Functional Medicine Approach to Chronic Diseases: A Review of the Process & Case Study

Tal Cohen, DAOM, MS-HNFM

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Diagnosis with Functional Medicine

- Your Functional Medicine journey starts by thinking about the connection between the different organs or systems of the body and how they interact
- Does this patient have any of the 'trigger' as an immune activation that led to chronic inflammation?
- Review of studies can help you establish these connections: e.g. by searching "Type 2 Diabetes and BPA **NCBI**"
- *(National Center for Biotechnology Information, U.S. National Library of Medicine)*

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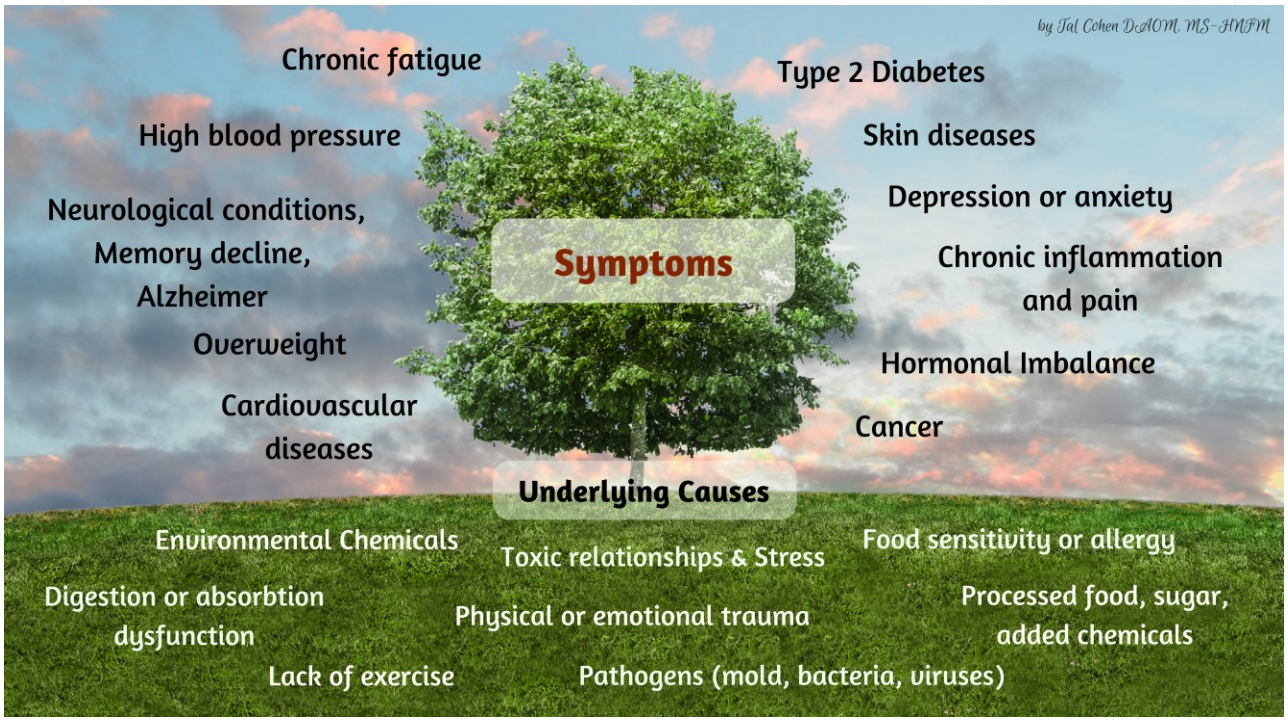
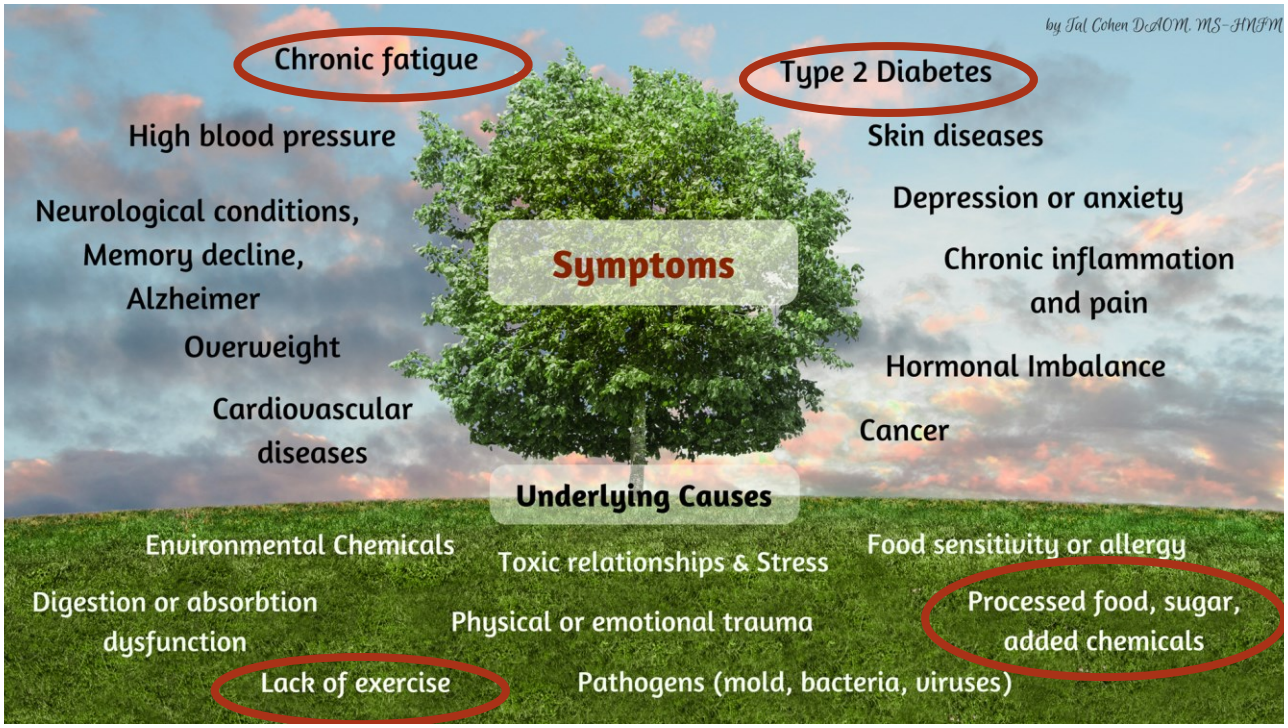

by Tal Cohen DcAOM, MS-HNFM
Chronic fatigue
Type 2 Diabetes
High blood pressure
Skin diseases
Depression or anxiety
Neurological conditions,
Memory decline,
Alzheimer
Symptoms
Chronic inflammation
and pain
Overweight
Hormonal Imbalance
Cardiovascular
diseases
Cancer
Underlying Causes
Environmental Chemicals
Toxic relationships & Stress
Food sensitivity or allergy
Digestion or absorbtion
dysfunction
Physical or emotional trauma
Processed food, sugar,
added chemicals
Lack of exercise
Pathogens (mold, bacteria, viruses)

