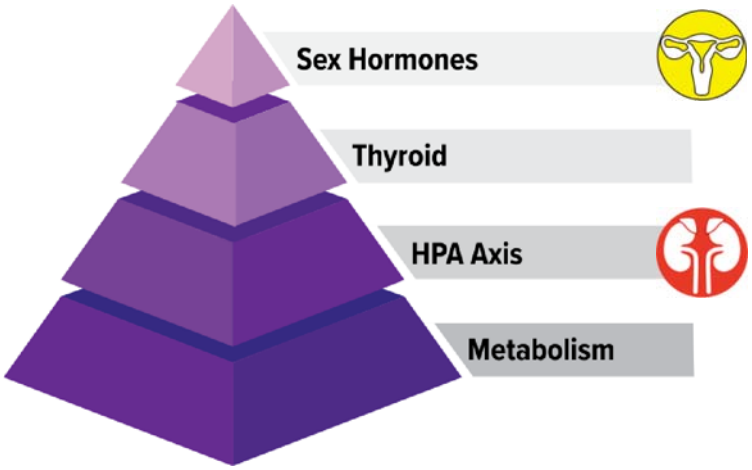
GENOVA DIAGNOSTICS
63 Zillicoa Street
Asheville, NC 28801

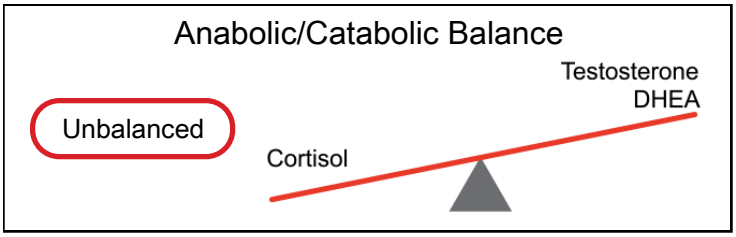
WOMEN'S HEALTH+

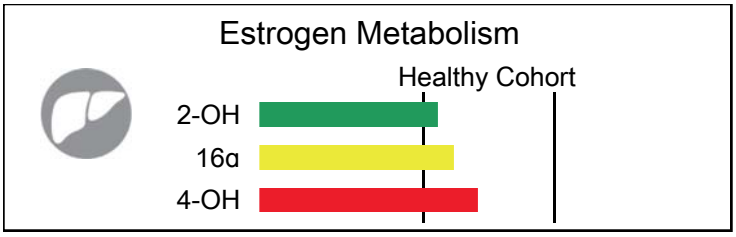
Patient: **SAMPLE PATIENT**
DOB:
Sex:
MRN:

4121 Women's Health+ - Saliva, Urine

Results Overview







Functional Imbalance Scores

Key (< 2) : Low Need for Support | (2-3) : Optional Need for Support | (4-6) : Moderate Need for Support | (7-10) : High Need for Support

Need For HPA Axis Support	Need For Sex Hormone Support	Need For Detoxification Support
HPA AXIS	SEX HORMONES	ESTROGEN METABOLISM
10	4	2
Cortisol Curve ▼	Estradiol ▲	Methylation Activity ▲
DHEA ▽	Testosterone ▼	2-OH-E1/E2 ●
DHEA:Cortisol ▽	Estrone ▽	4-OH-E1/E2 ●
Morning Cortisol ●	Progesterone ●	2/16 Ratio ●

Therapeutic Support Options

• Stress Reduction • Mindfulness Training • HRV Biofeedback • Breathwork Training • Exercise/Yoga/Tai Chi • Herbal Adaptogens • Lower Blood Sugar • B-Vitamins • Phosphoserine • Glandulars	• Address Thyroid Imbalance • Address HPA Axis • Phytoestrogens (for estrogen support) • Phytoandrogens (for testosterone support) • Consider Glandulars • Consider Hormone Precursors • Consider BHRT	• Methylation Support: B-Vitamins, Mg, Betaine • Cruciferous vegetables, berries, rosemary • Soy isoflavones, DIM, I3C • Bioflavanoids, Glutathione • Reduce sugar, stress, environmental toxicity • Reduce adiposity • Physical activity

Nutrient Need Overview

	Nutrient Need (0 1 2 3 4 5 6 7 8 9 10)	DRI	Suggested Recommendations	Provider Recommendations
Antioxidants				
Glutathione				
B-Vitamins				
Thiamin - B1		1.1 mg	25 mg	
Riboflavin - B2		1.1 mg	25 mg	
Niacin - B3		14 mg	20 mg	
Pyridoxine - B6		1.3 mg	50 mg	
Biotin - B7		30 mcg	200 mcg	
Folate - B9		400 mcg	400 mcg	
Cobalamin - B12		2.4 mcg	100 mcg	
Minerals				
Magnesium		320 mg	400 mg	
Manganese		1.8 mg	5.0 mg	
Zinc		8 mg	10 mg	
GI Support				
Digestive Support/Enzymes			5,000 IU	
Microbiome Support/Probiotics			25 billion CFU	

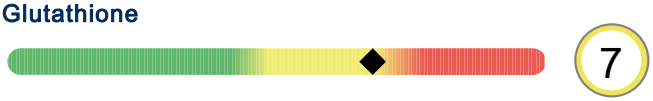
Recommendations for age and gender-specific supplementation are set by comparing levels of nutrient functional need to optimal levels as described in the peer-reviewed literature. They are provided as guidance for short-term support of nutritional deficiencies only.

The Nutrient Need Overview is provided at the request of the ordering practitioner. Any application of it as a therapeutic intervention is to be determined by the ordering practitioner.

Interpretation At-A-Glance

Antioxidant Needs

Glutathione



- Glutathione (GSH) is composed of cysteine, glutamine & glycine. GSH is a source of sulfate and plays a key role in antioxidant activity and detoxification of toxins.
- GSH requirement is increased with high-fat diets, cigarette smoke, cystinuria, chronic alcoholism, chronic acetaminophen use, infection, inflammation and toxic exposure.
- Deficiency may result in oxidative stress & damage, impaired detoxification, altered immunity, macular degeneration and increased risk of chronic illness.
- Food sources of GSH precursors include meats, poultry, fish, soy, corn, nuts, seeds, wheat germ, milk and cheese.

