **Optimal Range: 5 - 8**
WR Range – < 2.5 or > 12

Used for white cell enumeration, identifies leukopenia (low WBC) and leukocytosis (increase WBC). White blood cells or leukocytes are divided into 2 groups - granulocytes and non-granulocytes cells and these categories are:

Granulocytes: Polymorphonuclear neutrophils (segmented and bands)
Eosinophils
Basophils

Non-granulocytes: Lymphocytes
Monocytes

CPT - 85048

272

White Blood Cell (WBC)

INCREASED	***DECREASED***
Acute viral or bacterial infection	Chronic viral or bacterial infection
Childhood diseases- chickenpox, measles, mumps	Systemic lupus erythematosus
Intestinal parasites	Hepatitis
Infectious mononucleosis	Vitamin B6, B12, and folate anemia
Acute and chronic myelocytic leukemia	Adrenal dysfunction
Adrenal dysfunction	Anterior pituitary dysfunction
Pelvic inflammatory disease	Hyperparathyroidism
Asthma	Chronic intestinal parasites
Emphysema	Rheumatoid arthritis

273

White Blood Cell (WBC)

INCREASED

Treat underlying pathology appropriately

IAG
Bio-Immunozyme Forte
Cytozyme THY

DECREASED

Treat underlying pathology appropriately

IAG
Bio-Immunozyme Forte
Cytozyme THY

274

Red Blood Count (RBC)

Laboratory Range: 3.77 - 5.28 xc10 E6/uL (F) 4.14 – 5.80 (M) Optimal Range: 4 – 5
WR Range – < 3.50 or > 6.0

The RBC is used to evaluate anemia, loss of red blood cells, and suspected polycythemic condition.

Red blood cells transport hemoglobin, and hemoglobin transports oxygen. The accessible tissue oxygen is dependent upon the function and availability of hemoglobin, effective blood flow patterns, and the health of the tissue itself.

CPT - 8504

275

Red Blood Count (RBC)

INCREASED

Polycythemia
Dehydration
Iron overload
High altitudes
Pulmonary fibrosis
Cardiopathy
Asthma
Emphysema
Adrenal cortical hyperfunction

DECREASED

Anemia
B6, B12, and or folate deficiency
Hepatic dysfunction
Renal Dysfunction
Leukemia

276

Red Blood Count (RBC)

INCREASED	DECREASED
Vitamin A	Vitamin B6
Vitamin E	Vitamin B12
Phlebotomy	Folate
Water	Molybdenum
Treat the underlying pathology	Copper
Bio-Ae-Mulsion (Forte) - BRC	B6 phosphate – BRC
Bio-E-Mulsion Forte - BRC	B12 - 2000

277

Erythrocytosis

When the RBC count is above clinical ranges, erythrocytosis is present. Polycythemia is a disease state in which the hematocrit and/or hemoglobin concentration are elevated in peripheral blood. It can be due to an increase in the number of red blood cells or to a decrease in the volume of plasma.

With erythrocytosis the WBC and platelet count may be normal. Polycythemia is divided into 3 classes-primary, secondary and relative. Primary and secondary polycythemia show an increase in RBCs and HCT of the plasma volume is normal or possibly increased.

Primary polycythemia, also call polycythemia rubre vera, is a proliferation of RBCs that are concerned due to the possibility of occlusive vascular disease, cerebral vascular accident, hemorrhage and the possibility of progression to leukemia. Symptoms may consist of peripheral joint inflammation and an enlarged spleen.

Secondary polycythemia may be due to

1. Heart disease
2. Living at higher altitudes
3. Chronic lung disease
4. Smoking

278

Hemoglobin

Laboratory Range: 11.1-15.9 g/dL (F) 13.0 – 17.7 (M)
Optimal Range: 14 - 17
WR range – < 10.0 or > 19.0

Hemoglobin is a combination of heme and globin. It reveals the amount intracellular iron and is a heavy molecule contributing greatly to the weight of the blood, Hgb is the major component of red blood cell, it functions in the transport of oxygen. It also helps to buffer carbon dioxide performed during normal metabolic activity. There may be considerable variations in normal Hgb levels in healthy adults.

Hemoglobin does not require insulin for uptake of iron, making the glucose hemoglobin an excellent test for glucose metabolism (hemoglobin A1c).

