DR. HYMAN+

Where Genetics and Epigenetics intersect.

A Histamine Intolerance Case Demonstration

Conflict Disclosure

I am the past Director of Education at Seeking Health.

This is a Nutraceutical and Gene Analysis company based in Bellingham, WA.

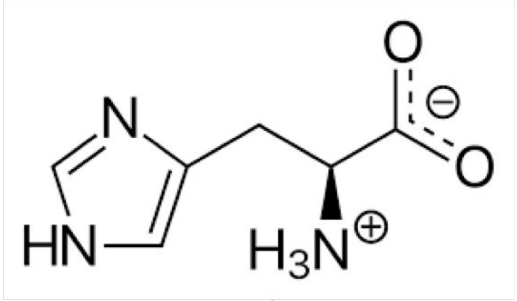
The information I will be sharing will mention some Seeking Health Products.

Disease is caused by two primary things.

1. Too many things you don’t need.
    a. Irritants

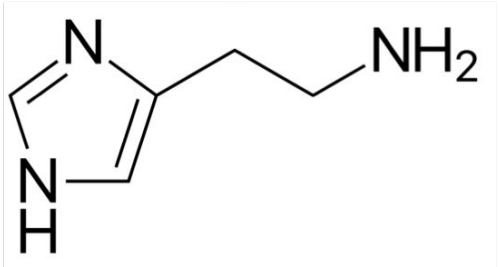
2. Not enough of the things you do.
    a. Nutrients

Histidine



Histidine Decarboxylase → Cu

Histamine



Histamine Intolerance

1. More histamine in your system than you can metabolize safely.

2. The term is most often reserved for excessive histamine in the intestinal tract.

   When Excess histamine in the intestinal tract gets take up into the circulation, symptoms may be see systemically.

Histamine Intolerance

1. Not enough things you do need
2. Two primary enzymes to break apart histamine
    a. DAO or Di-Amine-Oxidase
        i. Needs copper as cofactor
            1. Look for copper deficiency
        ii. Secreted from intestinal lining
            1. Look for intestinal damage
                a. Celiac, Crohn's, CF, SIBO, C-Diff, etc..
        iii. Inhibited by Subtances
            1. Prescription Meds
            2. Aldehydes/Alcohol
    b. HNMT- Histamine N-Methyltransferase
        i. Methylating nutrients needed.
            1. B12, Folates, TMG/Betaine

Histamine Intolerance

1. Too many things you don't need.
    a. Ingestion of high histamine foods and beverages.
        i. Alcohol/Fermented Beverages :
            1. Champagne highest, wine, beer, etc…
        ii. Meats:
            1. Spoiled Fish
                a. Scrombroid Poisoning
            2. Cured Meats
                a. Salami, smoked meats, deli meats, etc…
        iii. Fermented Foods:
            1. Cheese, yogurt , sauerkraut, vinegar, etc…

Symptoms of Histamine Intolerance

1. Cardiovascular
    a. Dizziness, Headache
2. Respiratory
    a. Post Nasal Drip, Congestion, Sneezing
3. Skin
    a. Itching, Flushing, Eczema
4. Gastrointestinal
    a. Bloating, Fullness, Diarrhea, Abdominal Pain, Constipation

Primary Symptoms of Anti-Histmine Drugs- Drowsiness

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6667364/

Histamine Intolerance Case

1. 70 yo Female
2. Presents with frequent HA, Eczema, “Burning Lips”
3. “Gut is fine if I do not eat dairy or irritating foods”
4. “Dairy causes constipation.”
5. “Foods like smoked salmon, cheese, or champagne will trigger migraines and give me diarrhea for at least a day.”
6. “Now many foods are triggering me. Things got better when I took out bacon and lunch meat before. But now…I can’t do many foods. I can’t even do citrus at all.”
7. Taking multiple H1 antihistamine medications to control symptoms

Histamine Intolerance

1. What are the irritants?

2. What are the supportive nutrients that she may be missing?
   a. Can we tell from the information we have?
   b. Or do we need to dig with further testing?

Histamine Intolerance- Reduce Irritants

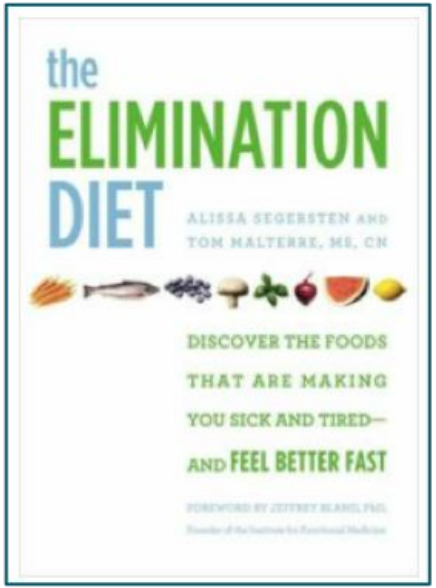
1. REDUCE the IRRITANTS in the gut.
    a. Lessen histamine burden from foods.
        i. Client-”dairy, smoke salmon, cured meats, champagne, cheese, citrus”
    b. Lessen mast cell and basophil activation which reduces histamine.
        i. Food sensitivities/Elimination Diet (esp. gluten and dairy)
    c. Balance intestinal environment/microbes.
        i. Probiotics, Prebiotics, Microbial Balancing Herbs
    d. Lower inhibitors
        i. Alcohol and Medications

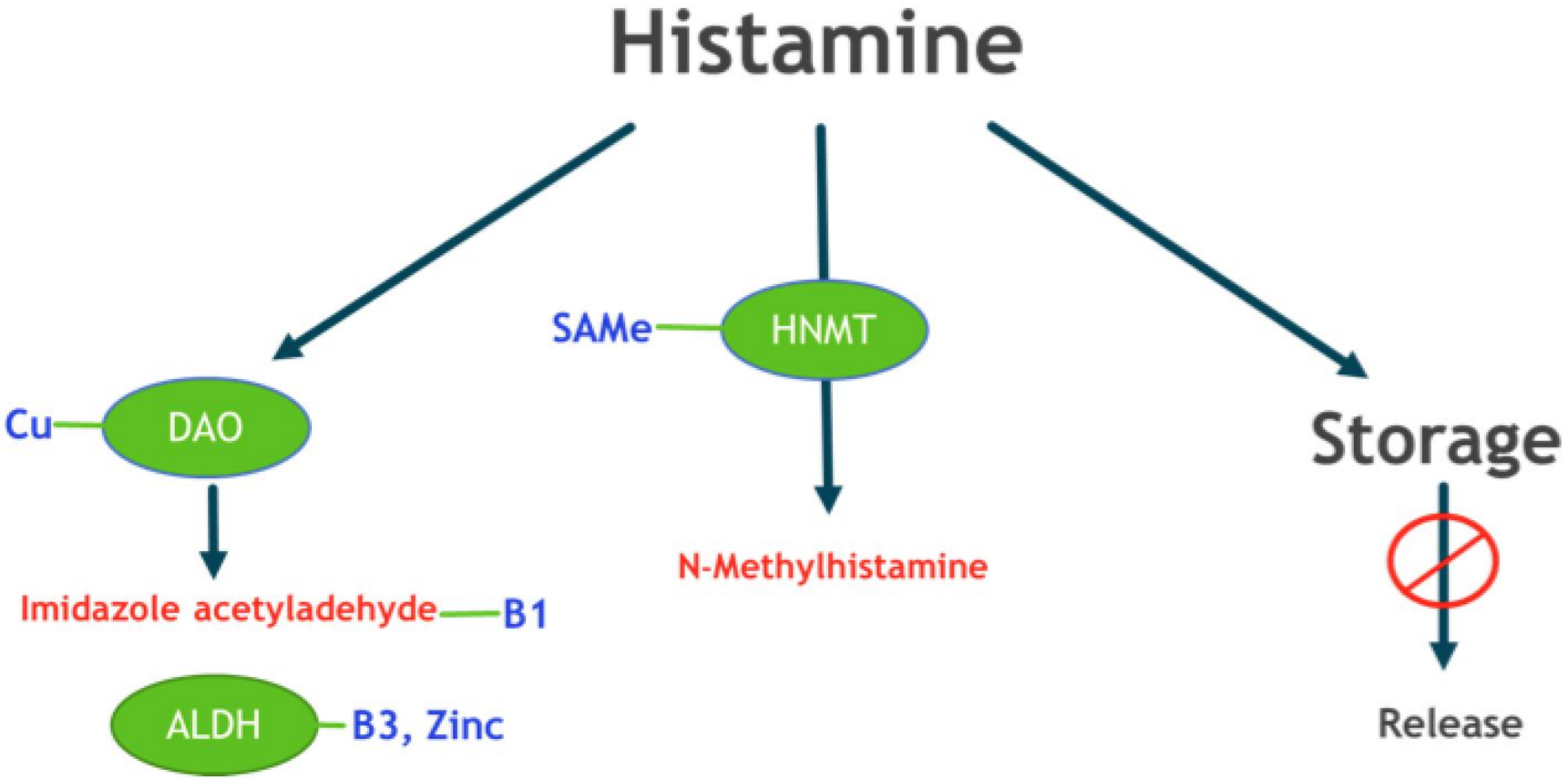
Histamine Intolerance- Nutrients/Support