4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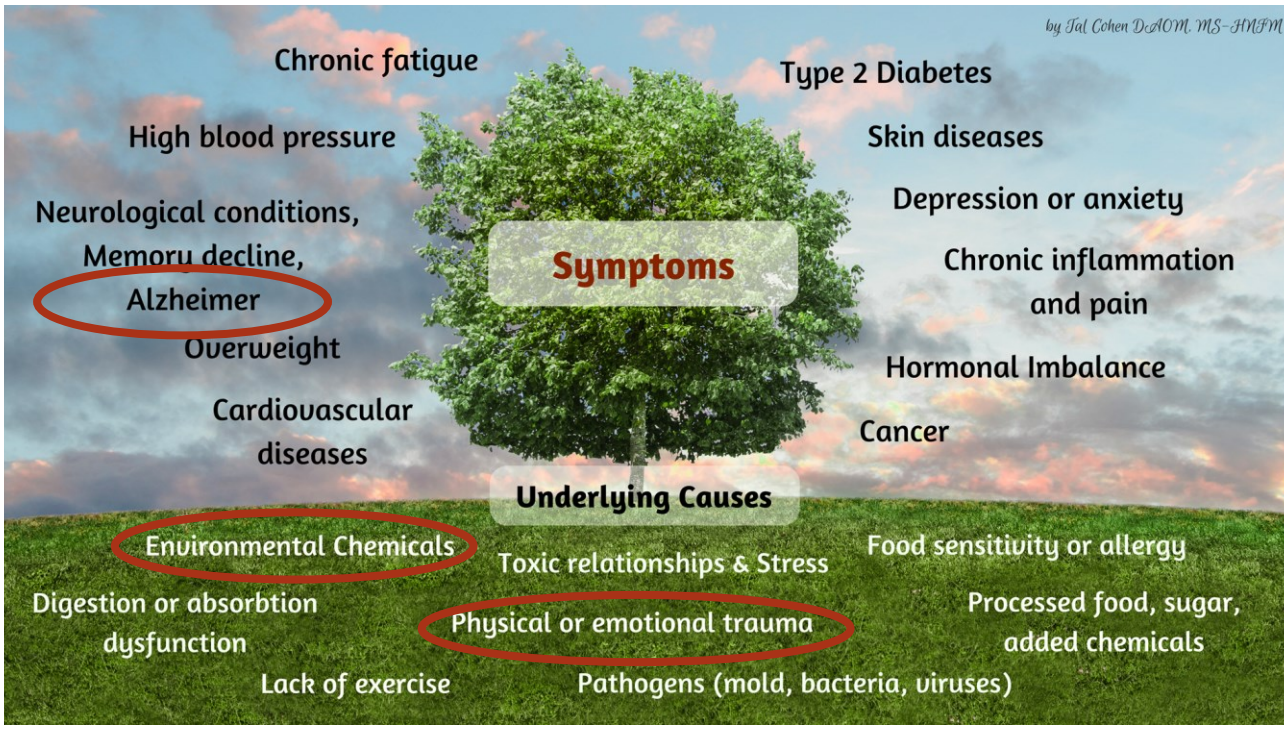
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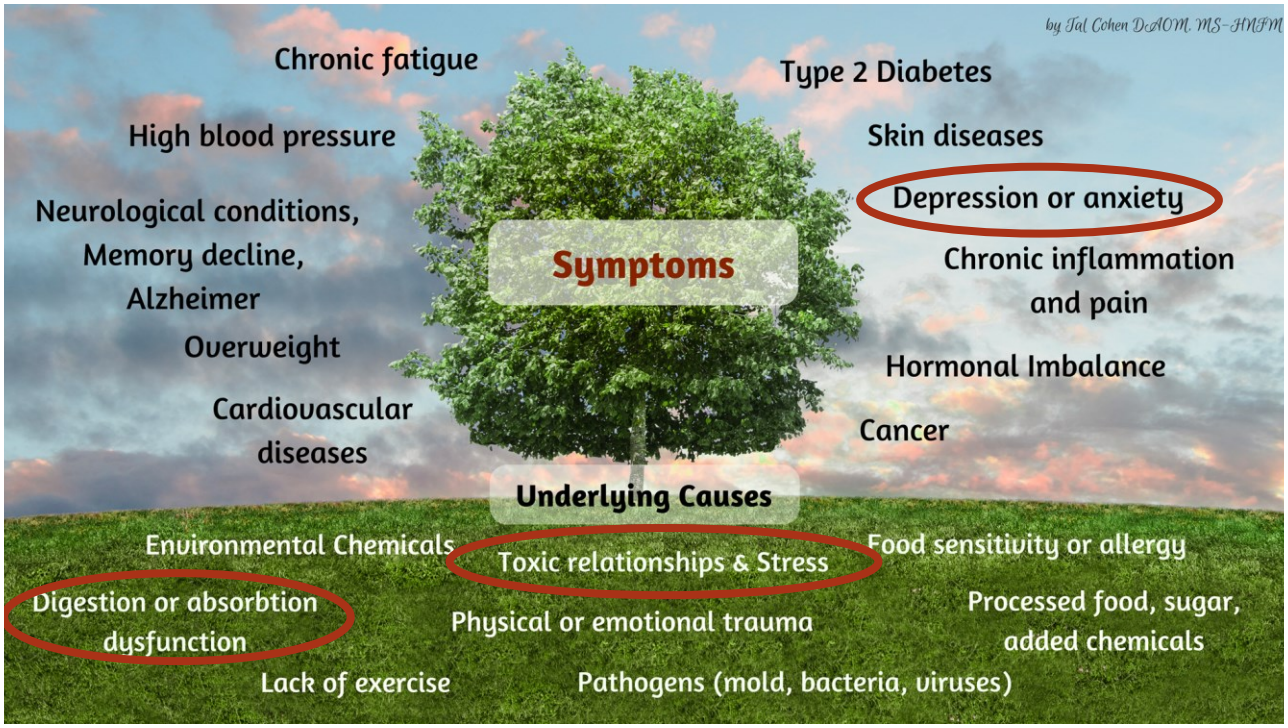
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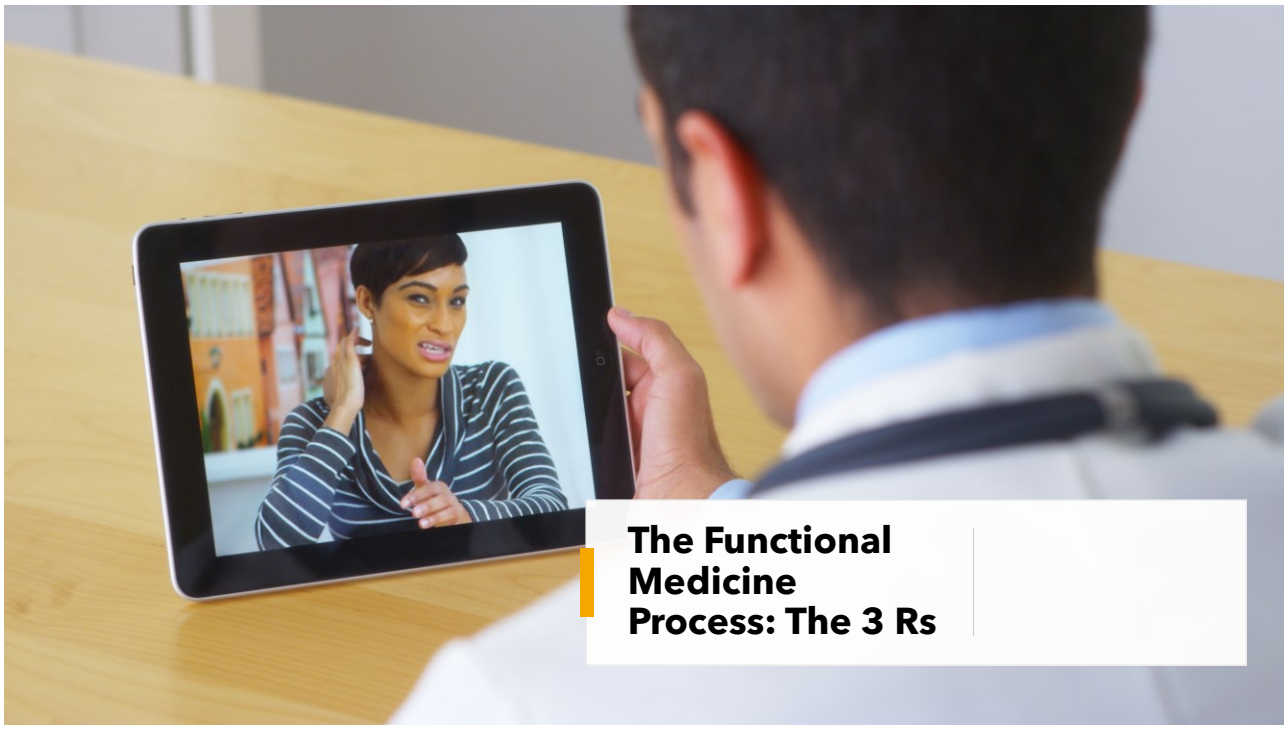