KEY

Function of Nutrient | Cause of Deficiency | Complications of Deficiency | Food Sources of Nutrient

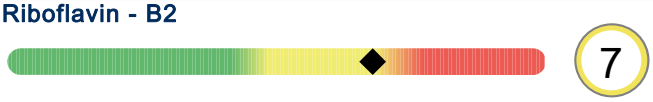
Interpretation At-A-Glance

B-Vitamin Needs

Thiamin - B1

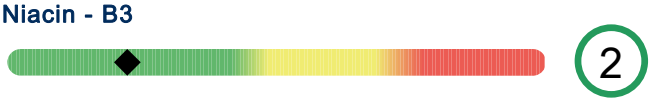
- B1 is a required cofactor for enzymes involved in energy production from food, and for the synthesis of ATP, GTP, DNA, RNA and NADPH.
- Low B1 can result from chronic alcoholism, diuretics, digoxin, oral contraceptives and HRT, or large amounts of tea & coffee (contain anti-B1 factors).
- B1 deficiency may lead to dry beriberi (e.g., neuropathy, muscle weakness), wet beriberi (e.g., cardiac problems, edema), encephalopathy or dementia.
- Food sources include lentils, whole grains, wheat germ, Brazil nuts, peas, organ meats, brewer's yeast, blackstrap molasses, spinach, milk & eggs.

Riboflavin - B2



- B2 is a key component of enzymes involved in antioxidant function, energy production, detoxification, methionine metabolism and vitamin activation.
- Low B2 may result from chronic alcoholism, some anti-psychotic medications, oral contraceptives, tricyclic antidepressants, quinacrine or adriamycin.
- B2 deficiency may result in oxidative stress, mitochondrial dysfunction, low uric acid, low B3 or B6, high homocysteine, anemia or oral & throat inflammation.
- Food sources include milk, cheese, eggs, whole grains, beef, chicken, wheat germ, fish, broccoli, asparagus, spinach, mushrooms and almonds.

Niacin - B3

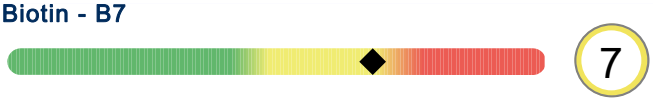


- B3 is used to form NAD and NADP, involved in energy production from food, fatty acid & cholesterol synthesis, cell signaling, DNA repair & cell differentiation.
- Low B3 may result from deficiencies of tryptophan (B3 precursor), B6, B2 or Fe (cofactors in B3 production), or from long-term isoniazid or oral contraceptive use.
- B3 deficiency may result in pellagra (dermatitis, diarrhea, dementia), neurologic symptoms (e.g., depression, memory loss), bright red tongue or fatigue.
- Food sources include poultry, beef, organ meats, fish, whole grains, peanuts, seeds, lentils, brewer's yeast and lima beans.

Pyridoxine - B6

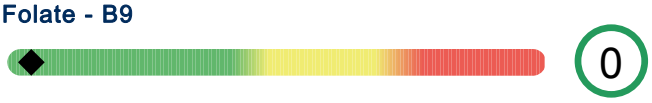
- B6 (as P5P) is a cofactor for enzymes involved in glycogenolysis & gluconeogenesis, and synthesis of neurotransmitters, heme, B3, RBCs and nucleic acids.
- Low B6 may result from chronic alcoholism, long-term diuretics, estrogens (oral contraceptives and HRT), anti-TB meds, penicillamine, L-DOPA or digoxin.
- B6 deficiency may result in neurologic symptoms (e.g., irritability, depression, seizures), oral inflammation, impaired immunity or increased homocysteine.
- Food sources include poultry, beef, beef liver, fish, whole grains, wheat germ, soybean, lentils, nuts & seeds, potato, spinach and carrots.

Biotin - B7



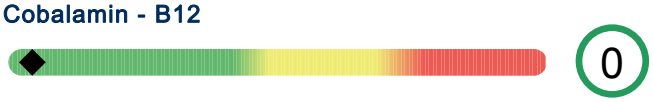
- Biotin is a cofactor for enzymes involved in functions such as fatty acid synthesis, mitochondrial FA oxidation, gluconeogenesis and DNA replication & transcription.
- Deficiency may result from certain inborn errors, chronic intake of raw egg whites, long-term TPN, anticonvulsants, high-dose B5, sulfa drugs & other antibiotics.
- Low levels may result in neurologic symptoms (e.g., paresthesias, depression), hair loss, scaly rash on face or genitals or impaired immunity.
- Food sources include yeast, whole grains, wheat germ, eggs, cheese, liver, meats, fish, wheat, nuts & seeds, avocado, raspberries, sweet potato and cauliflower.

Folate - B9



- Folate plays a key role in coenzymes involved in DNA and SAMe synthesis, methylation, nucleic acids & amino acid metabolism and RBC production.
- Low folate may result from alcoholism, high-dose NSAIDs, diabetic meds, H2 blockers, some diuretics and anti-convulsants, SSRIs, methotrexate, trimethoprim, pyrimethamine, triamterene, sulfasalazine or cholestyramine.
- Folate deficiency can result in anemia, fatigue, low methionine, increased homocysteine, impaired immunity, heart disease, birth defects and CA risk.
- Food sources include fortified grains, green vegetables, beans & legumes.

Cobalamin - B12



- B12 plays important roles in energy production from fats & proteins, methylation, synthesis of hemoglobin & RBCs, and maintenance of nerve cells, DNA & RNA.
- Low B12 may result from alcoholism, malabsorption, hypochlorhydria (e.g., from atrophic gastritis, H. pylori infection, pernicious anemia, H2 blockers, PPIs), vegan diets, diabetic meds, cholestyramine, chloramphenicol, neomycin or colchicine.
- B12 deficiency can lead to anemia, fatigue, neurologic symptoms (e.g., paresthesias, memory loss, depression, dementia), methylation defects or chromosome breaks.
- Food sources include shellfish, red meat, poultry, fish, eggs, milk and cheese.

KEY

Function of Nutrient | Cause of Deficiency | Complications of Deficiency | Food Sources of Nutrient

Interpretation At-A-Glance

Mineral Needs

Magnesium

- Magnesium is involved in >300 metabolic reactions. Key areas include energy production, bone & ATP formation, muscle & nerve conduction and cell signaling.
- Deficiency may occur with malabsorption, alcoholism, hyperparathyroidism, renal disorders (wasting), diabetes, diuretics, digoxin or high doses of zinc.
- Low Mg may result in muscle weakness/spasm, constipation, depression, hypertension, arrhythmias, hypocalcemia, hypokalemia or personality changes.
- Food sources include dark leafy greens, oatmeal, buckwheat, unpolished grains, chocolate, milk, nuts & seeds, lima beans and molasses.

Manganese

- Manganese plays an important role in antioxidant function, gluconeogenesis, the urea cycle, cartilage & bone formation, energy production and digestion.
- Impaired absorption of Mn may occur with excess intake of Fe, Ca, Cu, folic acid, or phosphorous compounds, or use of long-term TPN, Mg-containing antacids or laxatives.
- Deficiency may result in impaired bone/connective tissue growth, glucose & lipid dysregulation, infertility, oxidative stress, inflammation or hyperammonemia.
- Food sources include whole grains, legumes, dried fruits, nuts, dark green leafy vegetables, liver, kidney and tea.