1. Increase cofactors/coenzymes
    a. Minerals
        i. Copper (DAO), Zn (ALDH)
    b. Vitamins
        i. B12, Folates, Betaine/TMG = (SAMe)
2. Add enzymes (DAO)
    a. Use a DiamineOxidase enzyme after eating high histamine meals with fermented foods, cured meats, or alcohol
3. Add in gut support
    a. Pre- and Probiotics

Histamine Intolerance Actions

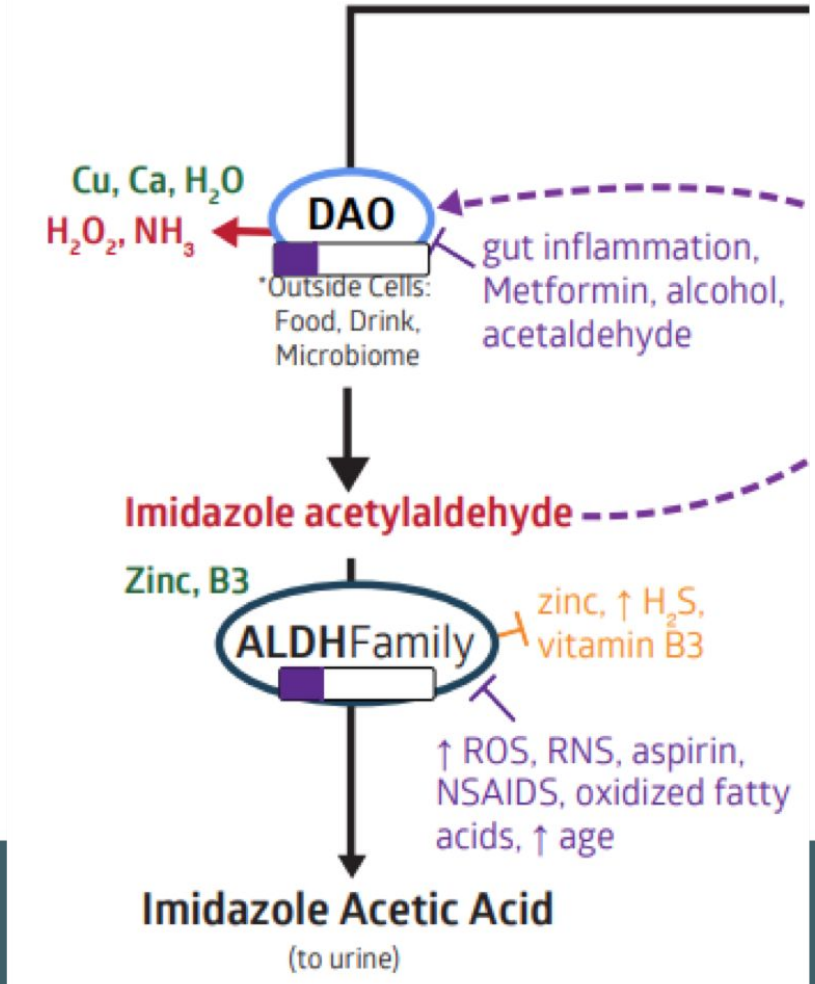
1. Lower level of histamine foods consumed
2. Do elimination diet for food sensitivities
3. Balance Missing Nutrients
    a. Vitamins and Minerals (need data/labs)
    b. DAO Enzymes
    c. Intestinal Microbes (need data/labs)
4. Run Gene and Nutrient Panels

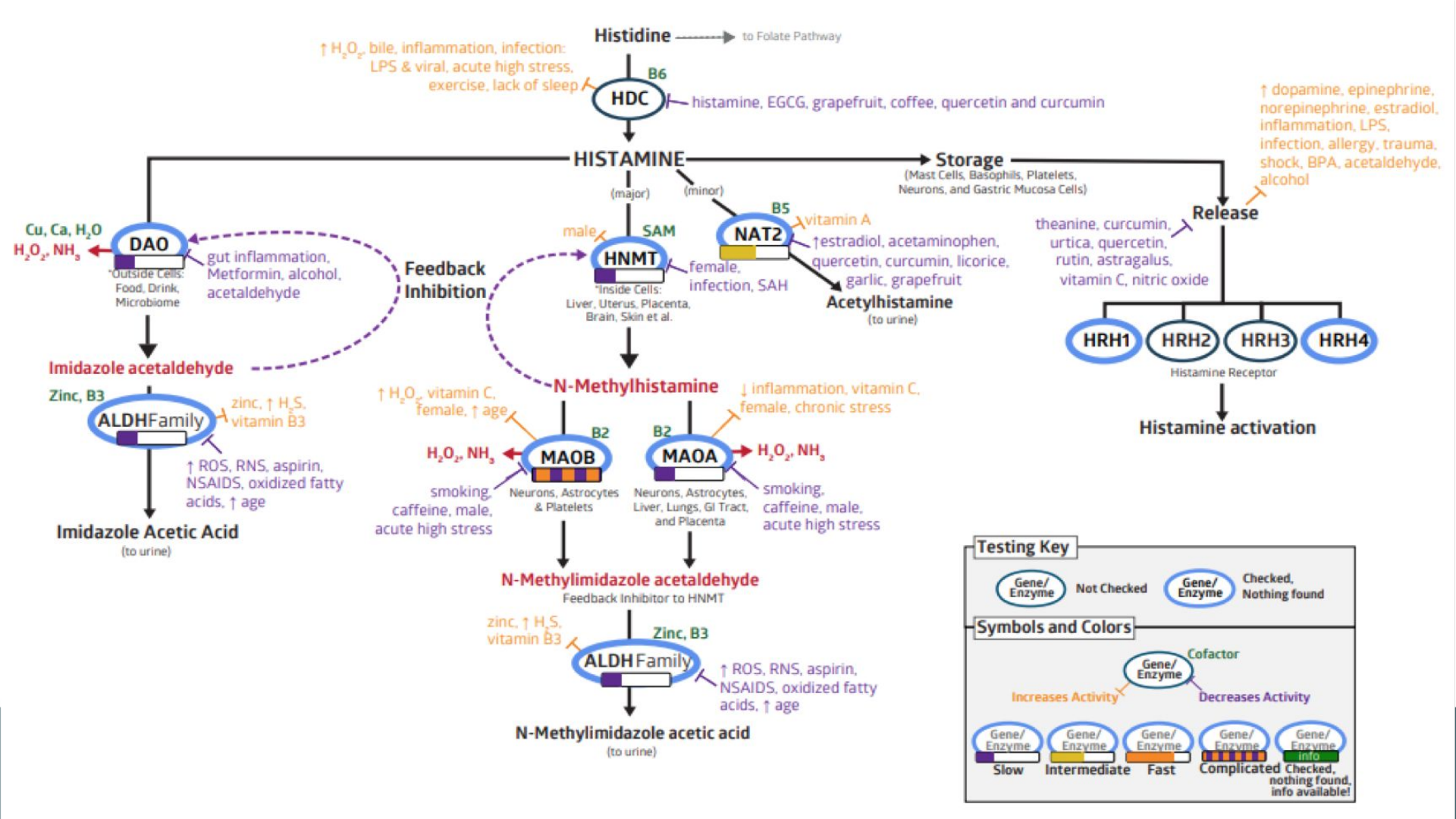



Histamine
SAMe
HNMT
Cu
DAO
N-Methylhistamine
Storage
Imidazole acetyladehyde
B1
ALDH
B3, Zinc
Release

Gene Analysis: Strategene Panel

1. Looks at common gene variants for histamine metabolism
    a. **DAO**: Diamineoxidase
    b. **HNMT**: Histamine N-Methyltransferase
    c. MAOA/MAOB: Monoamineoxidase A and B
    d. ALDH: Aldehyde Dehydrogenase
2. Examines challenges in Methylation
    a. Folate Metabolism
    b. Betaine Metabolism
    c. Methionine Metabolism


Cu, Ca, H_2O
H_2O_2, NH_3
DAO
*Outside Cells: Food, Drink, Microbiome
gut inflammation, Metformin, alcohol, acetaldehyde
Imidazole acetylaldehyde
Zinc, B3
ALDHFamily
zinc, ↑ H_2S, vitamin B3
↑ ROS, RNS, aspirin, NSAIDS, oxidized fatty acids, ↑ age
Imidazole Acetic Acid
(to urine)