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The Functional Medicine Process: The 3 Rs

- The 3 'R' approach to healing is simple, straightforward, and should be used in the healing of every chronic disease.
- Start by asking your patient about their physical, cognitive, and emotional state that might have led to the development of the dysfunction.
- Remember that dysfunction could start months and years before symptoms are noticed or reported

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The 3 Rs in Patient with Chronic Gut Dysfunction

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The 3 Rs in Patient with Chronic Gut Dysfunction

- **REMOVE:** Eliminate the 'trigger' of disease, e.g. pathogens (bacterial overgrowth, parasite, yeast) or chronic and long term NSAIDs use
- **REPLACE:** Support healthy function in a state of imbalance, e.g. adding HCL or enzymes to support metabolism of food
- **REPAIR:** Stimulate healthy function, e.g. L-glutamine, vitamin C, Aloe-Vera, and Licorice to support healthy gut lining

The 3 Rs in Patient with Chronic Joint Pain

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The 3 Rs in Patient with Chronic Joint Pain

- **REMOVE:** Eliminate the 'trigger' of disease, e.g. Chemical accumulation
- **REPLACE:** Support healthy function in a state of imbalance, e.g. calm immune reaction, inhibit IL-6 and increase IL-10 with Curcumin and Boswellia, and increase Treg with green tea polyphenols
- **REPAIR:** Stimulate elimination of chemicals, e.g. milk thistle, Indole-3-Carbinol, vitamin C, and NAC to stimulate Phase II detoxification and activity of glutathione s-transferase

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The 3 Rs in Patient with Chronic Joint Pain

- **Epigallocatechin-3-gallate (EGCG), the major polyphenol in green tea, significantly increased Treg frequencies and numbers in spleen and lymph nodes and had inhibited T cell response.**
- Wong, C. P., Nguyen, L. P., Noh, S. K., Bray, T. M., Bruno, R. S., & Ho, E. (2011). Induction of regulatory T cells by green tea polyphenol EGCG. Immunology letters, 139(1-2), 7–13. https://doi.org/10.1016/j.imlet.2011.04.009
- **Curcumin: An Effective Inhibitor of Interleukin-6**
- Ghandadi M, Sahebkar A. Curcumin: An Effective Inhibitor of Interleukin-6. Curr Pharm Des. 2017;23(6):921-931. doi:10.2174/1381612822666161006151605
- **Curcumin induces the expression and production of IL-10**
- Mollazadeh H, Cicero AFG, Blesso CN, Pirro M, Majeed M, Sahebkar A. Immune modulation by curcumin: The role of interleukin-10. Crit Rev Food Sci Nutr. 2019;59(1):89-101. doi:10.1080/10408398.2017.1358139

The 3 Rs in Patient with Psoriasis

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The 3 Rs in Patient with Psoriasis