Zinc

- Zinc plays a vital role in immunity, protein metabolism, heme synthesis, growth & development, reproduction, digestion and antioxidant function.
- Low levels may occur with malabsorption, alcoholism, chronic diarrhea, diabetes, excess Cu or Fe, diuretics, ACE inhibitors, H2 blockers or digoxin.
- Deficiency can result in hair loss and skin rashes, also impairments in growth & healing, immunity, sexual function, taste & smell and digestion.
- Food sources include oysters, organ meats, soybean, wheat germ, seeds, nuts, red meat, chicken, herring, milk, yeast, leafy and root vegetables.

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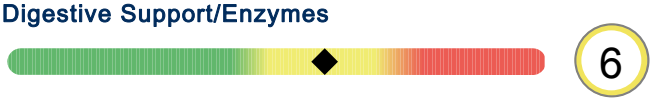
Interpretation At-A-Glance

Microbiome & Digestive Support

Microbiome Support/Probiotics

- Probiotics have many functions. These include: production of some B vitamins and vitamin K; enhance digestion & absorption; decrease severity of diarrheal illness; modulate of immune function & intestinal permeability.
- Alterations of gastrointestinal microflora may result from C-section delivery, antibiotic use, improved sanitation, decreased consumption of fermented foods and use of certain drugs.
- Some of the diseases associated with microflora imbalances include: IBS, IBD, fibromyalgia, chronic fatigue syndrome, obesity, atopic illness, colic and cancer.
- Food sources rich in probiotics are yogurt, kefir and fermented foods.

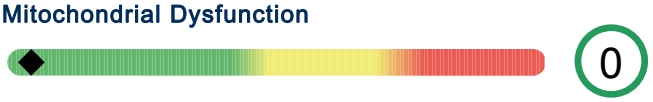
Digestive Support/Enzymes



- Pancreatic enzymes are secreted by the exocrine glands of the pancreas and include protease/peptidase, lipase and amylase.
- Pancreatic exocrine insufficiency may be primary or secondary in nature. Any indication of insufficiency warrants further evaluation for underlying cause (i.e., celiac disease, small intestine villous atrophy, small bowel bacterial overgrowth).
- A high functional need for digestive enzymes suggests that there is an impairment related to digestive capacity.
- Determining the strength of the pancreatic enzyme support depends on the degree of functional impairment. Supplement potency is based on the lipase units present in both prescriptive and non-prescriptive agents.

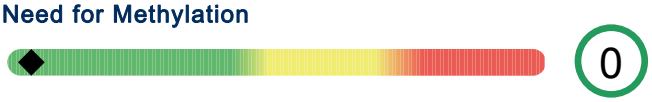
Functional Imbalances

Mitochondrial Dysfunction



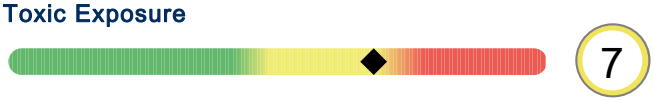
- Mitochondria are a primary site of generation of reactive oxygen species. Oxidative damage is considered an important factor in decline of physiologic function that occurs with aging and stress.
- Mitochondrial defects have been identified in cardiovascular disease, fatigue syndromes, neurologic disorders such as Parkinson's and Alzheimer's disease, as well as a variety of genetic conditions. Common nutritional deficiencies can impair mitochondrial efficiency.

Need for Methylation



- Methylation is an enzymatic process that is critical for both synthesis and inactivation. DNA, estrogen and neurotransmitter metabolism are all dependent on appropriate methylation activity.
- B vitamins and other nutrients (methionine, magnesium, selenium) functionally support catechol-O-methyltransferase (COMT), the enzyme responsible for methylation.

Toxic Exposure



- Methyl tert-Butyl Ether (MTBE) is a common gasoline additive used to increase octane ratings, and has been found to contaminate ground water supplies where gasoline is stored. Inhalation of MTBE may cause nose and throat irritation, as well as headaches, nausea, dizziness and mental confusion. Animal studies suggest that drinking MTBE may cause gastrointestinal irritation, liver and kidney damage and nervous system effects.
- Styrene is classified by the US EPA as a "potential human carcinogen," and is found widely distributed in commercial products such as rubber, plastic, insulation, fiberglass, pipes, food containers and carpet backing.
- Levels of these toxic substances should be examined within the context of the body's functional capacity for methylation and need for glutathione.

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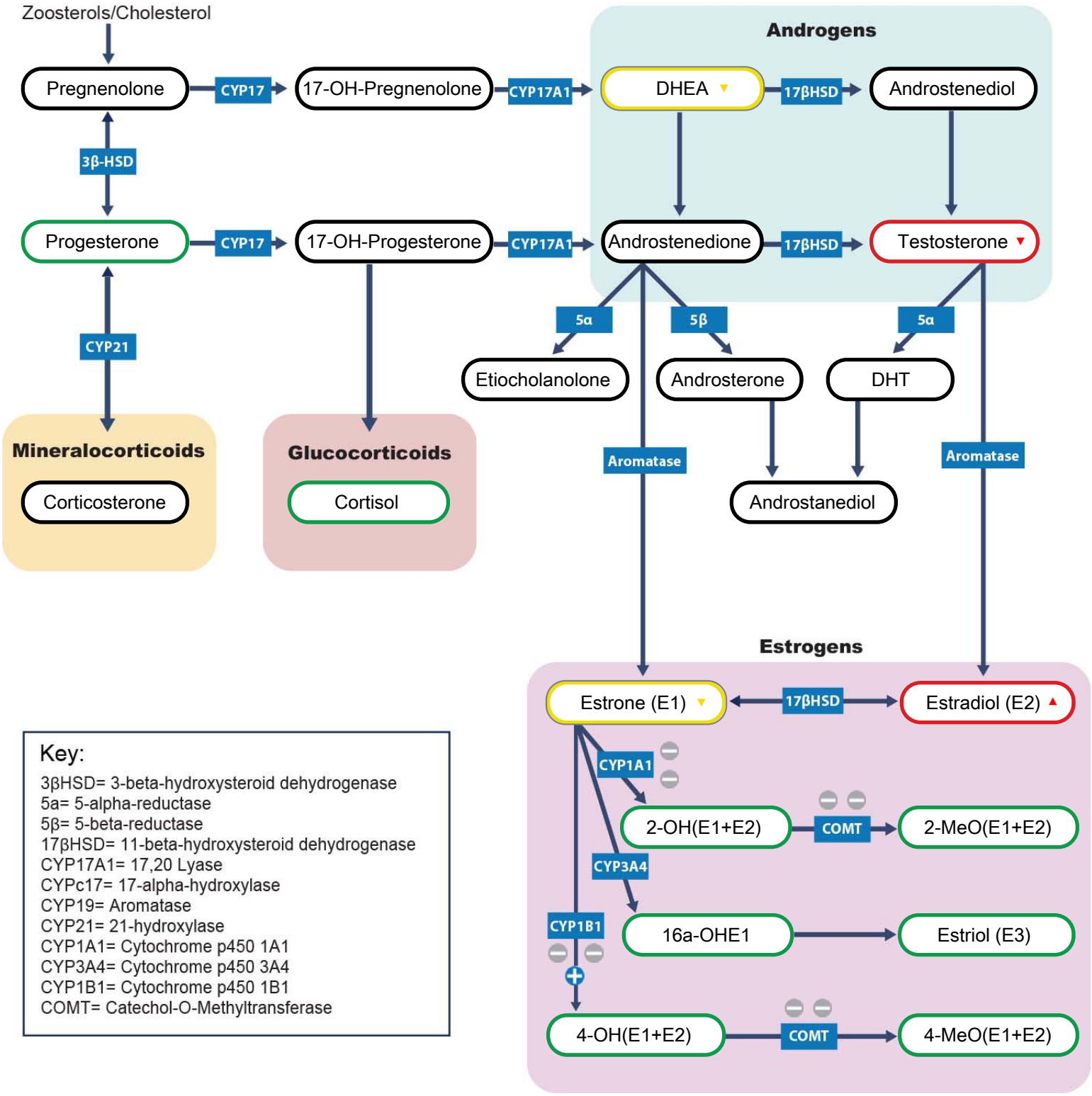
Steroidogenic Pathway