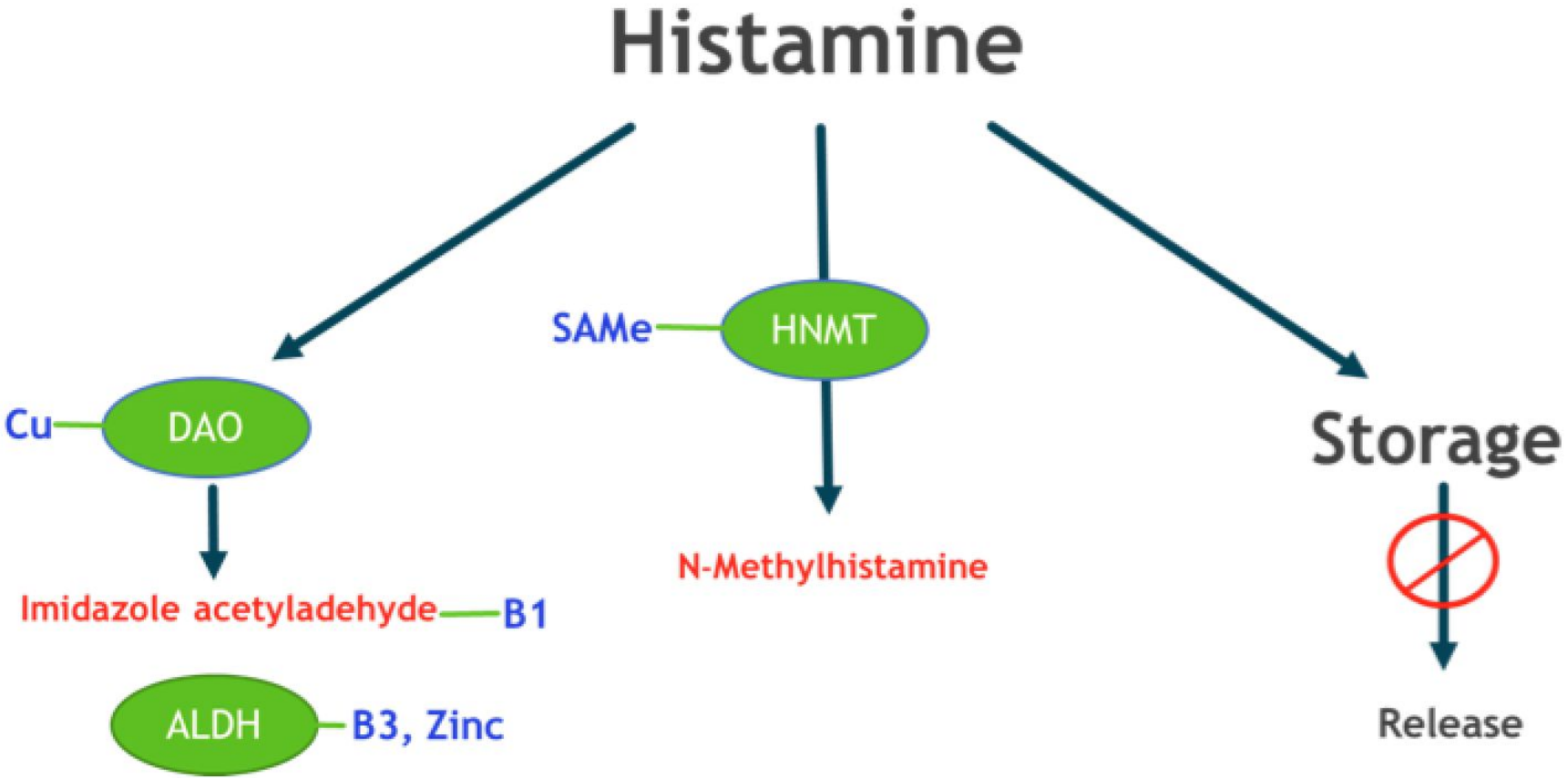

Histidine
to Folate Pathway
↑ H_2O_2, bile, inflammation, infection: LPS & viral, acute high stress, exercise, lack of sleep
B6
HDC
histamine, EGCG, grapefruit, coffee, quercetin and curcumin
HISTAMINE
(major)
(minor)
Storage
(Mast Cells, Basophils, Platelets, Neurons, and Gastric Mucosa Cells)
↑ dopamine, epinephrine, norepinephrine, estradiol, inflammation, LPS, infection, allergy, trauma, shock, BPA, acetaldehyde, alcohol
Release
theanine, curcumin, urtica, quercetin, rutin, astragalus, vitamin C, nitric oxide
HRH1
HRH2
HRH3
HRH4
Histamine Receptor
Histamine activation
Cu, Ca, H_2O
H_2O_2, NH_3
DAO
*Outside Cells: Food, Drink, Microbiome
gut inflammation, Metformin, alcohol, acetaldehyde
Feedback Inhibition
male
SAM
HNMT
*Inside Cells: Liver, Uterus, Placenta, Brain, Skin et al.
female, infection, SAH
B5
NAT2
vitamin A
↑estradiol, acetaminophen, quercetin, curcumin, licorice, garlic, grapefruit
Acetylhistamine
(to urine)
Imidazole acetaldehyde
Zinc, B3
ALDHFamily
zinc, ↑ H_2S, vitamin B3
↑ ROS, RNS, aspirin, NSAIDS, oxidized fatty acids, ↑ age
Imidazole Acetic Acid
(to urine)
N-Methylhistamine
↑ H_2O_2, vitamin C, female, ↑ age
↓ inflammation, vitamin C, female, chronic stress
B2
MAOB
Neurons, Astrocytes & Platelets
B2
MAOA
Neurons, Astrocytes, Liver, Lungs, GI Tract, and Placenta
H_2O_2, NH_3
H_2O_2, NH_3
smoking, caffeine, male, acute high stress
smoking, caffeine, male, acute high stress
N-Methylimidazole acetaldehyde
Feedback Inhibitor to HNMT
zinc, ↑ H_2S, vitamin B3
Zinc, B3
ALDH Family
↑ ROS, RNS, aspirin, NSAIDS, oxidized fatty acids, ↑ age
N-Methylimidazole acetic acid
(to urine)
Testing Key
Gene/ Enzyme
Not Checked
Gene/ Enzyme
Checked, Nothing found
Symbols and Colors
Gene/ Enzyme
Cofactor
Increases Activity
Decreases Activity
Gene/ Enzyme
Slow
Gene/ Enzyme
Intermediate
Gene/ Enzyme
Fast
Gene/ Enzyme
Complicated
Gene/ Enzyme
info
Checked, nothing found, info available!