CPT - 83051

279

Hemoglobin

INCREASED	DECREASED
Dehydration	Anemia
Polycythemia	Vitamin C deficiency
Emphysema	Internal bleeding
Asthma	Chronic intestinal parasites
	Folate deficiency
	B12 deficiency
	Thiamine deficiency

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Hemoglobin

INCREASED	DECREASED
Water	Iron
Phlebotomy	Vitamin C
	Folate
	Vitamin B12
	Thiamine
	Locate the source of the bleeding
	Fe-Zyme – BRC
	Bio-C Plus - BRC
	Thiamine 50 – BRC
	B12 – 2000 – BRC

281

Hematocrit

Laboratory Range: 34.0 – 46.6% (F) 37.5 – 51.0 (M)
Optimal Range: 40 - 45
WR range – < 30 or > 50

Hematocrit indicates the amount of RBC production. HCT values together with hemoglobin are commonly used expressed a degree of anemia. These 2 values are usually paralleled with a disproportionate value if RBC's have an abnormal shape or size about them. The MCV and MCH values are considered along with HCT.

Is used to evaluate anemia, blood loss, state of hydration, and suspected polycythemia and the results of treatment.

The hematocrit is a percentage of the total volume occupied by the red blood cells when given volume of blood is centrifuged.

CPT - 85014

282

Hematocrit

INCREASED	DECREASED
Dehydration	Anemia
Polycythemia	Vitamin C deficiency
Emphysema	Internal bleeding
Asthma	Chronic intestinal parasites
Spleen hyperfunction	Thymus hypofunction
	Folate deficiency
	B12 deficiency
	Thiamine deficiency

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Hematocrit

INCREASED	DECREASED
Water	Iron
Phlebotomy	Vitamin C
	Folate
	Vitamin B12
	Thiamine
	Locate the source of the bleeding
	Fe-Zyme – BRC
	Thiamine 50 – BRC
	B12 – 2000 – BRC

284

Mean corpuscular volume (MCV)

Laboratory Range: 79 - 97 fL **Optimal Range: 83 - 90**
WR range – < 75 or > 100

The MCV helps to identify the average size of the RBC and provides a convenient basis for separating anemias into groups: microcytic, normocytic or macrocytic. A low MCV value identifies microcytosis while an elevated value would indicate macrocytosis, and normal values would indicate normal sized RBCs.

The MCV indicates the volume in cubic microns occupied an average single red blood cell. MCV and MCH should always be viewed together to determine a possible B6, B12 or folate anemia.

If elevated it may be your first clue to possible methylation problems.

285

Mean corpuscular volume (MCV)

INCREASED	DECREASED
Vitamin B12/folate anemia	Iron anemia
Dehydration	Microscopic internal bleeding
High-altitude	Intestinal parasites
Thyroid hypofunction	Vitamin C anemia
Alcoholism	Vitamin B6 anemia
Vitamin C anemia	Heavy-metal burden
Multiple sclerosis	Thyroid hyperfunction
Hepatic disease	

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Mean corpuscular hemoglobin (MCH)

Laboratory Range: 26.6 - 33 pg **Optimal Range: 27 - 32.5**
WR range – < 22.0 or > 37.0

The MCH is the weight of hemoglobin in a single red blood cells. MCV is a measurement of the average size of your red blood cells. MCH results tend to mirror MCV results. This is because bigger red blood cells generally contain more hemoglobin while smaller red blood cells tend to have less.

MCH increase or decrease along with an increase or decrease in MCV and is a significant finding for B12, folate, iron, copper and vitamin B6 anemia. MCV and MCH should always be evaluated together.

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Mean corpuscular hemoglobin (MCH)

INCREASED	DECREASED
Vitamin B12/folate anemia	Iron anemia
Dehydration	Microscopic internal bleeding
High-altitude	Intestinal parasites
Thyroid hypofunction	Vitamin C anemia
Alcoholism	Vitamin B6 anemia
Vitamin C anemia	Heavy-metal burden
Multiple sclerosis	Thyroid hyperfunction
Hepatic disease	

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Mean corpuscular hemoglobin concentration (MCHC)

Laboratory Range: 31.5 – 35.7 g/dL **Optimal Range: 32 - 35**

The mean corpuscular hemoglobin concentration is a measure of the concentration of hemoglobin in a given volume of packed red blood cell. It is calculated by multiplying the hemoglobin result from the CBC panel by 100 and then dividing by the hematocrit.

The mean corpuscular hemoglobin concentration indicates the amount intracellular iron contained in the red blood cells. The same things that can cause increases or decreases in the MCH and MCV can be applied to the MCHC as well.

289

Red blood cell distribution width (RDW)

Laboratory Range: 11.7 - 15.4% **Optimal Range: 11.5 – 13.0**
WR range: > 14

The red blood cell distribution width identifies variation in red blood cell size. The greater the number the greater the variation (anisocytosis). An arbitrary value of 10+ or -1.5 has been assigned.

A normal value shows consistency or same size. Increased RDW is primarily indicative of an iron deficiency anemia; however, it can be increased with vitamin B12 or folate anemia.

The same things that affect MCV and MCH will also affect RDW.