Key:

3βHSD= 3-beta-hydroxysteroid dehydrogenase
5a= 5-alpha-reductase
5β= 5-beta-reductase
17βHSD= 11-beta-hydroxysteroid dehydrogenase
CYP17A1= 17,20 Lyase
CYPc17= 17-alpha-hydroxylase
CYP19= Aromatase
CYP21= 21-hydroxylase
CYP1A1= Cytochrome p450 1A1
CYP3A4= Cytochrome p450 3A4
CYP1B1= Cytochrome p450 1B1
COMT= Catechol-O-Methyltransferase

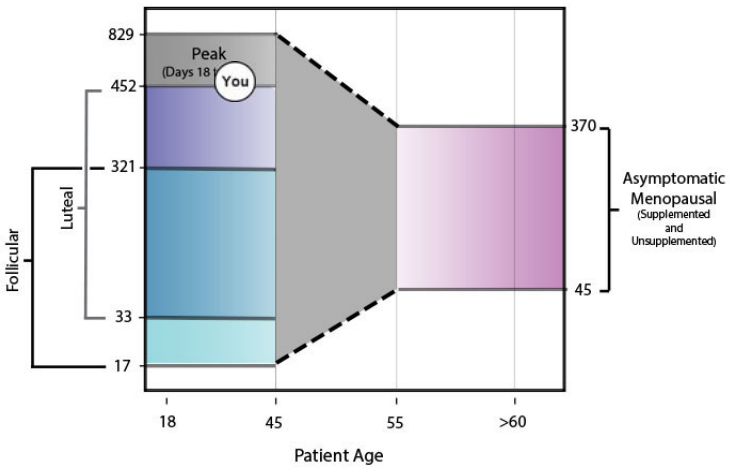
The results shown on pages 1 and 7 default to salivary results. If no salivary results are available, urine results are used.

Methodology: EIA, LIA

Salivary Sex Hormones

Progesterone

Progesterone



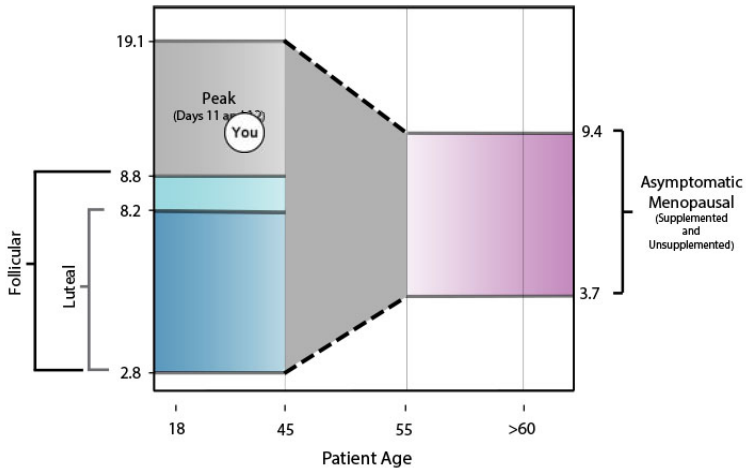
		Reference Range
Progesterone ♦	481	See Chart Below

Androgens

DHEA	85	71-640 pg/mL
Testosterone, Free ♦	<30	34-148 pmol/L

Estrogens

Estradiol (E2)



		Reference Range
Estradiol (E2) ♦	9.5	See Chart Below
Estrone (E1) *	41.5	31.9-183.4 pmol/L
Estriol (E3) *	<70	<= 133 pmol/L

**Reference ranges for Estrone and Estriol are based on menopausal patients.*

Reference Range Information

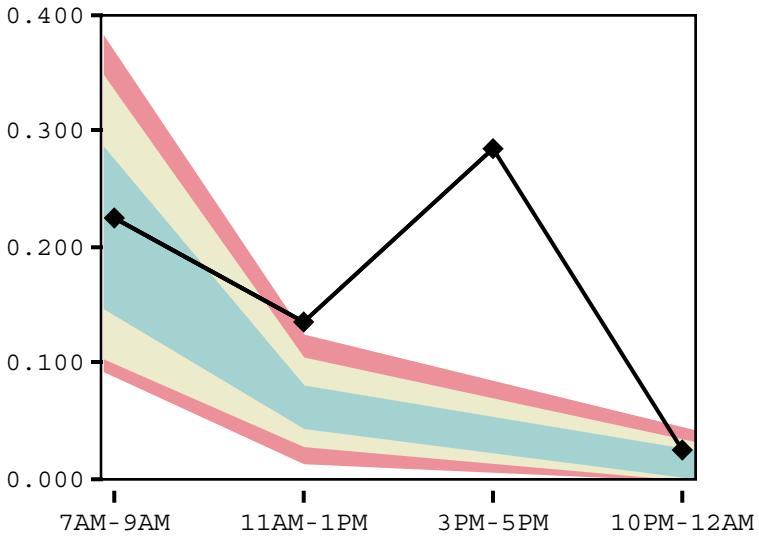
Saliva Analyte	Luteal	Follicular	Menopausal	Male	Patient Result
Estrone (pmol/L)	N/A	N/A	31.9 - 183.4	N/A	41.5
Estradiol (pmol/L)	2.8 - 8.2	2.8 - 8.8	3.7 - 9.4	3.1 - 7.4	9.5
Estriol (pmol/L)	N/A	N/A	<=133	N/A	<70
Progesterone (pmol/L)	33 - 452	17 - 321	45 - 370	31 - 280	481
Testosterone, Free (pmol/L)	34 - 148	34 - 148	34 - 148	110 - 513	<30
DHEA (pg/mL)	71 - 640	71 - 640	71 - 640	71 - 640	85

These reference ranges are based on luteal premenopausal samples. If patient is menopausal, refer to the chart above to determine the appropriate clinical ranges. Each individual is unique and evaluation of hormone status should be within the context of the patient's clinical picture.