Histamine

DAO

HNMT

Gene	SNP rsID	Call	Impact	Variant Allele	Alias	Result
HRH1	rs901865	CC		T	-17T>C	-/-
HRH4	rs11665084	CC		T	413C>T	-/-
HRH4	rs11662595	AA		G	249A>G	-/-
DAO/ AOC1	rs2052129	GT		T	-691G>T	+/-
DAO/ AOC1	rs10156191	CT		T	47C>T	+/-
HNMT	rs11558538	CT		T	C314T	+/-
NAT2	rs1801279	GG		A		-/-
MAOA	rs6323	TT		G	T941G	-/-
MAOA	rs1137070	CC		T	1410T>C	-/-
MAOB	rs1799836	TC		C	-36A>G	+/-
MAOB	rs2311013	TT		A	1155T>A	-/-
MAOB	rs5905512	AG		A	15106T>C	+/-
ALDH1B1	rs2228093	CT		T	ALDH1B1*2	+/-
ALDH2	rs671	GG		A	ALDH2*2	-/-
ALDH2	rs737280	TT		C	699T>C	-/-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Imidazole acetyladehyde
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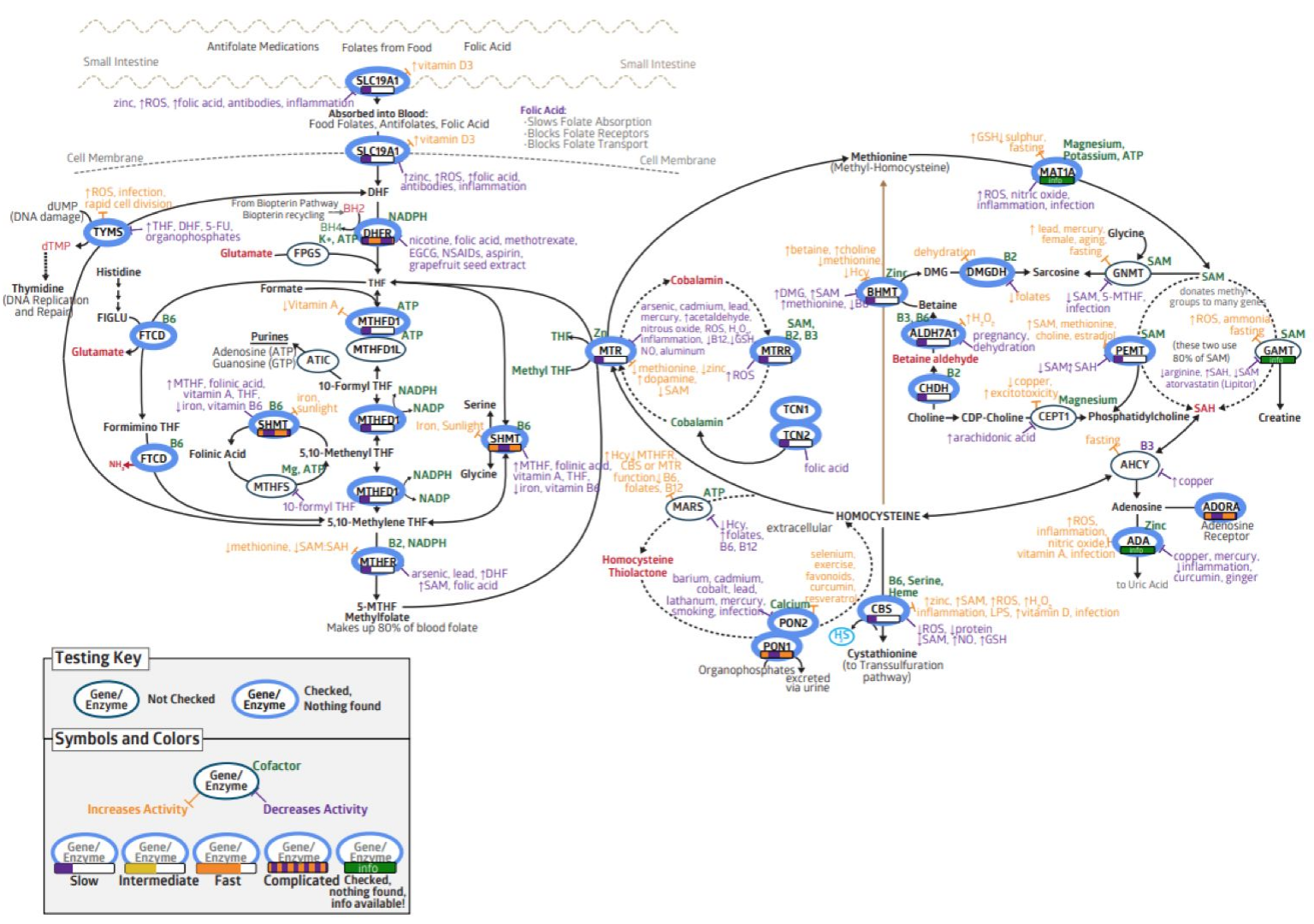
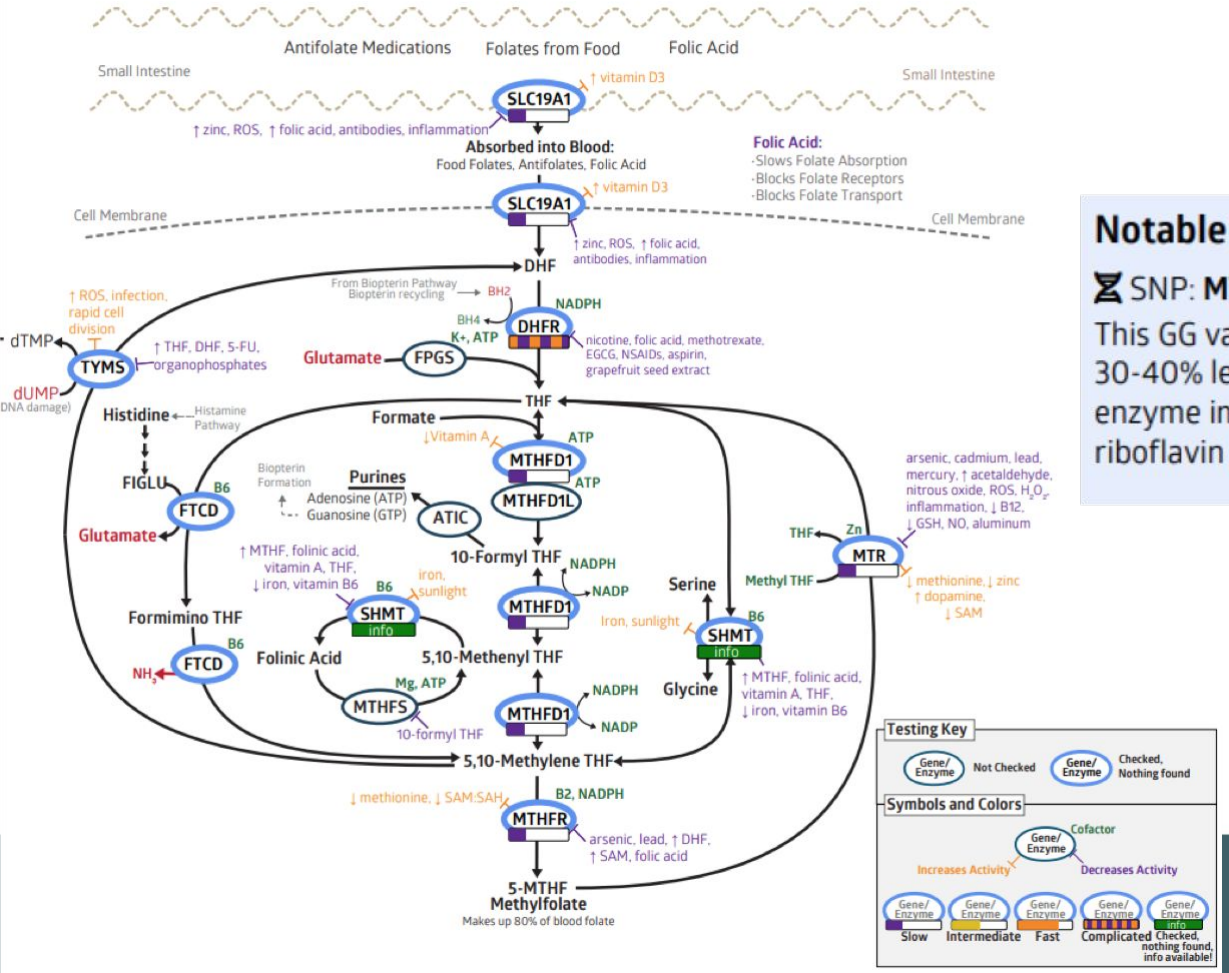
B3, Zinc
Release


Antifolate Medications
Folates from Food
Folic Acid
Small Intestine
Small Intestine
↑vitamin D3
SLC19A1
zinc, ↑ROS, ↑folic acid, antibodies, inflammation
Absorbed into Blood:
Food Folates, Antifolates, Folic Acid
Folic Acid:
·Slows Folate Absorption
·Blocks Folate Receptors
·Blocks Folate Transport
Cell Membrane
Cell Membrane
↑zinc, ↑ROS, ↑folic acid, antibodies, inflammation
DHF
↑ROS, infection, rapid cell division
dUMP (DNA damage)
TYMS
↑THF, DHF, 5-FU, organophosphates
dTMP
Thymidine (DNA Replication and Repair)
From Biopterin Pathway
Biopterin recycling
BH2
BH4
NADPH
K+, ATP
DHFR
nicotine, folic acid, methotrexate, EGCG, NSAIDs, aspirin, grapefruit seed extract
Glutamate
FPGS
Histidine
THF
Formate
↓Vitamin A
ATP
MTHFD1
MTHFD1L
FIGLU
B6
FTCD
Glutamate
Purines
Adenosine (ATP)
Guanosine (GTP)
ATIC
10-Formyl THF
NADPH
NADP
↑MTHF, folinic acid, vitamin A, THF, ↓iron, vitamin B6
iron, sunlight
Formimino THF
B6
FTCD
NH3
SHMT
B6
Folinic Acid
5,10-Methenyl THF
Mg, ATP
MTHFS
10-formyl THF
MTHFD1
NADPH
NADP
Iron, Sunlight
Serine
SHMT
B6
Glycine
↑MTHF, folinic acid, vitamin A, THF, ↓iron, vitamin B6
5,10-Methylene THF
↓methionine, ↓SAM:SAH
B2, NADPH
MTHFR
arsenic, lead, ↑DHF ↑SAM, folic acid
5-MTHF
Methylfolate
Makes up 80% of blood folate
THF
Zn
Methyl THF
MTR
Cobalamin
arsenic, cadmium, lead, mercury, ↑acetaldehyde, nitrous oxide, ROS, H2O2, inflammation, ↓B12,↓GSH
NO, aluminum
↑methionine, ↓zinc, ↑dopamine, ↓SAM
Cobalamin
SAM, B2, B3
MTRR
↑ROS
TCN1
TCN2
folic acid
↑Hcy,↓MTHFR, CBS or MTR function,↓B6, folates, B12
ATP
MARS
↓Hcy, ↑folates, B6, B12
extracellular
Homocysteine Thiolactone
barium, cadmium, cobalt, lead, lathanum, mercury, smoking, infection
selenium, exercise, favonoids, curcumin, resveratrol
Calcium
PON2
PON1
Organophosphates excreted via urine
B6, Serine, Heme
CBS
↑zinc, ↑SAM, ↑ROS, ↑H2O2, inflammation, LPS, ↑vitamin D, infection
↓ROS, ↓protein ↓SAM, ↑NO, ↑GSH
Cystathionine (to Transsulfuration pathway)
HOMOCYSTEINE
Methionine (Methyl-Homocysteine)
↑GSH,↓sulphur, fasting
Magnesium, Potassium, ATP
MAT1A
info
↑ROS, nitric oxide, inflammation, infection
↑ lead, mercury, female, aging, fasting
Glycine
SAM
GNMT
↑betaine, ↑choline ↓methionine ↓Hcy
dehydration
Zinc
DMG
B2
DMGDH
Sarcosine
↓folates
↓SAM, ↑MTHF, infection
↑DMG, ↑SAM ↑methionine, ↓B6
BHMT
Betaine
B3, B6
ALDH7A1
↑H2O2, pregnancy, dehydration
Betaine aldehyde
B2
CHDH
↑SAM, methionine, choline, estradiol
SAM
PEMT
↓SAM↑SAH
↓copper, ↑excitotoxicity
Magnesium
Choline
CDP-Choline
CEPT1
Phosphatidylcholine
↑arachidonic acid
SAH
donates methyl groups to many gens
↑ROS, ammonia fasting
SAM
GAMT
info
Creatine
(these two use 80% of SAM)
↓arginine, ↑SAH, ↓SAM atorvastatin (Lipitor)
fasting
B3
AHCY
↑copper
Adenosine
ADORA
Adenosine Receptor
↑ROS, inflammation, nitric oxide,H vitamin A, infection
Zinc
ADA
info
copper, mercury, ↓inflammation, curcumin, ginger
to Uric Acid
Testing Key
Gene/ Enzyme
Not Checked
Gene/ Enzyme
Checked, Nothing found
Symbols and Colors
Gene/ Enzyme
Cofactor
Increases Activity
Decreases Activity
Gene/ Enzyme
Slow
Gene/ Enzyme
Intermediate
Gene/ Enzyme
Fast
Gene/ Enzyme
Complicated
Gene/ Enzyme
info
Checked, nothing found, info available!