- **REMOVE:** Eliminate the 'trigger' of disease, e.g. Foods that cause allergy/sensitivity leading to autoimmune reaction
- **REPLACE:** Support healthy function in a state of imbalance, e.g. replace with anti-inflammatory diet and Salvia Miltiorrhiza to inhibit the growth of keratinocytes
- **REPAIR:** Reduce inflammatory reaction in GI, e.g. Quercetin to reduce inflammation in GI, vitamin A and D to regulate/normalize keratinocyte proliferation, differentiation and apoptosis, and probiotics to support healthy gut flora

The 3 Rs in Patient with Psoriasis

- **Therapeutical effect of Salvia miltiorrhiza on Psoriasis**

Tang L, He S, Wang X, et al. Cryptotanshinone reduces psoriatic epidermal hyperplasia via inhibiting the activation of STAT3. Exp Dermatol. 2018;27(3):268-275. doi:10.1111/exd.13511

- **Vitamin A and D for Psoriasis**
- Huang, T. H., Lin, C. F., Alalaiwe, A., Yang, S. C., & Fang, J. Y. (2019). Apoptotic or Antiproliferative Activity of Natural Products against Keratinocytes for the Treatment of Psoriasis. International journal of molecular sciences, 20(10), 2558. https://doi.org/10.3390/ijms20102558
- **The role of gut microbiome in the pathogenesis of psoriasis and the therapeutic effects of probiotics**
- Alesa, D. I., Alshamrani, H. M., Alzahrani, Y. A., Alamssi, D. N., Alzahrani, N. S., & Almohammadi, M. E. (2019). The role of gut microbiome in the pathogenesis of psoriasis and the therapeutic effects of probiotics. Journal of family medicine and primary care, 8(11), 3496–3503. https://doi.org/10.4103/jfmpc.jfmpc_709_19

Case Study: Diabetes

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Male Patient in 60s

- Digestion problems: Diarrhea, pain ,discomfort
- Chronic fatigue
- HbA1c 6.9
- Kidney damage (got off metformin)
- Overweight
- Severe neuropathy
- Knee and back pain
- Hypertension uncontrolled (on 7 medication)

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Very deficient, Anemic

Tests	In Range	Out of Range	Reference Range	Units
WBC		25.6	4.0-11.0	K/UL
RBC		3.68	4.10-5.70	M/UL
HEMOGLOBIN		11.5	13.0-17.0	G/DL
HEMATOCRIT		34.0	37.0-49.0	%
MCV	92.4		80.0-100.0	fL
MCH	31.3		27.0-34.0	PG
MCHC	33.8		32.0-35.5	G/DL
RDW	13.0		11.0-15.0	%

Comprehensive Thyroid

Thyroid Only

Tests	In Range	Out of Range	Reference Range	Units
T3, Free	3.4		2.2-4.0	pg/mL
T4, Free	1.38		0.76-1.46	ng/dL
T4, Total	8.9		4.5-12.5	µg/dL
TSH	0.849		0.358-3.740	µIU/mL
Anti-TPO Ab (ATA)	<10.0		0.0-35.0	IU/mL
Thyroxine-binding globulin (TBG)	14.1		14.0-31.0	µg/mL
Thyroglobulin (TG)	8.9		<=55.0	ng/mL
Anti-Thyroglobulin Ab (ATG)	<20		0-40	IU/mL

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RT3 is estimate to block T3 receptors

Reverse T3

Tests	In Range	Out of Range	Reference Range	Units
REVERSE T3		27.4	9.0-27.0	ng/dL

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Reverse T3: A Strong 'Anti-T3 Hormone'

rT3 is not just an inactive metabolite, it is also **a powerful inhibitor of the conversion of T4 to T3.**

Chopra, I. J. (1977). A Study of Extrathyroidal Conversion of Thyroxine (T4) to 3,3',5-Triiodothyronine (T3) in Vitro*. Endocrinology, 101(2), 453-463. doi:10.1210/endo-101-2-453

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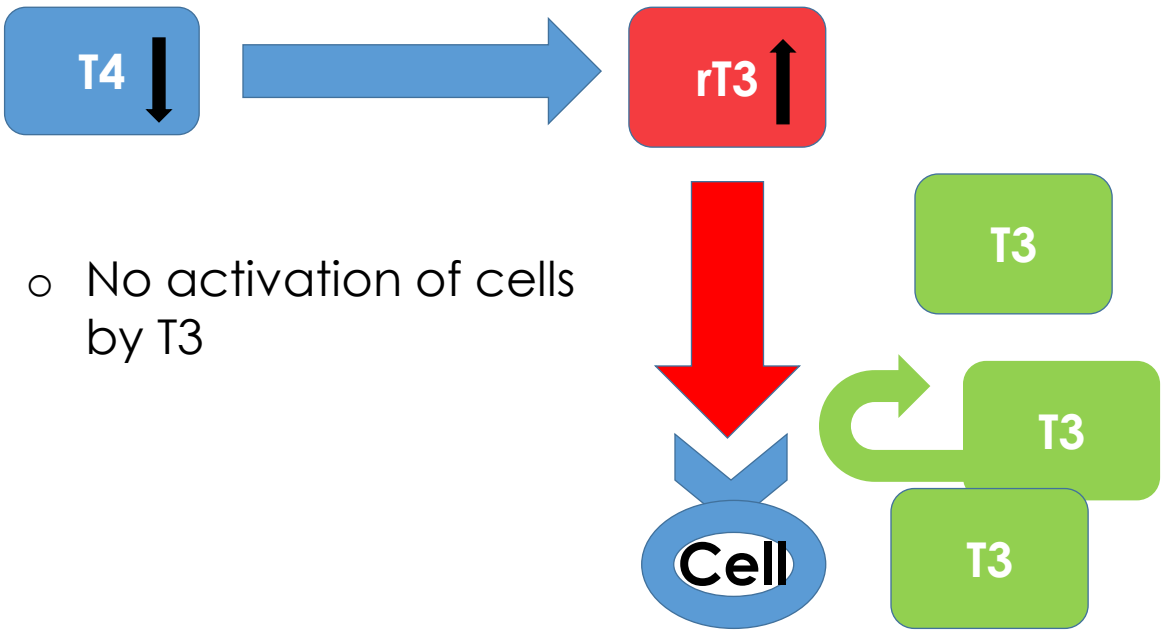

- No activation of cells by T3

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- Stress
- Trauma
- Low-calorie diet
  Inflammation
- Toxins
- Infections
- Liver/kidney dysfunction

Jones, D. (2010). Textbook of functional medicine. Gig Harbor, WA: Institute for Functional Medicine.