Methodology: EIA

HPA Axis

Diurnal Cortisol Curve



Cortisol, Free (Salivary)

		Reference Range
7AM-9AM Cortisol ◆	0.225	0.097-0.337 mcg/dL
11AM-1PM Cortisol ◆	0.135	0.027-0.106 mcg/dL
3PM-5PM Cortisol ◆	0.285	0.013-0.068 mcg/dL
10PM-12AM Cortisol ◆	0.025	<= 0.034 mcg/dL

Androgens

		Reference Range
DHEA	85	71-640 pg/mL
DHEA:Cortisol Ratio	378	358-2,538

Results

Cortisol, Free (Salivary)	Morning Cortisol 7AM-9AM**	Midday Cortisol 11AM-1PM**	Afternoon Cortisol 3PM-5PM**	Evening Cortisol 10PM-12AM**
Patient Result (mcg/dL) >>	**0.225**	**0.135**	**0.285**	**0.025**
Reference Range (mcg/dL) **Based on Collection Times	0.097-0.337	0.027-0.106	0.013-0.068	<=0.034
Actual Collection Time	9:08AM	1:00PM	5:00PM	12:00AM

Methodology: LC/MS/MS

Estrogen Metabolism

Urine Estrogens

		Reference Range
Estrone (E1)	9.2	2.0-26.2 mcg/g Creat.
Estradiol (E2)	2.9	0.6-11.2 mcg/g Creat.
Estriol (E3)	2.2	0.6-19.9 mcg/g Creat.

Phase 1 Estrogen Metabolites

		Reference Range
2-Hydroxyestrone+ 2-Hydroxyestradiol 2-OH(E1+E2)	5.4	1.3-36.3 mcg/g Creat.
16α-Hydroxyestrone 16a-OHE1	2.4	0.5-8.9 mcg/g Creat.
4-Hydroxyestrone+ 4-Hydroxyestradiol 4-OH(E1+E2)	2.4	<= 5.9 mcg/g Creat.

Enzyme Activity

2-OH(E1+E2)/ 16α-OHE1 Ratio	2.3	0.3-13.7
Methylation Activity 2-OH/2-MeO Ratio	0.9 Poorer Methylation	1.6-10.7

Phase 2 Estrogen Metabolites

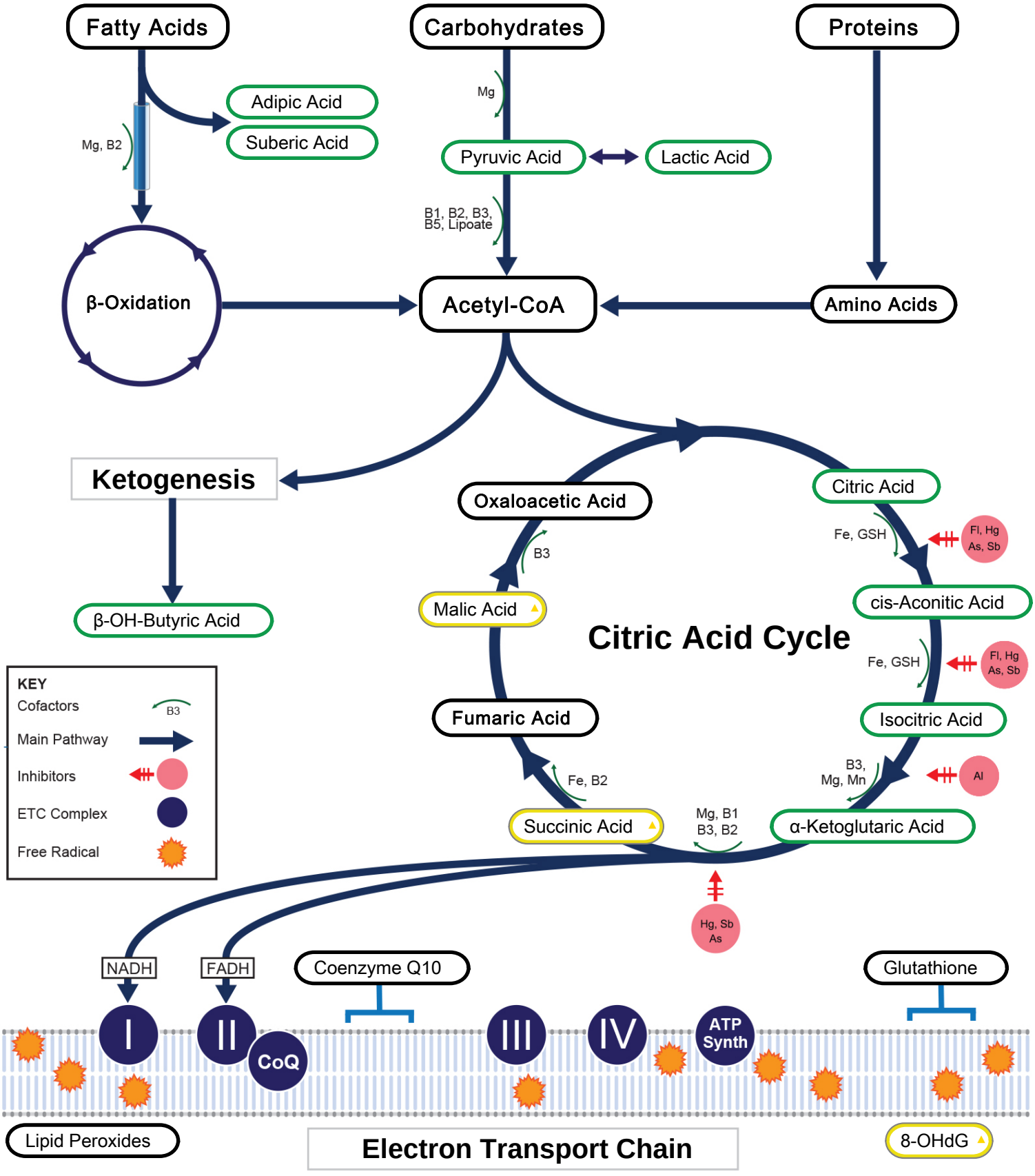
2-Methoxyestrone+ 2-Methoxyestradiol 2-MeO(E1+E2)	6.2	0.2-8.6 mcg/g Creat.
4-Methoxyestrone+ 4-Methoxyestradiol 4-MeO(E1+E2)	<dl	<= 1.0 mcg/g Creat.