DR. HYMAN+

Folate



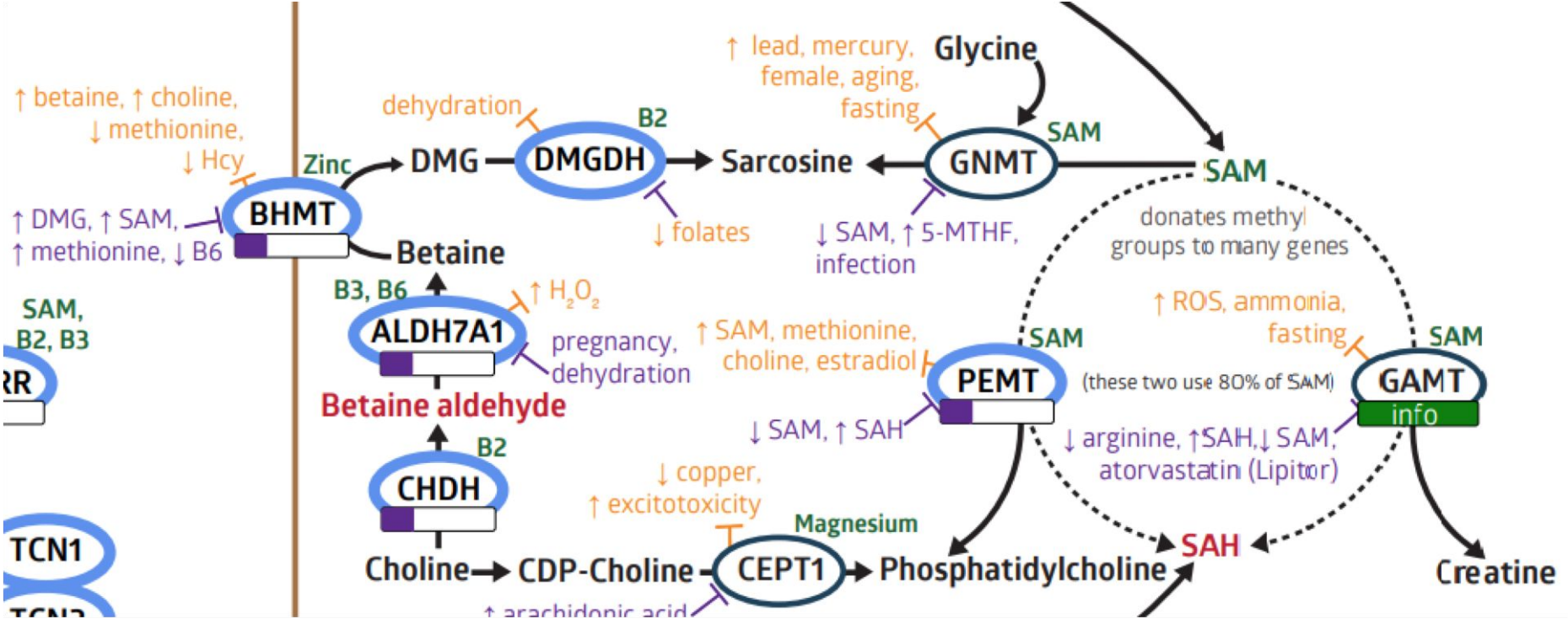
Notable variation:

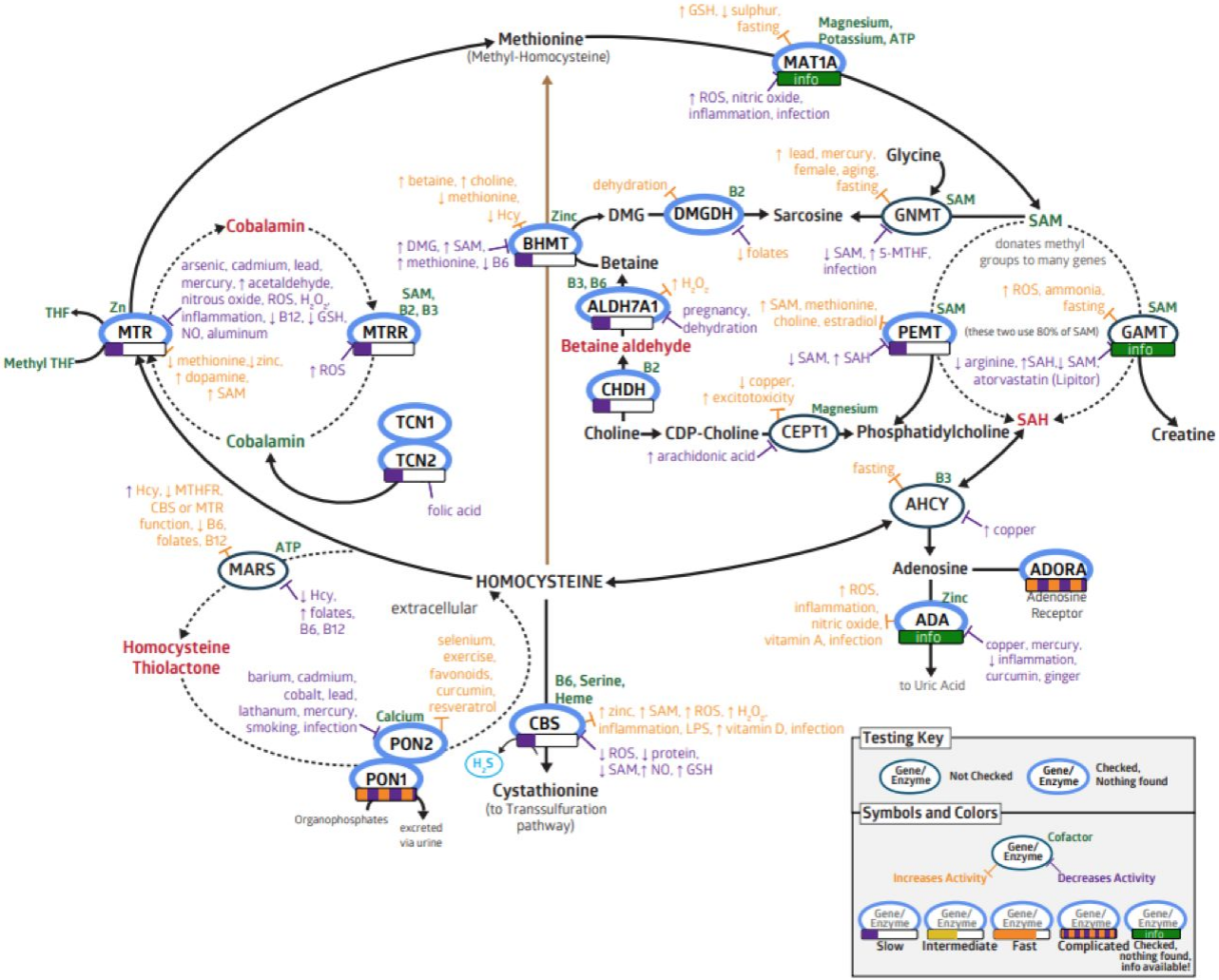
SNP: **MTHFR A1298C rs1801131 (+/+, GG)**

This GG variant reduces enzyme activity by approximately 30-40% less than wild type. The activity and stability of the enzyme improves by consuming sufficient folate (B9) and riboflavin (B2).