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Mitochondria: Metabolic Analysis Profile

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Results Overview
Normal
Borderline
High Need
Supplementation for High Need
Antioxidants
Vitamin A / Carotenoids
Vitamin C
Vitamin E / Tocopherols
B-Vitamins
Thiamin - B1
Riboflavin - B2
Niacin - B3
Pyridoxine - B6
Biotin - B7
Cobalamin - B12
Folic Acid - B9
Folic Acid - B9 - Dose = 1,200 mcg
Minerals
Magnesium
Manganese
Molybdenum
Zinc

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Studies to review

- **"Vitamin B12 deficiency has been demonstrated to be highly prevalent among patients with type 1 and type 2 diabetes mellitus. It presents with diverse clinical manifestations ranging from impaired memory, dementia, delirium, peripheral neuropathy"**
- Kibirige, D., & Mwebaze, R. (2013). Vitamin B12 deficiency among patients with diabetes mellitus: is routine screening and supplementation justified?. Journal of diabetes and metabolic disorders, 12(1), 17. https://doi.org/10.1186/2251-6581-12-17
- **Chronic folate deficiency induces glucose and lipid metabolism disorders**
- Zhao, M., Yuan, M. M., Yuan, L., Huang, L. L., Liao, J. H., Yu, X. L., Su, C., Chen, Y. H., Yang, Y. Y., Yu, H., & Xu, X. (2018). Chronic folate deficiency induces glucose and lipid metabolism disorders and subsequent cognitive dysfunction in mice. PloS one, 13(8), e0202910. https://doi.org/10.1371/journal.pone.0202910

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SUGGESTED SUPPLEMENT SCHEDULE

Supplements	Daily Recommended Intake (DRI)	Patient's Daily Recommendations	Provider Daily Recommendations
Antioxidants			
Vitamin A / Carotenoids	3,000 IU	3,000 IU	
Vitamin C	90 mg	250 mg	
Vitamin E / Tocopherols	22 IU	100 IU	
B-Vitamins			
Thiamin - B1	1.2 mg	10 mg	
Riboflavin - B2	1.3 mg	10 mg	
Niacin - B3	16 mg	20 mg	
Pyridoxine - B6	1.7 mg	10 mg	
Biotin - B7	30 mcg	100 mcg	
Folic Acid - B9	400 mcg	1,200 mcg	
Cobalamin - B12	2.4 mcg	500 mcg	
Minerals			
Magnesium	420 mg	400 mg	
Manganese	2.3 mg	3.0 mg	
Molybdenum	45 mcg	75 mcg	
Zinc	11 mg	10 mg	
Digestive Support			
Probiotics		25 billion CFU	
Pancreatic Enzymes		0 IU	

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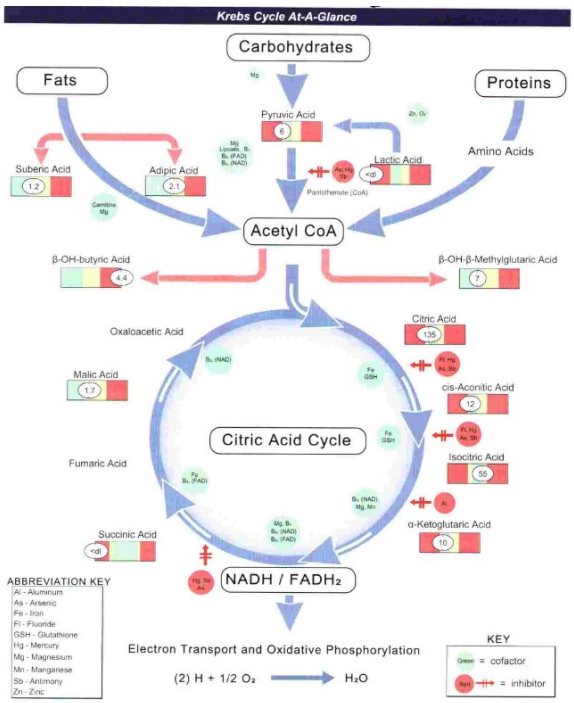
Krebs Cycle At-A-Glance
Carbohydrates
Fats
Proteins
Pyruvic Acid
6
Lactic Acid
<dl
Amino Acids
Suberic Acid
1.2
Adipic Acid
2.1
Pantothenate (CoA)
Acetyl CoA
β-OH-butyric Acid
4.4
β-OH-β-Methylglutaric Acid
7
Oxaloacetic Acid
Citric Acid
135
Malic Acid
1.7
cis-Aconitic Acid
12
Citric Acid Cycle
Isocitric Acid
35
Fumaric Acid
α-Ketoglutaric Acid
10
Succinic Acid
<dl
NADH / FADH₂
ABBREVIATION KEY
Al - Aluminum
As - Arsenic
Fe - Iron
Fl - Fluoride
GSH - Glutathione
Hg - Mercury
Mg - Magnesium
Mn - Manganese
Sb - Antimony
Zn - Zinc
Electron Transport and Oxidative Phosphorylation
(2) H + 1/2 O₂
H₂O
KEY
= cofactor
= inhibitor