Reference Range Information

Urine Analyte	Premenopause Luteal	Menopause	Male	Patient Result
Estrone (mcg/g Creat.)	2.0 - 26.2	1.1 - 26.2	1.6 - 8.6	9.2
Estradiol (mcg/g Creat.)	0.6 - 11.2	0.6 - 15.4	0.8 - 4.3	2.9
Estriol (mcg/g Creat.)	0.6 - 19.9	0.7 - 30.8	0.3 - 5.1	2.2
2-OH(E1+E2) (mcg/g Creat.)	1.3 - 36.3	0.9 - 43.8	0.7 - 12.5	5.4
16a-OHE1 (mcg/g Creat.)	0.5 - 8.9	0.4 - 7.7	<=2.0	2.4
4-OH(E1+E2) (mcg/g Creat.)	<=5.9	<=8.8	<=1.6	2.4
2-MeO(E1+E2) (mcg/g Creat.)	0.2 - 8.6	0.3 - 5.9	0.2 - 2.5	6.2
4-MeO(E1+E2) (mcg/g Creat.)	<=1.0	<=1.0	<=1.0	<dl
2-OH(E1+E2)/16a-OHE1 Ratio	0.3 - 13.7	0.3 - 15.1	0.8 - 12.9	2.3
2-OH/2-MeO Ratio	1.6 - 10.7	0.4 - 11.6	1.0 - 8.8	0.9

These reference ranges are based on luteal premenopausal samples. If patient is menopausal, refer to the chart above to determine the appropriate clinical ranges. Each individual is unique and evaluation of hormone status should be within the context of the patient's clinical picture.

Oxidative Stress & Mitochondrial Dysfunction



All biomarkers reported in mmol/mol creatinine unless otherwise noted.

Organic Acids

Malabsorption & Dysbiosis Markers

Malabsorption Markers

		Reference Range
Indoleacetic Acid	1.9	<= 4.2
Phenylacetic Acid	0.16	<= 0.12

Dysbiosis Markers

		Reference Range
Dihydroxyphenylpropionic Acid (DHPPA)	4.6	<= 5.3
3-Hydroxyphenylacetic Acid	2.8	<= 8.1
4-Hydroxyphenylacetic Acid	12	<= 29
Benzoic Acid	0.07	<= 0.05
Hippuric Acid	719	<= 603

Yeast / Fungal Dysbiosis Markers

		Reference Range
D-Arabinitol	104	<= 36
Citramalic Acid	3.7	<= 5.8
Tartaric Acid	<dl	<= 15

Vitamin Markers

Branched-Chain Catabolites (B1, B2, B3, ALA)

		Reference Range
α-Ketoadipic Acid	0.7	<= 1.7
α-Ketoisovaleric Acid	0.97	<= 0.97
α-Ketoisocaproic Acid	0.64	<= 0.89
α-Keto-β-Methylvaleric Acid	2.0	<= 2.1
Glutaric Acid	0.35	<= 0.51
Isovalerylglycine	3.4	<= 3.7

Methylation Markers (Folate, B12)

		Reference Range
Formiminoglutamic Acid (FIGlu)	0.7	<= 1.5
Methylmalonic Acid	0.8	<= 1.9

Biotin Markers

		Reference Range
3-Hydroxypropionic Acid	11	5-22
3-Hydroxyisovaleric Acid	20	<= 29

Cellular Energy & Mitochondrial Markers

Fatty Acid Metabolism

		Reference Range
Adipic Acid	1.2	<= 2.8
Suberic Acid	0.9	<= 2.1

Carbohydrate Metabolism

		Reference Range
Pyruvic Acid	21	7-32
Lactic Acid	8.9	1.9-19.8
α-Hydroxybutyric Acid	0.45	<= 0.83
β-OH-Butyric Acid	1.5	<= 2.8
β-OH-β-Methylglutaric Acid	7	<= 15

Energy Metabolism

		Reference Range
Citric Acid	216	40-520
cis-Aconitic Acid	19	10-36
Isocitric Acid	50	22-65
α-Ketoglutaric Acid	18	4-52
Succinic Acid	3.9	0.4-4.6
Malic Acid	1.8	<= 3.0

Methodology: GCMS, LC/MS/MS, Alkaline Picrate, Colorimetric

Neurotransmitter Metabolites

Kynurenine Markers (Vitamin B6)

		Reference Range
Kynurenic Acid	4.0	<= 7.1
Quinolinic Acid	9.0	<= 9.1
Kynurenic / Quinolinic Ratio	0.44	>= 0.44
Xanthurenic Acid	1.04	<= 0.96

Catecholamine Markers

		Reference Range
Homovanillic Acid	2.5	1.2-5.3
Vanilmandelic Acid	2.2	0.4-3.6
3-Methyl-4-OH-phenylglycol	0.19	0.02-0.22

Serotonin Markers

		Reference Range
5-OH-indoleacetic Acid	>87.2	3.8-12.1

Toxin & Detoxification Markers

		Reference Range
Pyroglutamic Acid	72	16-34
α-Ketophenylacetic Acid (from Styrene)	0.29	<= 0.46
α-Hydroxyisobutyric Acid (from MTBE)	7.1	<= 6.7
Orotic Acid	0.63	0.33-1.01

Organic Acid Reference Ranges are Age Specific

Methodology: Colorimetric, Alkaline Picrate, GC/MS, LC/MS/MS

Organic Acids

Oxalate Markers

		Reference Range
Glyceric Acid	14.2	3.5-16.4
Glycolic Acid	52	<= 67
Oxalic Acid	14	<= 78

All biomarkers reported in mmol/mol creatinine.