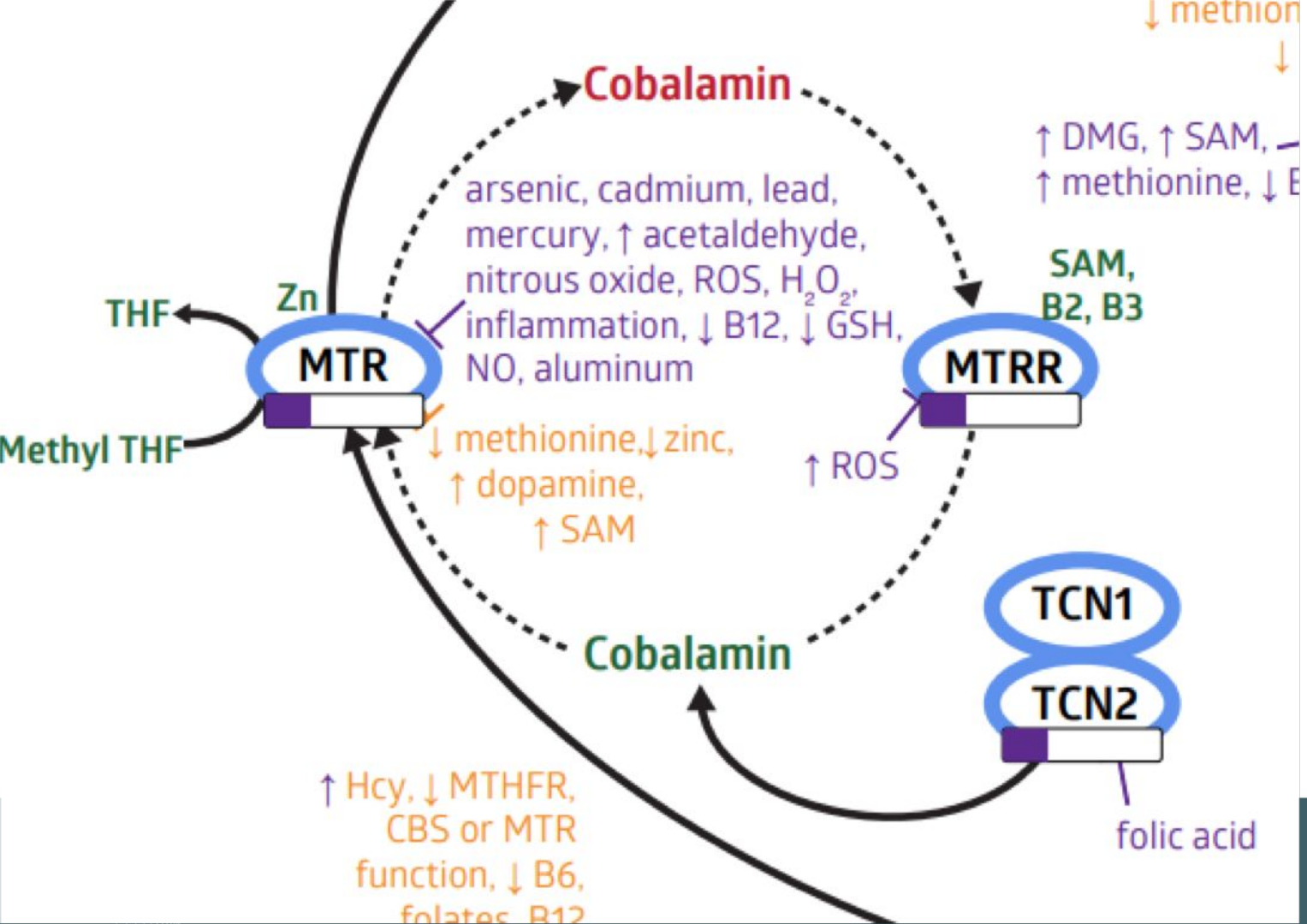
DR. HYMAN+

Gene	SNP rsID	Call	Impact	Variant Allele	Alias	Result
SLC19A1	rs1051266	TC		T	G80A	+/-
DHFR	rs70991108	DI		D	19bp Del/Ins	+/-
MTHFD1	rs2236225	AA		A	G1958A	+/+
MTHFD1	rs1076991	TT		T	T105C	+/+
MTHFR	rs1801133	GG		A	C677T	-/-
MTHFR	rs1801131	GG		G	A1298C	+/+
FTCD	rs61735836	CC		T	C301T	-/-
SHMT1	rs1979277	-		A	C1420T	NC
TYMS	rs16430	II		D	Ins/Del	-/-


↑ betaine, ↑ choline,
↓ methionine,
↓ Hcy
↑ DMG, ↑ SAM,
↑ methionine, ↓ B6
BHMT
Zinc
DMG
dehydration
DMGDH
B2
Sarcosine
↓ folates
↑ lead, mercury,
female, aging,
fasting
Glycine
GNMT
SAM
↓ SAM, ↑ 5-MTHF,
infection
SAM
donates methyl
groups to many genes
Betaine
B3, B6
ALDH7A1
↑ H_2O_2
pregnancy,
dehydration
Betaine aldehyde
↑ SAM, methionine,
choline, estradiol
SAM
PEMT
(these two use 80% of SAM)
↑ ROS, ammonia,
fasting
SAM
GAMT
info
↓ SAM, ↑ SAH
↓ arginine, ↑SAH, ↓ SAM,
atorvastatin (Lipitor)
B2
CHDH
↓ copper,
↑ excitotoxicity
Magnesium
Choline
CDP-Choline
CEPT1
Phosphatidylcholine
SAH
Creatine
SAM,
B2, B3
TCN1


Methionine
(Methyl-Homocysteine)
↑ GSH, ↓ sulphur, fasting
Magnesium, Potassium, ATP
MAT1A
info
↑ ROS, nitric oxide, inflammation, infection
SAM
donates methyl groups to many genes
Glycine
↑ lead, mercury, female, aging, fasting
GNMT
SAM
↓ SAM, ↑ 5-MTHF, infection
Sarcosine
DMGDH
B2
dehydration
↓ folates
DMG
Zinc
BHMT
↑ betaine, ↑ choline, ↓ methionine, ↓ Hcy
↑ DMG, ↑ SAM, ↑ methionine, ↓ B6
Betaine
Cobalamin
arsenic, cadmium, lead, mercury, ↑ acetaldehyde, nitrous oxide, ROS, H_2O_2, inflammation, ↓ B12, ↓ GSH, NO, aluminum
THF
Zn
MTR
Methyl THF
MTRR
SAM, B2, B3
↑ ROS
↓ methionine,↓ zinc, ↑ dopamine, ↑ SAM
Cobalamin
TCN1
TCN2
folic acid
B3, B6
ALDH7A1
↑ H_2O_2
pregnancy, dehydration
Betaine aldehyde
B2
CHDH
↑ SAM, methionine, choline, estradiol
PEMT
SAM
(these two use 80% of SAM)
↓ SAM, ↑ SAH
↓ copper, ↑ excitotoxicity
Magnesium
Choline
CDP-Choline
CEPT1
Phosphatidylcholine
↑ arachidonic acid
SAH
GAMT
info
SAM
↑ ROS, ammonia, fasting
↓ arginine, ↑SAH,↓ SAM, atorvastatin (Lipitor)
Creatine
fasting
B3
AHCY
↑ copper
↑ Hcy, ↓ MTHFR, CBS or MTR function, ↓ B6, folates, B12
ATP
MARS
↓ Hcy, ↑ folates, B6, B12
HOMOCYSTEINE
extracellular
Homocysteine Thiolactone
Adenosine
ADORA
Adenosine Receptor
↑ ROS, inflammation, nitric oxide, vitamin A, infection
Zinc
ADA
info
copper, mercury, ↓ inflammation, curcumin, ginger
to Uric Acid
selenium, exercise, favonoids, curcumin, resveratrol
barium, cadmium, cobalt, lead, lathanum, mercury, smoking, infection
Calcium
PON2
PON1
Organophosphates
excreted via urine
B6, Serine, Heme
CBS
↑ zinc, ↑ SAM, ↑ ROS, ↑ H_2O_2, inflammation, LPS, ↑ vitamin D, infection
↓ ROS, ↓ protein, ↓ SAM,↑ NO, ↑ GSH
H_2S
Cystathionine
(to Transsulfuration pathway)
Testing Key
Gene/ Enzyme
Not Checked
Checked, Nothing found
Symbols and Colors
Cofactor
Increases Activity
Decreases Activity
Slow
Intermediate
Fast
Complicated
Checked, nothing found, info available!