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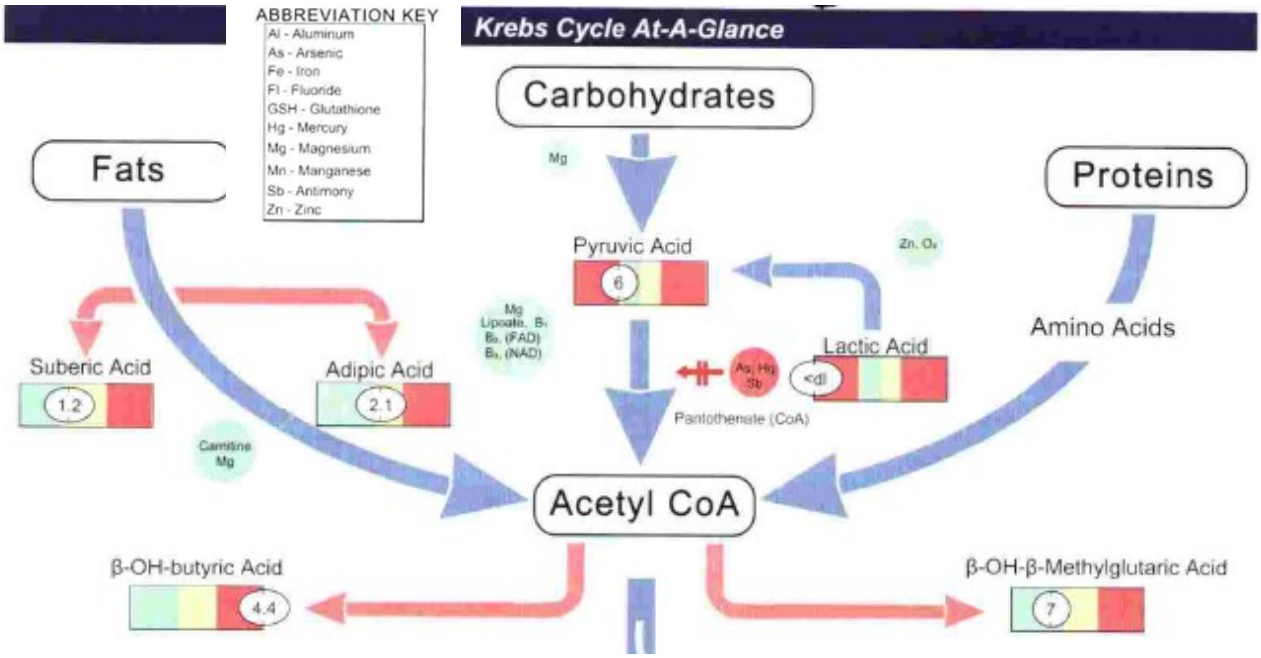
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Sb - Antimony
Zn - Zinc
Krebs Cycle At-A-Glance
Carbohydrates
Mg
Fats
Proteins
Pyruvic Acid
6
Zn, O2
Mg
Lipoate, B1
B2 (FAD)
B3 (NAD)
Lactic Acid
<dl
As, Hg
Sb
Pantothenate (CoA)
Amino Acids
Suberic Acid
1.2
Adipic Acid
2.1
Carnitine
Mg
Acetyl CoA
β-OH-butyric Acid
4.4
β-OH-β-Methylglutaric Acid
7

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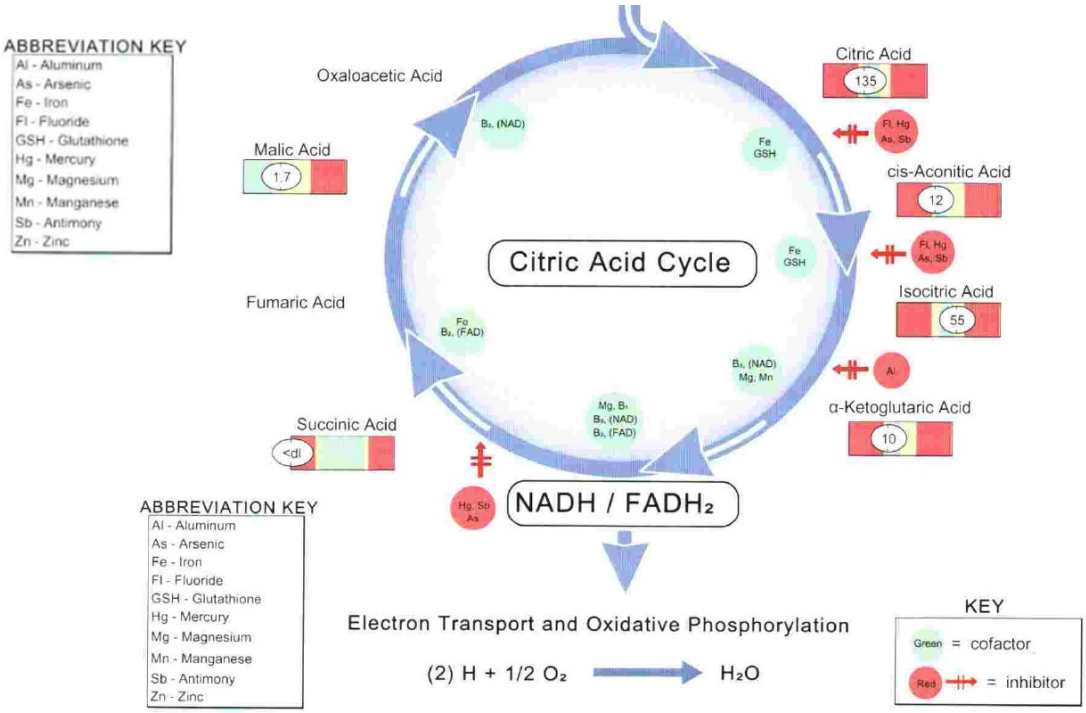
Studies to review

- **Chronic Health Effects in People Exposed to Arsenic via the Drinking Water: Dose-Response Relationships in Review**
- Yoshida T, Yamauchi H, Fan Sun G. Chronic health effects in people exposed to arsenic via the drinking water: dose-response relationships in review. Toxicol Appl Pharmacol. 2004;198(3):243-252. doi:10.1016/j.taap.2003.10.022
- **Deficiency of Pyruvate Dehydrogenase Activity in the pancreas of diabetic animals**
- Zhou YP, Ostenson CG, Ling ZC, Grill V. Deficiency of pyruvate dehydrogenase activity in pancreatic islets of diabetic GK rats. Endocrinology. 1995;136(8):3546-3551. doi:10.1210/endo.136.8.7628391
- **"Arsenic can interfere with cellular longevity by inhibiting essential metabolic enzymes"**
- Giri B, Dey S. Is it possible to avert arsenic effects on cells and tissues bypassing its toxicity and suppressive consequences of energy production? A hypothesis. BLDE Univ J Health Sci [serial online] 2017 [cited 2020 May 31];2:91-6. Available from: http://www.bldeujournalhs.in/text.asp?2017/2/2/91/220945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Oxaloacetic Acid
Malic Acid
1.7
Fumaric Acid
Succinic Acid
<dl
Citric Acid
135
cis-Aconitic Acid
12
Isocitric Acid
55
α-Ketoglutaric Acid
10
Citric Acid Cycle
NADH / FADH₂
Electron Transport and Oxidative Phosphorylation
(2) H + 1/2 O₂
H₂O
KEY
Green = cofactor
Red = inhibitor