290

Microcytic Anemias

The 3 main microcytic anemias will exhibit a low MCV. The degree of MCV depression may imply a specific cause but should be analyzed with other findings

✓Iron deficiency anemia (IDA) is a common cause of microcytic anemia and will exhibit a poor MCV. Hypochromatic, microcytic anemias may be due to inadequate iron consumption, iron assimilation or blood loss.

✓Thalassemias - (genetic disorder) occur at approximately the same incidence as IDA. A thalassemia victim is usually asymptomatic with a lower MCV value due to a lower RDW. A thalassemia victim may only exhibited a decreased MCV. A mathematical formula has been devised to aid in differentiating IDA from thalassemia. Divide MCV by RBC, if the answer is > 13.5, IDA should be the diagnosis

✓Anemia from chronic disease is the third most common form and frequently accompanies chronic infections, inflammatory diseases such as arthritis and cancers. While this type of anemia maybe microcytic it is more often normocytic, but hypochromatic.

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Macrocytic Anemias

When the patient has been diagnosed as anemic with the MCV elevated, a macrocytic anemia is the diagnosis. This may be due to the results of reticulocytosis (reticulocytes are larger than mature erythrocyte) in, this occurs nutritional deficiencies of iron, B12 or folate deficiency

Reticulocytosis (TIC) - suggests deficiencies in vitamin B12, especially when accompanied with more than 5% of the circulating segmented neutrophils having hypersegmented nuclei. This finding is reported to have greater significance for megaloblastic anemia and elevated MCV.

292

Sideroblastic Anemias

Sideroblastic anemia is a less common anemia but should always be considered when the RBCs are microcytic and hypochromic. Several cells in sideroblastic anemia may be slightly macrocytic but always quite hypochromatic.

It can be inherited, almost always in males, but are more commonly acquired from medications, toxins, or neoplasms.

The anemia developed due to an inability of the developing RBCs to add iron to the heme complex. The RBCs have a ring of iron "surrounding the nucleus" in other terms "ring sideroblasts" like thalassemia, sideroblastic anemia requires reduction in the body's iron stores.

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Anemias

Microcytic	***Normocytic***	***Macrocytic***
Iron deficiency	Hemolysis	Folate deficiency
Thalassemia	Systemic disease	B12 deficiency
Chronic inflammation	Bone marrow failure	Chronic hepatic disease
Lead poisoning	Acute hemorrhage	Hypothyroidism

294

Platelets

Laboratory Range: 150 - 450 x 10E3 /uL **Optimal Range: 170 - 300**
WR range – <100 or > 500

The formation and breakdown of clots involve platelets. Platelets are approximately 2-3 µ in diameter; but large forms appear one production is increased. The evaluation of platelets his to aid in evaluation, diagnosis and or followup for bleeding disorders, drug-induced thrombocytopenia, idiopathic thrombocytopenia purpura, intravascular coagulation, leukemia states, chemotherapeutic management of malignant diseases, and petechia.

The production of blood platelets is under the control of thrombopoietin. Platelets have an average survival time of 8-10 days. Circadian rhythms play a major role with the highest platelet count occurring being mid day.

CPT - 85049

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Platelets

INCREASED	***DECREASED***
Arteriosclerosis	Cancer
Cancer	Anemia
Polycythemia	Hepatic dysfunction
Inflammatory arthritis	
BCP	
Pregnancy may slightly increase	

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Platelets

INCREASED	***DECREASED***
Chlorophyll	Sesame seed oil
Essential fatty acids	
Sesame seed oil	

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Cells of the Immune System

White Blood Cells:

- **Phagocytes – Neutrophils (45 – 65%)**
- **Lymphocytes – (25 – 40%)**
- **Monocytes – Macrophages (3 – 7%)**
- **Eosinophils – (1 – 3%)**
- **Basophils - (<1%)**

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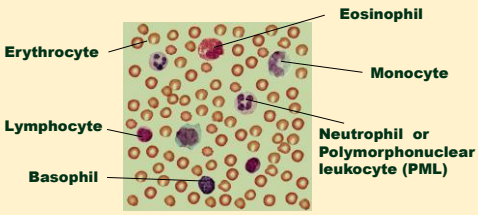
The Cells of the Immune System



299

Neutrophils (segs)

Laboratory Range: 40 - 74% of total WBC **Optimal Range: 45 - 65%**
WR range – <20% or > 80%

Primary function of the neutrophils is phagocytosis. It is the body's first line of defense.

As a general rule, an increased neutrophil percentage is a result of an active viral or bacterial infection.

As a general rule, a decreased neutrophil percentage is a result of a chronic viral or bacterial infection.

300

Nonsegmented neutrophils (Bands)

Laboratory Range: 0 - 2% of total WBC **Optimal Range: <2%**
WR range – > 7% of total WBC

Nonsegmented neutrophils (metamyelocytes) are immature neutrophils. They are increased with acute infections; they may be increased without affecting total WBC, there are just more of them in response to the infection.