DR. HYMAN+

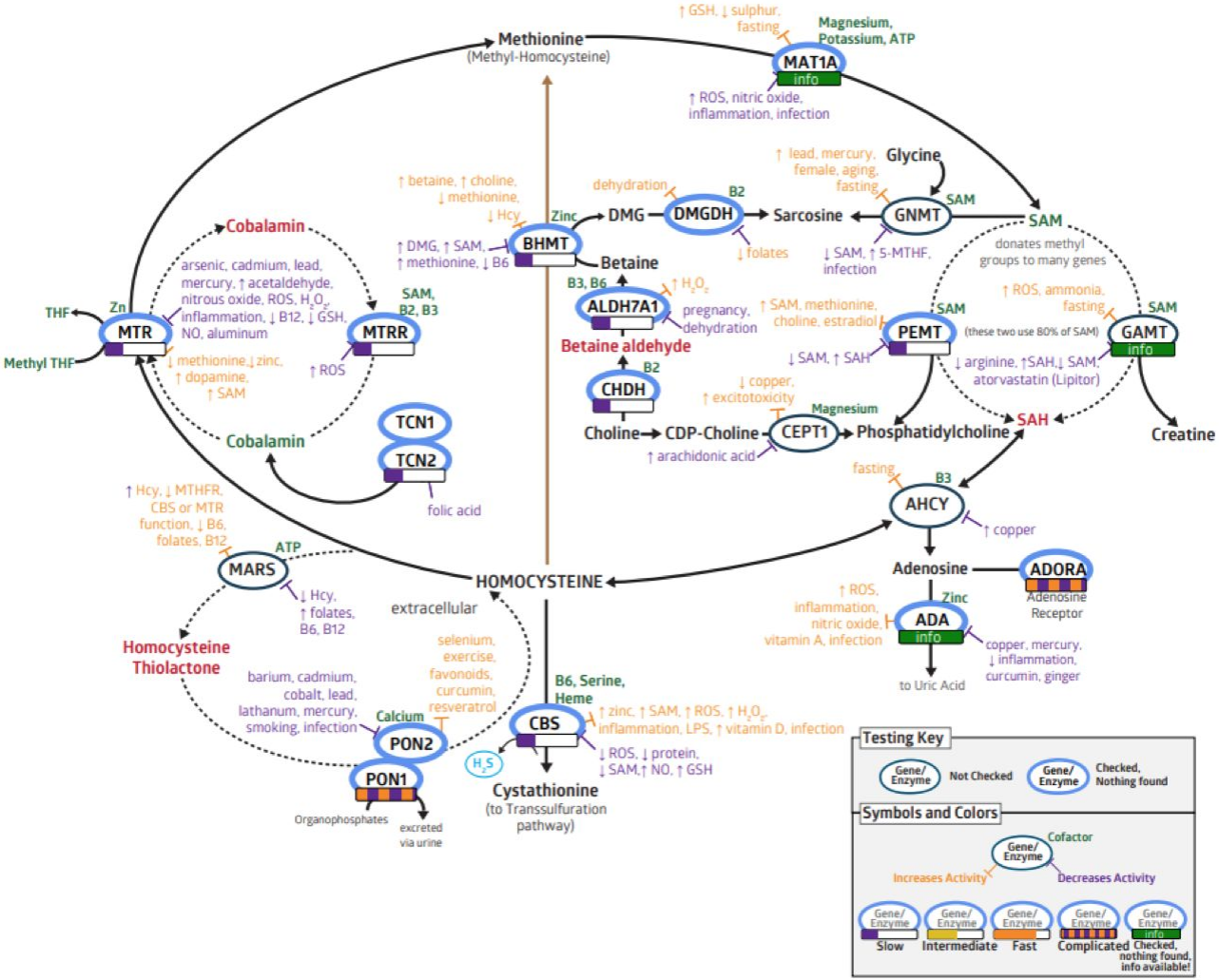

↓ methion
↓
Cobalamin
↑ DMG, ↑ SAM,
↑ methionine, ↓ B
arsenic, cadmium, lead,
mercury, ↑ acetaldehyde,
nitrous oxide, ROS, H_2O_2,
inflammation, ↓ B12, ↓ GSH,
NO, aluminum
SAM,
B2, B3
THF
Zn
MTR
MTRR
Methyl THF
↓ methionine, ↓ zinc,
↑ dopamine,
↑ SAM
↑ ROS
TCN1
TCN2
Cobalamin
↑ Hcy, ↓ MTHFR,
CBS or MTR
function, ↓ B6,
folates, B12
folic acid

DR. HYMAN+

B12

PC
Choline
TMG

Gene	SNP rsID	Call	Impact	Variant Allele	Alias	Result
MTR	rs3768142	GG		G	1710G>T	+/+
MTR	rs28372871	GG		G	-186G>T	+/+
MTR	rs1805087	AA		G	A2756G	-/-
MTRR	rs1532268	CC		T	C524T	-/-
MTRR	rs1801394	AG		G	G66A	+/-
TCN1	rs34324219	CC		A	901G>T	-/-
TCN2	rs526934	AA		G		-/-
TCN2	rs1801198	GG		G	c.776G>C	+/+
TCN2	rs9606756	AA		G	67A>G	-/-
MAT1A	rs72558181	CC		T	791G>A	-/-
PEMT	rs7946	TT		T	G5465A	+/+
PEMT	rs3760188	CT		T	29420C>T	+/-
CHDH	rs12676	AC		A	G233T	+/-
CHDH	rs9001	TT		G	A119C	-/-
ALDH7A1	rs13182402	AG		G	395T>C	+/-
BHMT	rs3733890	GG		A	716G>A	-/-
DMGDH	rs121908331	TT		C	326A>G	-/-
ADA	rs73598374	-		T	G22A	NC
ADORA2A	rs5751876	-		T	C1976T	NC
ADORA2A	rs2236624	CC		T		-/-
ADORA2A	rs35320474	II		I	Del/Ins	+/+
PON1	rs662	TC		T	575A>G	+/-
PON1	rs854560	AA		T	L55M	-/-
PON2	rs7493	GG		C	896C>G	-/-


Methionine
(Methyl-Homocysteine)
↑ GSH, ↓ sulphur, fasting
Magnesium, Potassium, ATP
MAT1A
info
↑ ROS, nitric oxide, inflammation, infection
SAM
donates methyl groups to many genes
Glycine
↑ lead, mercury, female, aging, fasting
GNMT
SAM
↓ SAM, ↑ 5-MTHF, infection
Sarcosine
DMGDH
B2
dehydration
↓ folates
DMG
Zinc
BHMT
↑ betaine, ↑ choline, ↓ methionine, ↓ Hcy
↑ DMG, ↑ SAM, ↑ methionine, ↓ B6
Betaine
Cobalamin
arsenic, cadmium, lead, mercury, ↑ acetaldehyde, nitrous oxide, ROS, H_2O_2, inflammation, ↓ B12, ↓ GSH, NO, aluminum
THF
Zn
MTR
Methyl THF
MTRR
SAM, B2, B3
↑ ROS
↓ methionine,↓ zinc, ↑ dopamine, ↑ SAM
Cobalamin
TCN1
TCN2
folic acid
B3, B6
ALDH7A1
↑ H_2O_2
pregnancy, dehydration
Betaine aldehyde
B2
CHDH
↑ SAM, methionine, choline, estradiol
PEMT
SAM
(these two use 80% of SAM)
↓ SAM, ↑ SAH
↓ copper, ↑ excitotoxicity
Magnesium
Choline
CDP-Choline
CEPT1
Phosphatidylcholine
↑ arachidonic acid
SAH
GAMT
info
SAM
↑ ROS, ammonia, fasting
↓ arginine, ↑SAH,↓ SAM, atorvastatin (Lipitor)
Creatine
fasting
B3
AHCY
↑ copper
↑ Hcy, ↓ MTHFR, CBS or MTR function, ↓ B6, folates, B12
ATP
MARS
↓ Hcy, ↑ folates, B6, B12
HOMOCYSTEINE
extracellular
Homocysteine Thiolactone
Adenosine
ADORA
Adenosine Receptor
↑ ROS, inflammation, nitric oxide, vitamin A, infection
Zinc
ADA
info
copper, mercury, ↓ inflammation, curcumin, ginger
to Uric Acid
selenium, exercise, favonoids, curcumin, resveratrol
barium, cadmium, cobalt, lead, lathanum, mercury, smoking, infection
Calcium
PON2
PON1
Organophosphates
excreted via urine
B6, Serine, Heme
CBS
↑ zinc, ↑ SAM, ↑ ROS, ↑ H_2O_2, inflammation, LPS, ↑ vitamin D, infection
↓ ROS, ↓ protein, ↓ SAM,↑ NO, ↑ GSH
H_2S
Cystathionine
(to Transsulfuration pathway)
Testing Key
Gene/ Enzyme
Not Checked
Checked, Nothing found
Symbols and Colors
Cofactor
Increases Activity
Decreases Activity
Slow
Intermediate
Fast
Complicated
Checked, nothing found, info available!

DR. HYMAN+

Nutrient Analysis: ION40 Plasma Panel

1. Looks at nutrient status to determine missing cofactors and coenzymes for histamine metabolism.
    a. Copper - DAO coenzyme
    b. Homocysteine-for HNMT
    c. MMA- B12 for HNMT
    d. FIGLU- for HNMT
    e. Methionine- for HNMT
    f. Cystine- for HNMT
    g. Microbial Metabolites- for Intestinal Health

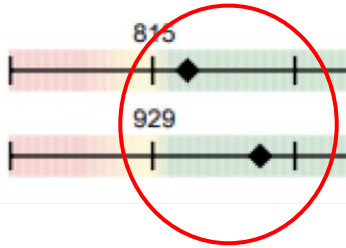
Nutrient Elements

Erythrocytes (packed cells)

1.	Potassium	2,991	2,672	2,303 - 3,374 ppm
2.	Magnesium	42	44	34 - 63 ppm
3.	Calcium*	37	44	24 - 65 ppm

Plasma

4.	Zinc	841	815	643 - 1,594 ppb
5.	Copper	1,032	929	753 - 1,920 ppb



Homocysteine Assay - Plasma

Methodology: Enzymatic Assay

Ranges: Ages 13 and over.

1.	Homocysteine	Hcy	13.2		3.0 - 14.0 nmol/mL

Nutrient Markers

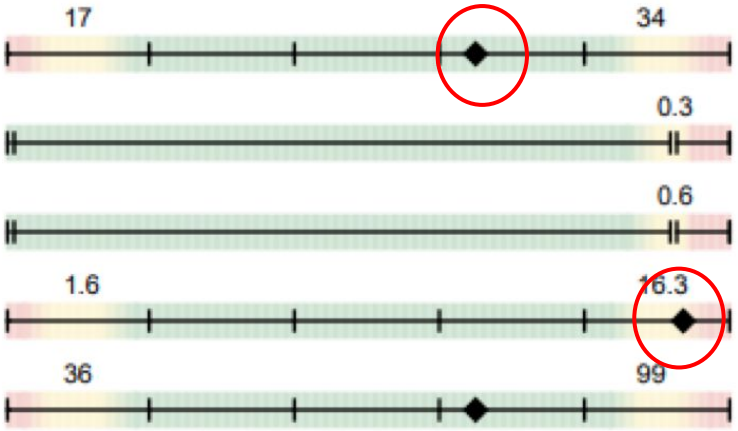
Methylation Cofactor Markers

(B12, Folate)

20.	Methylmalonate	MMA	1.8		<= 2.3
21.	Formiminoglutamate	FIGLU	0.5		<= 2.2

Sulfur Amino Acids (Glutathione - related)

26.	Methionine	24	14 - 48
27.	Cystathionine	<0.3	<= 0.3
28.	Homocystine	<0.6	<= 0.6
29.	Cystine	21.5	0.8 - 27.5
30.	Taurine	64	29 - 136