Creatinine Concentration

		Reference Range
Urine Creatinine ◆	4.8	3.1-19.5 mmol/L

Oxidative Stress Markers

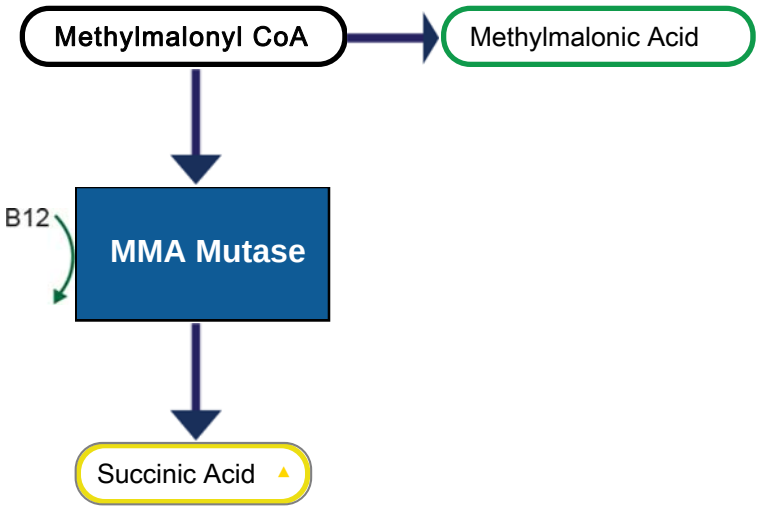
Oxidative Damage

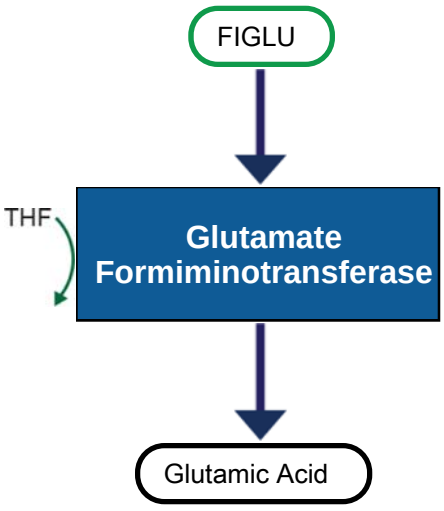
		Reference Range
8-OHdG (urine)	9	<= 15 mcg/g Creat.

The Oxidative Stress reference ranges are based on an adult population.

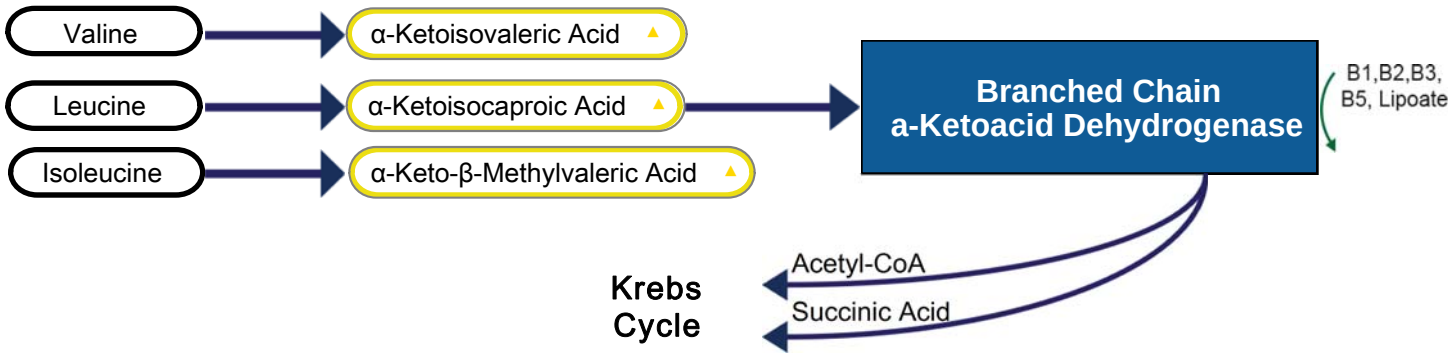
Pathways

Methylation Markers





Branched-Chain Amino Acid Metabolism



Commentary

Lab Comments
Testing Order Comments

:

Corrected result. Previous value was 1, verified by DBENT at 15:24 on 10/24/25.
Testing Result Comments

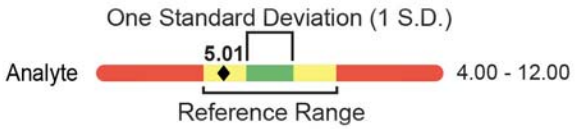
For more information regarding Endo+ clinical interpretation, please refer to the Endo+ Support Guide at **www.gdx.net/hormoneguide**

For more information regarding Organic Acids clinical interpretation, please refer to the Organic Acids Support Guide at **www.gdx.net/nutrevalguide**

The performance characteristics of all assays have been verified by Genova Diagnostics, Inc. Unless otherwise noted with ◆, the assay has not been cleared by the U.S. Food and Drug Administration.

<dl = Less than detection limit; >ul = greater than upper linearity limit; NR = Not Reportable

The **Reference Range** is a statistical interval representing 95% or 2 Standard Deviations (2 S.D.) of the reference range population. One Standard Deviation (1 S.D.) is a statistical interval representing ~68% of the reference population. Values between 1 and 2 S.D. are not necessarily abnormal. Clinical Correlation is suggested.



GENOVA DIAGNOSTICS
63 Zillicoa Street
Asheville, NC 28801

Genomics (Buccal Cells)

Patient: **SAMPLE PATIENT**
DOB:
Sex:
MRN:

Optional Add-on

Methodology: PCR/Sequencing

Apo E

Apolipoprotein E : CHOLESTEROL REGULATION

Apolipoprotein E (Apo E) plays a key role in lipid metabolism by helping to remove dietary cholesterol (chylomicrons and VLDL) from the bloodstream.

Location:
Chromosome 19
APOE
APO E2: cys / cys
APO E3: cys / arg
APO E4: arg / arg
Your Genotype:

2	3

The two SNPs lead to 3 possible variants for each chromosome, known as ApoE2, E3, & E4.

Health Implications

- The E2/E3 genotype is common, accounting for 10-15% of most populations.
- ApoE2 is associated with lower LDL-C and higher HDL-C, but also higher triglycerides (TGs).
- Slightly increased risk of type 2 diabetes and diabetic nephropathy
- ApoE2 is generally associated with lowest risk of atherosclerosis, MI and stroke; however, CAD and MI risk may increased with elevated TGs.
- Tendency toward higher plasma C-reactive protein despite lower CV risk.
- ApoE2 associated with reduced risk of osteoporosis and higher antioxidant activity.
- The APOE-ε2ε3 genotype and the APOE-ε2 allele are associated with serum uric acid levels in Chinese subjects, indicating that individuals carrying the APOE-ε2 allele have a higher risk of hyperuricemia than non-carriers.