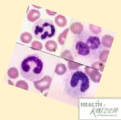
A metamyelocyte is a cell undergoing granulopoiesis, derived from a myelocyte, and leading to a band cell. It is characterized by the appearance of a bent nucleus, cytoplasmic granules, and the absence of visible nucleoli. Increase in the bands constitutes a shift to the left.

When the band cells are increased, additional thymus gland extract, IAG, and vitamin C should be used. Minimum consideration would be 3 – 4 weeks.

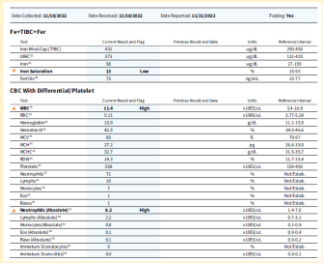
301

Neutrophils or polymorphonuclear leukocytes

Ideally 45 - 65% of WBCs
Recruited to sites of inflammation
'Patrol tissues' as they 'squeeze' out of the capillaries.
Large numbers are released during infections
Short lived – die after digesting bacteria (phagocytising and lysis)
Dead neutrophils make up a large proportion of "puss".



302



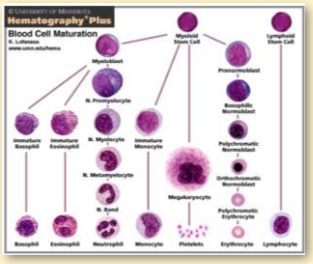
Fe+TIBC+Fer

Test	Current Result and Flag		Previous Result and Date	Units	Reference Interval
Iron Binding Capacity (TIBC)	431			ug/dL	250-450
UIBC	372			ug/dL	155-355
Iron	59			ug/dL	27-139
Iron Saturation	13	Low		%	15-55
Ferritin	53			ng/mL	10-232

CBC With Differential/Platelet

Test	Current Result and Flag		Previous Result and Date	Units	Reference Interval
WBC	11.4	High		x10E3/uL	3.4-10.8
RBC	5.11			x10E6/uL	3.77-5.28
Hemoglobin	15.9			g/dL	11.1-15.9
Hematocrit	46.5			%	34.0-46.6
MCV	91			fL	79-97
MCH	31.2			pg	26.6-33.0
MCHC	34.2			g/dL	31.5-35.7
RDW	14.5			%	11.7-15.4
Platelets	338			x10E3/uL	150-450
Neutrophils	72			%	Not Estab.
Lymphs	19			%	Not Estab.
Monocytes	7			%	Not Estab.
Eos	1			%	Not Estab.
Basos	1			%	Not Estab.
Neutrophils (Absolute)	8.2	High		x10E3/uL	1.4-7.0
Lymphs (Absolute)	2.2			x10E3/uL	0.7-3.1
Monocytes(Absolute)	0.8			x10E3/uL	0.1-0.9
Eos (Absolute)	0.1			x10E3/uL	0.0-0.4
Baso (Absolute)	0.1			x10E3/uL	0.0-0.2
Immature Granulocytes	0			%	Not Estab.
Immature Grans (Abs)	0.0			x10E3/uL	0.0-0.1

303



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Lymphocytes

Laboratory Range: 14 - 46% of total WBC **Optimal Range: 25 - 40%**
WR range – <15% or >70% of total WBC count.

Lymphocytes help to destroy the toxic byproducts of protein metabolism.

As a general rule, the lymphocyte percentage is increased in chronic viral and bacterial infections.

As a general rule, the lymphocyte percentage is decreased in active viral and bacterial infections. Often the lymphocytes will increase to level equal to or exceeding the neutrophil level.

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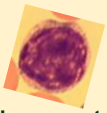
Lymphocytes



- **Produce antibodies**
- **B-cells develop mature in bone marrow then concentrate in lymph nodes and spleen**
- **T-cells mature in thymus**
- **B and T cells mature then circulate in the blood and lymph**
- **Circulation ensures they come in contact with pathogens and each other**

306

Monocytes

Laboratory Range: 4 - 13% of total WBC **Optimal Range: 3 - 7%**
WR range – > 15%

Monocytes become phagocytes once the leave the vascular system to become Macrophages. They phagocytize bacteria, particulate matter and protozoa.

In general the monocyte percentage is increased with recovery from infection, with chronic infection, with prostate hypertrophy and with ovarian or uterine dysfunction.

Always rule out liver dysfunction with an increase monocyte percentage. Increased monocytes indicate excessive tissue breakdown.

An increase in the monocytes with an increase in the basophils, above 1.0, and even a mild increase in eosinophils, above 3.0 is reason to suspect intestinal parasites.