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ABBREVIATION KEY

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- Hg - Mercury
- Mg - Magnesium
- Mn - Manganese
- Sb - Antimony
- Zn - Zinc

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Toxic & Essential Elements; Hair

TOXIC METALS		RESULT µg/g	REFERENCE INTERVAL	PERCENTILE 68th – 95th
Aluminum	(Al)	6.2	< 7.0	
Antimony	(Sb)	0.12	< 0.066	
Arsenic	(As)	0.030	< 0.080	
Barium	(Ba)	0.27	< 1.0	
Beryllium	(Be)	< 0.01	< 0.020	
Bismuth	(Bi)	0.004	< 2.0	
Cadmium	(Cd)	< 0.009	< 0.065	
Lead	(Pb)	0.28	< 0.80	
Mercury	(Hg)	1.0	< 0.80	
Platinum	(Pt)	< 0.003	< 0.005	
Thallium	(Tl)	< 0.001	< 0.002	
Thorium	(Th)	< 0.001	< 0.002	
Uranium	(U)	0.001	< 0.060	
Nickel	(Ni)	0.06	< 0.20	
Silver	(Ag)	0.02	< 0.08	
Tin	(Sn)	0.03	< 0.30	
Titanium	(Ti)	0.43	< 0.60	
Total Toxic Representation				

"people with high mercury exposure in young adulthood may have elevated risk of diabetes later in life."

He, K., Xun, P., Liu, K., Morris, S., Reis, J., & Guallar, E. (2013). Mercury exposure in young adulthood and incidence of diabetes later in life: the CARDIA Trace Element Study. Diabetes care, 36(6), 1584–1589. https://doi.org/10.2337/dc12-1842

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Zinc	(Zn)	170	130- 200
Manganese	(Mn)	0.08	0.08- 0.50
Chromium	(Cr)	0.34	0.40- 0.70
Vanadium	(V)	0.020	0.018- 0.065

"chromium, which has been shown reduce insulin resistance in some, but not all."

Hua, Y., Clark, S., Ren, J., & Sreejayan, N. (2012). Molecular mechanisms of chromium in alleviating insulin resistance. The Journal of nutritional biochemistry, 23(4), 313–319. https://doi.org/10.1016/j.jnutbio.2011.11.001

Inositol: "improving insulin resistance and reducing cardiovascular risk factors in women with PCOS and gestational diabetes mellitus or metabolic syndrome postmenopause"

Muscogiuri, G., Palomba, S., Laganà, A. S., & Orio, F. (2016). Inositols in the Treatment of Insulin-Mediated Diseases. International journal of endocrinology, 2016, 3058393. https://doi.org/10.1155/2016/3058393

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GI Microbiology Stool Testing

Microbiology Profile, stool

BACTERIOLOGY CULTURE		
Expected/Beneficial flora	**Commensal (Imbalanced) flora**	**Dysbiotic flora**
4+ Bacteroides fragilis group	1+ Enterobacter cloacae complex	
3+ Bifidobacterium spp.	3+ Gamma hemolytic strep	
2+ Escherichia coli	1+ Klebsiella pneumoniae ssp pneumoniae	
NG Lactobacillus spp.		
NG Enterococcus spp.		
4+ Clostridium spp.		
NG = No Growth		

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Alcat Test measures cellular reactions (WBC) to foods.

(Process using an impedance methodology-based flow cytometer)

SEVERE	MODERATE	MILD*
CANTALOUPE	ACORN SQUASH	ADZUKI BEANS*
COCOA	ALMOND	APPLE*
ICEBERG LETTUCE	ASPARAGUS	ARTICHOKE*
VANILLA	BLACK TEA	BAKER'S YEAST*
WHITE POTATO	BUTTERNUT SQUASH	BANANA*
	CINNAMON	BEEF*
	GREEN PEA	BLACK PEPPER*
	PEAR	BUCKWHEAT*
	STRING BEAN	CARROT*
		CAULIFLOWER*
		CELERY*
		CHIVES*
		CLOVE*
		COFFEE*
		CURRY*
		DANDELION LEAF*
		FLOUNDER*
		GARLIC*
		GRAPE*
		HONEYDEW MLN*
		JALAPEÑO PEPP*
		JICAMA*
		LAMB*
		MILLET*
		OKRA*
		OYSTER*
		PISTACHIO*
		PLANTAIN*
		PORK*
		QUINOA*
		RADISH*
		RICE (BRWN/WHT)*
		SEA BASS*

ACCEPTABLE / NO REACTION — Item Count: 250

VEGETABLES / LEGUMES

ARUGULA	BELL PEPPER MIX	BLACK BEANS	BLACK-EYED PEA
BOK CHOY	BOSTON BIBB LETTU	BROCCOLI	BRSSLS SPROUT
BUTTON MUSHROOM	CABBAGE	CANNELLINI BEANS	CAPERS
CHICKPEA	CHICORY	COLLARD GREENS	CUCUMBER
EGGPLANT	ENDIVE	ESCAROLE	FAVA BEAN
FENNEL SEED	HABANERO PEPPER	KALE	KELP
KIDNEY BEAN	LEAF LETT (RED/GR	LEEK	LENTIL BEAN
LIMA BEAN	MUNG BEAN	MUSTARD GREENS	NAVY BEAN
ONION	PARSNIP	PINTO BEAN	PORTOBELLO MUSHRM
RED BEET / SUGAR	RHUBARB	ROMAINE LETT	RUTABAGA
SCALLION	SHALLOTS	SHIITAKE MUSHRM	SPAGHETTI SQUASH
SPINACH	SWEET POTATO	SWISS CHARD	TOMATO
TURNIP	WAKAME SEAWEED	WATER CHESTNUT	WATERCRESS
YAM	YELLOW PEA	YELLOW SQUASH	ZUCCHINI SQUASH

FRUITS

APRICOT	AVOCADO	BLACK CURRANT	BLACKBERRY
BLUEBERRY	CHERRY	CRANBERRY	DATE
DRAGON FRUIT	FIG	GRAPEFRUIT	GUAVA
JACKFRUIT	KIWI	LEMON	LIME
LYCHEE	MANGO	MULBERRY	NECTARINE
OLIVE	ORANGE	PAPAYA	PEACH
PERSIMMON	PINEAPPLE	PLUM	POMEGRANATE
PUMPKIN	RASPBERRY	RED PALM FRUIT	STAR FRUIT
STRAWBERRY	WATERMELON		