Clinical Management Considerations

- The cholesterol-lowering effect of a low saturated fat and low cholesterol diet is least effective with E2 individuals.
- Minimize sugar and high-glycemic index foods, which produce the largest TG response in E2 carriers.
- Fish oils may reduce TGs the most effectively in E2 carriers.
- Alcohol may reduce LDL-C in men (neutral in women), but may increase risk of hemorrhagic stroke in men (at least in Asians).
- Lipid response to statins, and triglyceride response to fibrates, are usually the best in E2 > E3 > E4; studies are mixed.
- Gemfibrozil may help lower TGs and total cholesterol.
- HT appears to improve the lipid profile in this genotype, although oral estrogen may significantly increase TGs.

Key

- \- \- Neither chromosome carries the genetic variation.
- \+ \- One chromosome (of two) carries the genetic variation.
- \+ \+ Both chromosomes carry the genetic variation.

(You inherit one chromosome from each parent)

\+ ↑ Gene activity increased
\+ ↓ Gene activity decreased

CYP1B1	Cytochrome p450 1B1 : DETOXIFICATION
Location: Chromosome 2 **L432V Your Genotype:** **N453S Your Genotype:** 	Cytochrome P450 1B1 (CYP1B1) is a Phase I detoxification enzyme responsible for the 4-hydroxylation of estrogen as well as the activation of common environmental toxins such as polycyclic aromatic hydrocarbons (PAHs), polychlorinated biphenyls (PCBs), and aflatoxin B1. **Health Implications** · Hyper-induction of CYP1B1 upon exposure to its substrates or inducers · Increased production of 4-hydroxyestrogens and potentially carcinogenic compounds · Majority of studies have examined the L432V SNP, rather than the N453S SNP; as both SNPs are associated with increased enzyme activity, similar clinical associations may exist (but have not been confirmed) · L432V SNP linked to possible increased risk of breast cancer, especially in women smokers, those exposed to waste incinerator or agricultural pollutants, and women on HT for 4 years or longer (studies are mixed) · L432V SNP linked to possible increased risk of cancer of the ovary, uterus, prostate, or lung (studies are mixed) **Clinical Management Considerations** · Minimize exposure to xenobiotics (e.g., PAHs) and xenoestrogens (e.g., organochlorines), which increase CYP1B1 activity · Maintain a diet rich in antioxidants (colorful fruits and vegetables); consider supplementation · Consider redirecting estrogen metabolism away from 4-hydroxylation with cruciferous vegetables, and/or agents such as indole 3-carbinol (I3C), diindolylmethane (DIM), fish oils, or rosemary · Caution using long-term estrogen therapy, especially conjugated equine estrogens, which are preferentially 4-hydroxylated · Carcinogen-induced DNA damage may be minimized by agents such as curcumin, black cohosh, genistein, and DHEA

MTHFR	5,10-methyltetrahydrofolate reductase : METHYLATION
Location: Chromosome 1 **C677T** **Your Genotype:** **A1298C** **Your Genotype:** 	5,10-methylenetetrahydrofolate reductase (MTHFR) is a key enzyme in folate metabolism, facilitating the formation of methyltetrahydrofolate, a required cofactor in the remethylation of homocysteine (Hcy) to methionine. **Health Implications** · Heterozygosity for only 1298 (-/+) is associated with baseline "normal" MTHFR enzyme activity, suggesting efficient formation of methyl-THF · Risk of methylation impairment and elevated homocysteine is increased only when C677T polymorphism is also positive **Clinical Management Considerations** · Ensure adequate intake of dark-green leafy vegetables and other B vitamin-rich foods

COMT	Catechol-O-MethylTransferase : METHYLATION
Location: Chromosome 22.11q **V158M** **Your Genotype:**	Catechol-O-Methyltransferase (COMT) is a key enzyme involved in the deactivation of catechol compounds, including catecholamines, catechol estrogens, catechol drugs such as L-DOPA, and catechol metabolites of various chemicals and toxins, such as aryl hydrocarbons.

Health Implications

- Normal COMT enzyme activity, resulting in efficient methylation of catecholamines and estrogens
- Less sensitivity to stress, compared to the other genotypes, due to lower baseline catecholamine levels
- Lower baseline brain dopamine is associated with lower cognitive stability (e.g., focus) but greater cognitive flexibility (e.g., ability to adapt to external changes) compared to the other genotypes
- Superior cognitive function possible in Parkinson's disease patients; however, dopaminergic agents may compromise cognition
- Preliminary findings suggest possible decreased risk of cardiovascular events, which might be abolished by taking aspirin
- Possible increased risk of schizophrenia (conflicting studies), symptomology, and inferior cognitive performance in schizophrenics

Clinical Management Considerations

- Ensure adequate B6, B12, folate, magnesium, and methionine for general methylation support
- Cognitive efficiency may be improved by stimulation
- Possibly best methylphenidate (Ritalin®) response in children with ADHD (mixed studies)

CYP1A1	Cytochrome p450 1A1 : DETOXIFICATION
Location: Chromosome 15 ***2A (MSPI) Your Genotype:**	Cytochrome P450 1A1 (CYP1A1) is a Phase I detoxification enzyme found in extrahepatic tissues such as intestine, lung, skin, lymphocytes and placenta. CYP1A1 primarily metabolizes carcinogens such as polycyclic aromatic hydrocarbons (often activating them to carcinogens) but is also responsible for the 2-hydroxylation of estrogen.
***2C (I462V) Your Genotype:**	**Health Implications** · Baseline "normal" CYP1A1 enzyme activity · "Normal" degree of procarcinogen activation upon exposures to substrates **Clinical Management Considerations** · Regardless of CYP1A1 genotype, it is recommended to minimize exposure to CYP1A1 inducers such as polycyclic aromatic hydrocarbons (e.g. cigarette smoke and well-done meats), heterocyclic amines (e.g., fried meat), PCBs (e.g., contaminated fish or waste), and dioxins (e.g., contaminated meats, fish and dairy, chlorine bleaching, PVC plastics, incineration) · Maintain a diet rich in antioxidants (colorful fruits and vegetables)

Lab Comments
Testing Order Comments

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Corrected result. Previous value was 1, verified by DBENT at 15:24 on 10/24/25.
Testing Result Comments

This test has been developed and its performance characteristics determined by Genova Diagnostics, Inc. It has not been cleared by the U.S. Food and Drug Administration.

Commentary is provided to the practitioner for educational purposes, and should not be interpreted as diagnostic or treatment recommendations. Diagnosis and treatment decisions are the responsibility of the practitioner.

The accuracy of genetic testing is not 100%. Results of genetic tests should be taken in the context of clinical representation and familial risk. The prevalence and significance of some allelic variations may be population specific.

Any positive findings in your patient's test indicate genetic predisposition that could affect physiologic function and risk of disease. We do not measure every possible genetic variation. Your patient may have additional risk that is not measured by this test. Negative findings do not imply that your patient is risk-free.

DNA sequencing is used to detect polymorphisms in the patient's DNA sample. The sensitivity and specificity of this assay is <100%.