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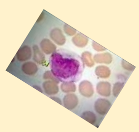
Monocytes



- **Larger than neutrophils.**
- **5 – 7 % of WBC's**
- **Found in the organs.**
- **Made in bone marrow, called macrophages once they reach organs.**
- **Long lived.**
- **Initiate immune responses as they display antigens from the pathogens to the lymphocytes.**

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npj | Aging and Mechanisms of Disease

REVIEW ARTICLE OPEN

Macrophages in age-related chronic inflammatory diseases

"Chronic inflammation is the common pathological basis for such age-associated diseases as cardiovascular disease, diabetes, cancer and Alzheimer's disease."

"Monocyte/macrophage lineage cells are crucial to these age-associated changes, which culminate in the development of chronic inflammatory diseases. In this review, <u>we will summarize the diverse physiological and pathological roles of macrophages in the chronic inflammation underlying age associated diseases."</u>

npj Aging and Mechanisms of Disease (2016) 2, 16018; doi:10.1038/npjamd.2016.18;

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NASHVILLE CHEST 2022 OCTOBER 16-19

Critical Care

ELEVATED CIRCULATING MONOCYTES AND MONOCYTE ACTIVATION IN PULMONARY POSTACUTE SEQUELAE OF SARS-CoV-2 INFECTION

CONCLUSIONS: This study present evidence that patients with COVID infection exhibit persistent alterations in monocytes even after the acute COVID infection period. Correlation of D-dimer level with CD169+ non-classical monocytes in patients with PPASC provides a further rational for determining if a specific monocyte subset contributes to the pathogenesis of PPASC.

CLINICAL IMPLICATIONS: Further studies are required for understanding of the development and progression of PPASC.

DISCLOSURES

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Atherosclerosis

Cardiovascular risk in ANCA-associated vasculitis: Monocyte phenotyping reveals distinctive signatures between serological subsets

Results: **Monocyte subset analysis showed increased classical monocytes during active disease, whereas non-classical monocytes were decreased compared to healthy controls (HC).**

Conclusions: **These findings highlight changes in monocyte subset composition and activation, but not in the intrinsic migration capacity of AAV monocytes. MPO-AAV monocytes are associated with sustained upregulation of inflammatory genes, whereas PR3-AAV monocytes exhibit chemokine receptor upregulation. These molecular changes may play a role in elevating cardiovascular risk as well as in the underlying pathophysiology of AAV.**

Vegting Y, Hanford KM, Jongejan A, Gajadin GR, Versloot M, van der Bom-Baylon ND, Dekker T, Penne EL, van der Heijden JW, Houben E, Bemelman FJ, Neele AE, Moerland PD, Vogt L, Kroon J, Hilhorst ML. Cardiovascular risk in ANCA-associated vasculitis: Monocyte phenotyping reveals distinctive signatures between serological subsets. Atherosclerosis. 2024 Aug 10;397:118559. doi: 10.1016/j.atherosclerosis.2024.118559. Epub ahead of print. PMID: 39186910.

311

Eosinophils

Laboratory Range: 0 - 7% of total WBC **Optimal Range: 1 - 3%**
WR range – > 10%*

Eosinophils are believed to have many functions once successfully in the body's bloodstream. These functions include the ability to fight off parasites, viruses, and bacteria. They can also kill off cells that happen to be aiding in allergic reactions, or forge inflammatory body responses and also mending already inflamed areas. They therefore play an important role in detoxification and the breakdown and removal of foreign proteins. They will be elevated in IgE mediated allergies and when there are intestinal parasites present.

- **Intestinal parasites**
- **Food and environmental allergy/sensitivity**

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Eosinophils

Increased eosinophil percentage may also be seen with:

- ✓**Asthma**
- ✓**Chronic obstructive pulmonary disease**
- ✓**Emphysema**

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Eosinophils

- ✓**1 – 3% of WBC's**
- ✓**Can ingest (phagocytize) bacteria and other foreign cells**
- ✓**Less active against bacteria than neutrophils**
- ✓**Their main function may to help immobilize and kill parasites**
- ✓**Participate in allergic reactions**
- ✓**Contribute to many of the pathologic processes in allergies**

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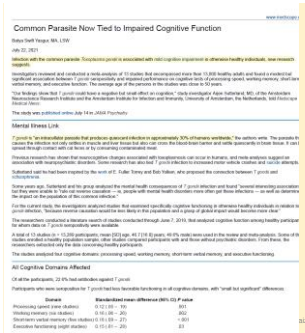

Common Parasite Now Tied to Impaired Cognitive Function

Infection with the common parasite *Toxoplasma gondii* is associated with mild cognitive impairment in otherwise healthy individuals, new research suggests.