MEAT

BISON	CHICKEN	CHICKEN LIVER	DUCK
TURKEY	VENISON		

Food Allergy vs Sensitivity

Allergy	Sensitivity
Immediate (mins to hours)	Not noticed or hours/day after
Stronger immune reaction (acute or dramatic)	Very mild reaction but inflammatory chronically

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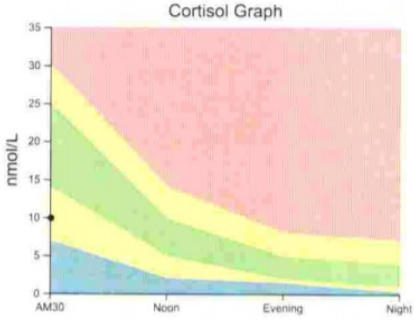
Low cortisol and DHEA indicates adrenal insufficiency

Analyte	Result	Unit	L	WRI	H	Optimal Range	Reference Interval
Cortisol AM30	9.9	nmol/L				14.0 – 25.0	7.0 – 30.0
DHEA*	23	pg/mL	↓				137 – 336

Cortisol Graph



Hormone Comments:

- The AM cortisol level is suboptimal. Additional cortisol testing is a consideration.
- DHEA levels typically decline with age and the level measured here is below the reference range. Note: Supplementation with DHEA may increase testosterone and/or estradiol levels.

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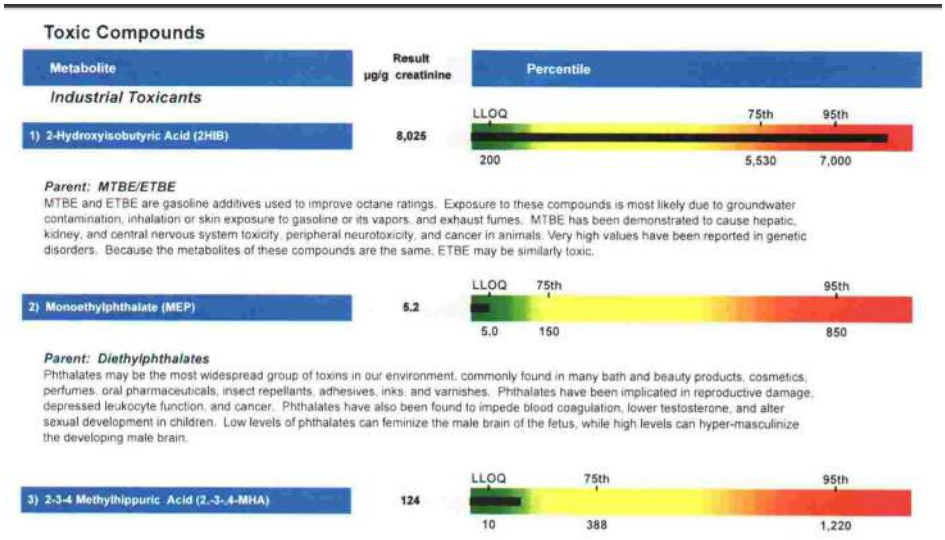
MTBE/ETBE (water contamination, exhaust fumes, inhalation or skin exposure) -> Neurotoxic



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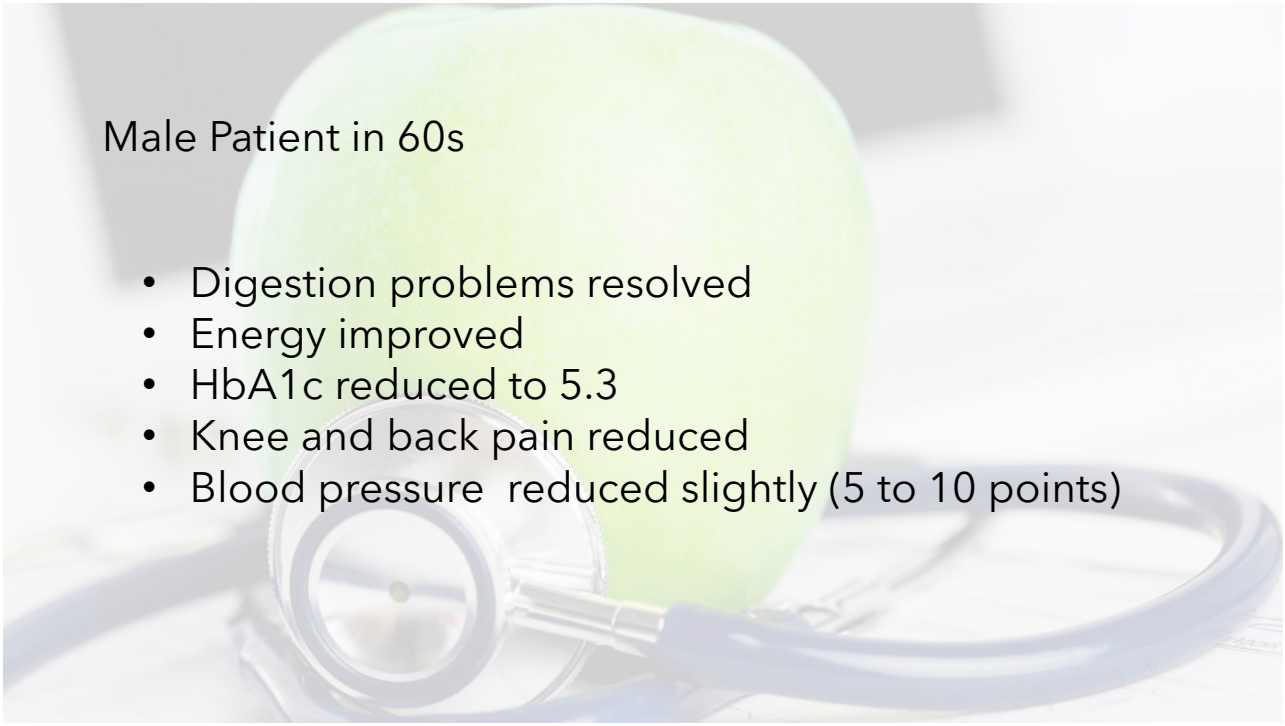

Male Patient in 60s

- Digestion problems resolved
- Energy improved
- HbA1c reduced to 5.3
- Knee and back pain reduced
- Blood pressure reduced slightly (5 to 10 points)

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Functional Medicine Approach to Chronic Diseases: A Review of the Process & Case Study

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