Mental Illness Link

All Cognitive Domains Affected

Infection with the common parasite *Toxoplasma gondii* is associated with mild cognitive impairment in otherwise healthy individuals, new research suggests.

***T gondii* is "an intracellular parasite that produces quiescent infection in approximately 30% of humans worldwide,"**

315

Basophils

Laboratory Range: 0 - 3% of total WBC **Optimal Range: <1%**
WR range – > 3% of total WBC count.

Basophils contain heparin, a blood-thinning substance and bring it to inflamed tissue to prevent clotting.

In addition to fighting parasitic infections, basophils play a role in mitigating allergic reactions: In allergic reactions, the immune system is exposed to an allergen. Basophils release histamine during allergic reactions. Basophils are also thought to play a role in causing the body to produce the antibody called immunoglobulin E (IgE). This antibody then binds to basophils and a similar type of cell called mast cells. These cells release substances such as histamines and serotonin. They mediate the inflammatory response in the area of your body that was exposed to the allergen.

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Basophils

<1% of WBC's
Do not ingest foreign material
Bone marrow derived granulocyte that release histamine
Structurally and functionally similar to mast cells produce a substance that attracts neutrophils and eosinophils
Recruited into sites where an antigen is present and may contribute to immediate hypersensitivity responses

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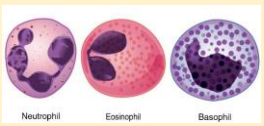
Immature Granulocytes

Immature granulocytes are immature white blood cells. The presence of immature granulocytes in blood test results usually means that the body is fighting an infection or inflammation. When the immune system must fight an infection or inflammation it increases the production of white blood cells in the bone marrow and immature white blood cells are released into the blood. When this occurs blood test results will show increased immature granulocyte count (IG count).



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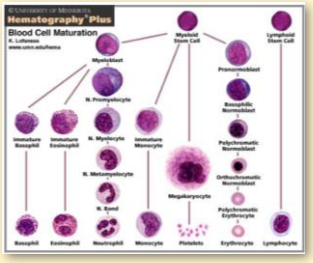

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BRIEF REPORT: ESOPHAGUS

Clinical Characteristics, Endoscopic Findings, and Treatment Outcomes in Lymphocytic Esophagitis Compared to Eosinophilic Esophagitis

Shaggi, Pierfrancesco[1,2]; Savarino, Eleonora[3]; Del Corso, Giulia[3]; Hardy, Rashmi[4]; Ghisa, Matteo[1,2]; Dunn, Jason M[5]; Marciano, Emanuele[1]; Wong, Terry[1]; Green, Michael[6]; de Bortoli, Nicola[7,8]; Zeki, Sebastian[9,4]

Author Information

The American Journal of Gastroenterology (10.14309/ajg.0000000000003046, August 20, 2024) | DOI: 10.14309/ajg.0000000000003046

Abstract

Introduction:

Lymphocytic and eosinophilic esophagitis (LyE and EoE) are immune-mediated esophageal diseases. Clinical characteristics, endoscopic findings, and treatment outcomes of LyE were compared to EoE.

Methods:

This was an international retrospective study on adults enrolled at three centres in Europe. We recorded clinical characteristics and endoscopy findings at baseline, and symptoms, histology, and endoscopy outcomes following treatment of LyE and EoE patients.

Results:

Demographics, clinical presentation, comorbidities, and endoscopy findings were largely different in 35 LyE compared to 59 EoE. Proton pump inhibitors (PPIs) response was generally lower in LyE.

Discussion:

LyE is clinically different from EoE, but differences in treatment response need further investigation.

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WHAT ARE OPPORTUNISTIC INFECTIONS – *STEALTH INFECTIONS*?

- **The human body carries many "germs" — bacteria, protozoa, fungi, mycoplasma, parasites and viruses. When the immune system is FUNCTIONING OPTIMALLY, it controls these organisms.**
- **However, when the immune system is weakened or out of balance, these organisms can get out of control and cause major health problems.**
- **Infections that take advantage of weakness in the immune defenses are called "opportunistic." The phrase "opportunistic infection" is often shortened to "OI."**
- **They modify Epigenetic Expression!!!!!!!**

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Microbiome - Stealth Infections

What are they?

- Viruses
- Bacteria
- Parasites
- Protozoa
- Fungi
- Mycoplasma

These infections Modify the Immune System causing inflammation, affecting the:

- Brain
- Joints
- Hormones
- Pain
- Virtually anything

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Microbiome - Stealth Infections

Where do these infections live?

- Wherever it is wet and warm
- Liver
- Kidney
- Gums
- Brain

- ✓ **Our job is to find them and create an environment that lets the body heal itself!**
- ✓ **Optimize pH- acidic pH depletes O2, virus, bacteria, mycoplasma, bacteria thrive in O2 depleted conditions**
- ✓ **Optimize blood sugar regulation**
- ✓ **Optimize the Microbiome**

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How to identify and treat Stealth Infections

- Use history and physical findings to determine more precise treatment plan: cold sores, warts, history of mono, recurring yeast infections, etc.
- For example using a CBC with differential
  - Total WBC under 5.0- means chronic infection
  - Total WBC greater than 8 – could be acute infection
  - Lymphocytes closer to Neutrophils suggest viral component

Monocytes over 7* suggest Microbiome Imbalances

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How to "assess " Stealth Infections

Polys	55 – 65	40 – 74	Also known as neutrophils, it makes up the majority of the white blood cells. It is the body's first line of defense.
Lymphocytes	25 – 40	14 – 46	The second most abundant white blood cell. They are aggressively antiviral. They manufacture globulins which react with antigens.
Monocytes	3 – 7	4 – 13	Derived from stem cells in the bone marrow. They are primarily phagocytic working outside the blood vessels.
Eosinophils	0 – 3	0 – 7	These white blood cells are elevated in IgE mediated allergies and when there are parasites present.
Basophils	<1	0 – 3	These white blood cells are elevated with toxic allergic reactions.
Sedimentation Rate (ESR)	0 – 8	0 – 30	This test is particularly important in chronic inflammatory disease. It measures how quickly red blood cells settle or coagulate.

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How to Treat Stealth Infections

Bacteria - Concomitantly addressing pH, adrenals, and digestion

- Caprin (4 – 6 tid)
- ADP (3 – 4 tid)
- NAC (N-Acetyl-L-Cysteine) (1 tid for 1 week, then 1 bid)
- Butyric-Cal-Mag
- Food-Grade Diatomaceous Earth (1/2 – 1 tsp bid) ????
- Additional considerations:
  - ✓ Bio-Immunozyme
  - ✓ Cytozyme THY
  - ✓ IAG

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How to Treat Stealth Infections

Virus - Concomitantly addressing pH, adrenals, and digestion. Generally, after bacteria, get the Low-Hanging Fruit.

- ADP (3 – 4 tid)
- UltraVir-X (1 – 2 tid)
- NAC (N-Acetyl-L-Cysteine) (1 tid for 1 week, then 1 bid)
- Food-Grade Diatomaceous Earth (1/2 – 1 tsp bid)
- Additional Considerations:
  - ✓ L-Lysine
  - ✓ Bio-Immunozyme
  - ✓ Cytozyme THY
  - ✓ IAG

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How to Treat Stealth Infections

Fungal Infections - Concomitantly addressing pH, adrenals, and digestion. Generally, after bacteria and virus; get the Low-Hanging Fruit first. Unless----

- Caprin (4 – 6 tid)
- ADP (3 – 4 tid)
- FC-Cidal (1 – 3 tabs tid)
- NAC (N-Acetyl-L-Cysteine) (1 tid for 1 week, then 1 bid)
- Food-Grade Diatomaceous Earth (1/2 – 1 tsp bid) ????
- Additional considerations:
  - ✓ Bio-Immunozyme
  - ✓ Cytozyme THY
  - ✓ IAG

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How to Treat Stealth Infections

Parasites - Concomitantly addressing pH, adrenals, and digestion. Generally, after bacteria and virus; get the Low-Hanging Fruit first.

- Dysbiocide (2 – 3 bid, 10 days on, 5 days off)
- ADP (2 – 3 tid)
- Food-Grade Diatomaceous Earth (1/2 – 1 tsp bid)
- NAC (N-Acetyl-L-Cysteine) (1 tid for 1 week, then 1 bid)
- Additional considerations:
  - ✓ Bio-Immunozyme
  - ✓ Cytozyme THY
  - ✓ IAG

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Nutrients that support the Innate Immune System

- **Bio-Immunozyme forte**
  - **Vitamin A, Zinc, Magnesium, Selenium, B-Vitamins, Vitamin E, Vitamin C**
- **Cyto-Zyme THY (Thymus)**
- **Bio DK Mulsion**
- **Bio-Mega 1000 (Fish oil)**
- **NAC**
- **Adult or Children ENT Pro**
- **IAG**

331

Erythrocyte sedimentation rate (ESR)

Reference Interval (Range): Male 0 – 30 Female 0 – 40 **Optimum Range: 0 - 8**
WR Range – > 50 mm/hr.

Erythrocyte sedimentation rate, also referred to as SED rate is related to C reactive protein, it is not specific for any particular disease pathology rather it is indicative of nonspecific activity of infections, inflammatory states, autoimmune disorders and plasma cell dyscrasias. Fibrinogen increased and the ESR and albumin will decrease the ESR. Since albumin is synthesized in the liver, hepatic damage will result in an increased ESR with a decrease in albumin.

Increase values for sedimentation rate are associated with tissue inflammation and destruction.

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Vitamin D, 25-Hydroxy

Laboratory Range: 30 – 100 ng/mL **Optimal Range: 75 - 110**
WR range - NA

Clinical Discussion:
What can I add?

If elevated look at:
- **Calcium**
- **Magnesium**
- **PTH**

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Vitamin D and the Thyroid: A Critical Review of the Current Evidence

Abstract: Vitamin D is necessary for the normal functioning of many organs, including the thyroid gland. It is, therefore, not surprising that vitamin D deficiency is considered a risk factor for the development of many thyroid disorders, including autoimmune thyroid diseases and thyroid cancer.

In conclusion, additional studies with larger numbers of participants are needed to fully understand the effect of vitamin D on thyroid function.

Babi´c Leko, M.; Jureško, I.; Rozi´c, I.; Plei´c, N.; Gunja´ca, I.; Zemunik, T. Vitamin D and the Thyroid: A Critical Review of the Current Evidence. Int. J. Mol. Sci. 2023, 24, 3586. https://doi.org/10.3390/ijms24043586

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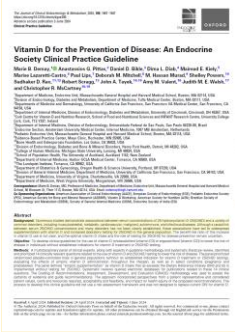

Vitamin D for the Prevention of Disease: An Endocrine Society Clinical Practice Guideline

Background: Numerous studies demonstrate associations between serum concentrations of 25-hydroxyvitamin D (25[OH]D) and a variety of common disorders, including musculoskeletal, metabolic, cardiovascular, malignant, autoimmune, and infectious diseases. Although a causal link between serum 25(OH)D concentrations and many disorders has not been clearly established, these associations have led to widespread supplementation with vitamin D and increased laboratory testing for 25(OH)D in the general population.

Marie B Demay, Anastassios G Pittas, Daniel D Bikle, Dima L Diab, Mairead E Kiely, Marise Lazaretti-Castro, Paul Lips, Deborah M Mitchell, M Hassan Murad, Shelley Powers, Sudhaker D Rao, Robert Scragg, John A Tayek, Amy M Valent, Judith M E Walsh, Christopher R McCartney, Vitamin D for the Prevention of Disease: An Endocrine Society Clinical Practice Guideline, *The Journal of Clinical Endocrinology & Metabolism*, Volume 109, Issue 8, August 2024, Pages 1907–1947, https://doi.org/10.1210/clinem/dgae290

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Conclusion: The panel suggests empiric vitamin D for those aged 1 to 18 years and adults over 75 years of age, those who are pregnant, and those with high-risk prediabetes. Due to the scarcity of natural food sources rich in vitamin D, empiric supplementation can be achieved through a combination of fortified foods and supplements that contain vitamin D. Based on the absence of supportive clinical trial evidence, the panel suggests against routine 25(OH)D testing in the absence of established indications. These recommendations are not meant to replace the current DRIs for vitamin D, nor do they apply to people with established indications for vitamin D treatment or 25(OH)D testing. Further research is needed to determine optimal 25(OH)D levels for specific health benefits.

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Anti-inflammatory nutrients

- **Fish oil – BioMega 1000, BioMega 3 Liquid**
- **Gamma Linoleic Acid (GLA) – Optimal EFA's, Black Current Seed oil**
- **Conguated Linoleic Acid (CLA) -CLA**
- **Alpha Linoleic Acid (ALA) -Optimal EFA's**
- **Proteolytic Enzymes- Intenzyme forte**
- **Vitamin D –Bio-DK Muision**
- **Curcumin –KappArest, CurcumRx**
- **Boswellia- KappArest**
- **Rosemary –KappArest**

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I can be reached at – dr.peterson@healthkaizenlife.com

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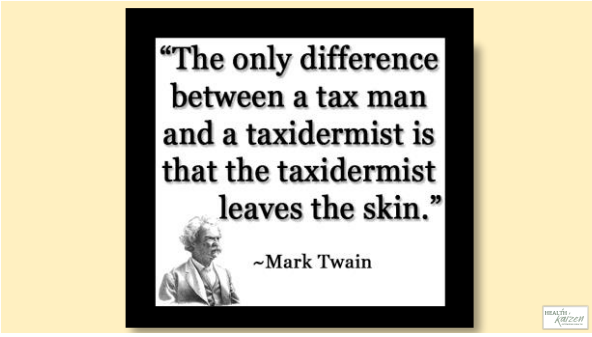
"The only difference between a tax man and a taxidermist is that the taxidermist leaves the skin."
~Mark Twain

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