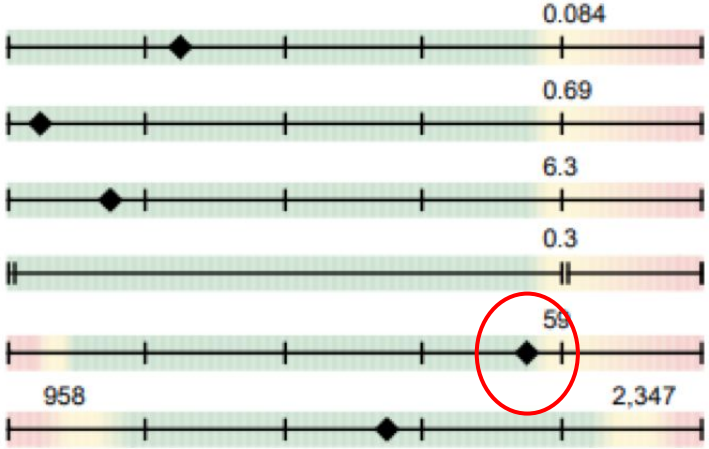


Toxicants and Detoxification

Detoxification Indicators

(Arg, NAC, Met, Mg, Antioxidants)

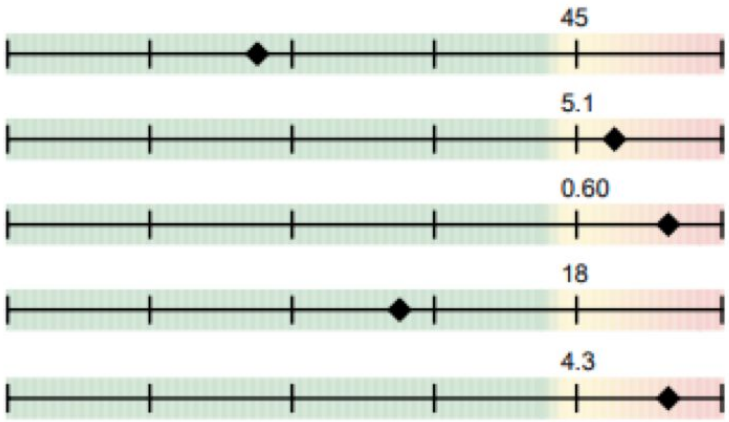
30.	2-Methylhippurate	0.023	0.084	<= 0.192
31.	Orotate	0.12	0.69	<= 1.01
32.	Glucarate	2.4	6.3	<= 10.7
33.	α-Hydroxybutyrate	<DL	0.3	<= 0.9
34.	Pyroglutamate	54	59	28 - 88
35.	Sulfate	1,643	958 – 2,347	690 - 2,988



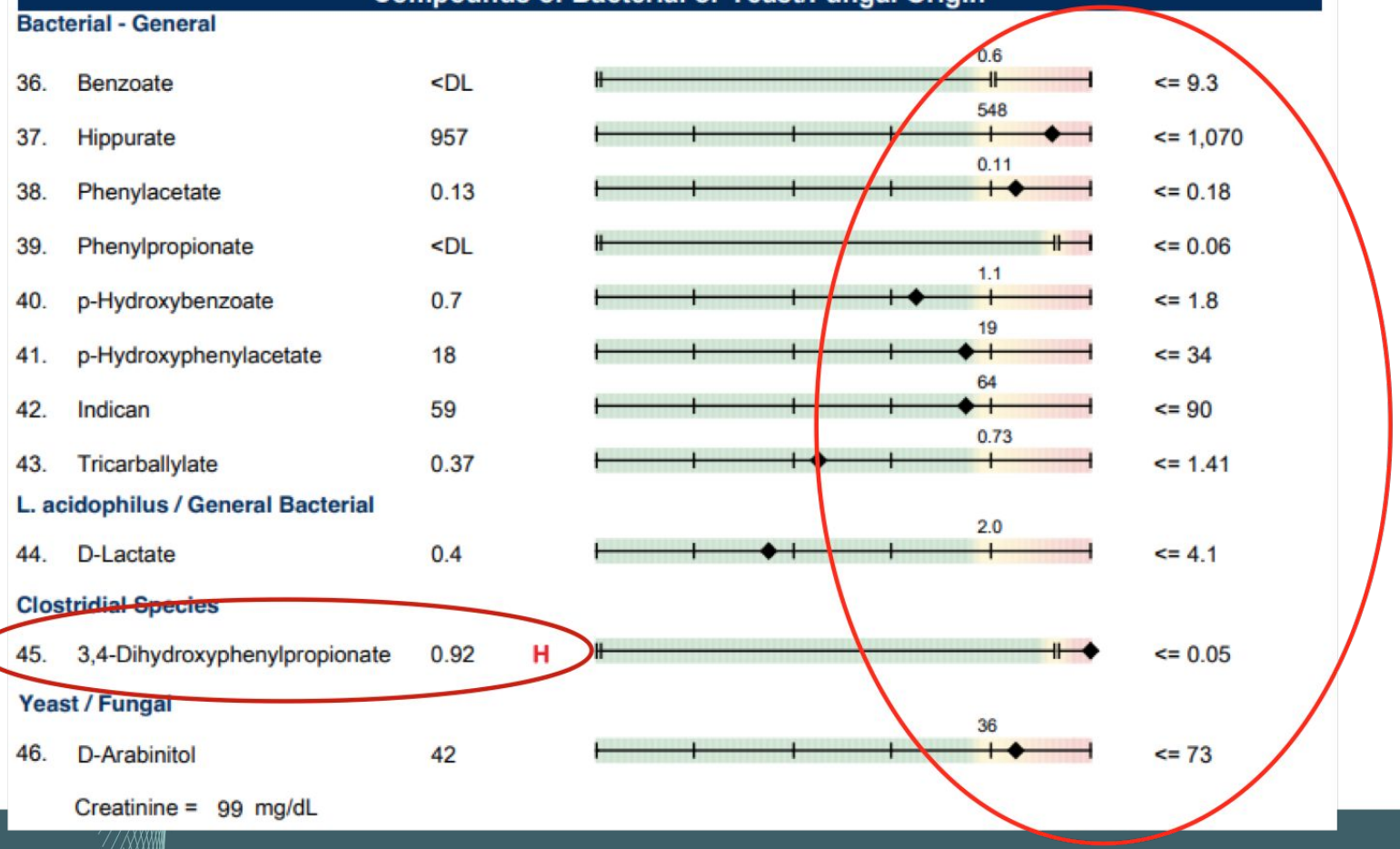
Toxic Elements

Whole Blood

7.	Aluminum	19	45	<= 113 ppb
8.	Arsenic	7.2	5.1	<= 10.0 ppb
9.	Cadmium	0.77	0.60	<= 1.10 ppb
10.	Lead	11	18	<= 29 ppb
11.	Mercury	7.2	4.3	<= 9.8 ppb



Compounds of Bacterial or Yeast/Fungal Origin



Bacterial - General					
36.	Benzoate	<DL		0.6	<= 9.3
37.	Hippurate	957		548	<= 1,070
38.	Phenylacetate	0.13		0.11	<= 0.18
39.	Phenylpropionate	<DL			<= 0.06
40.	p-Hydroxybenzoate	0.7		1.1	<= 1.8
41.	p-Hydroxyphenylacetate	18		19	<= 34
42.	Indican	59		64	<= 90
43.	Tricarballylate	0.37		0.73	<= 1.41
L. acidophilus / General Bacterial					
44.	D-Lactate	0.4		2.0	<= 4.1
Clostridial Species					
45.	3,4-Dihydroxyphenylpropionate	0.92	H		<= 0.05
Yeast / Fungal					
46.	D-Arabinitol	42		36	<= 73

Creatinine = 99 mg/dL

INFECTION AND IMMUNITY, June 1998, p. 2755–2761 Vol. 66, No. 6
0019-9567/98/$04.00+0

Effects of Toxin A from *Clostridium difficile* on Mast Cell Activation and Survival

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Received 11 December 1997/Returned for modification 2 February 1998/Accepted 11 March 1998

Toxins A and B from *Clostridium difficile* are the main cause of antibiotic-associated diarrhea and pseudomembranous colitis. They cause fluid accumulation, necrosis, and a strong inflammatory response when inoculated in intestinal loops. Since mast cells are a rich source of inflammatory mediators, abundant in the gut, and known to be involved in *C. difficile*-induced enteritis, we studied the in vitro effect of toxin A on isolated mast cells. Normal rats sensitized by infection with *Nippostrongilus brasiliensis* were used to isolate peritoneal mast cells (PMC). PMC from naive rats were stimulated with calcium ionophore A23187 as a model of antigen-independent activation, and PMC from sensitized rats were stimulated with *N. brasiliensis* antigens to study immunoglobulin E-dependent mast cell activation. After 4 h, toxin A did not induce release of nitric oxide or histamine in naive PMC. However, 10 ng of toxin per ml caused a significant release of tumor necrosis factor alpha (TNF-α). In contrast, 1 μg of toxin per ml inhibited antigen or A23187-induced histamine release by PMC. Toxin A at 1 μg/ml for 4 h caused disruption of actin which aggregated in the cytoplasm and around the nucleus. After 24 h, chromatin condensation, cytoplasmic blebbing, and apoptotic-like vesicles were observed; DNA fragmentation was documented also. These results suggest that mast cells may participate in the initial inflammatory response to *C. difficile* infection by releasing TNF-α upon interaction with toxin A. However, longer exposure to toxin A affects the release of inflammatory mediators, perhaps because of the alteration of the cytoskeleton and induction of apoptosis. The impaired functions and survival of mast cells by *C. difficile* toxin A could hamper the capacity of these cells to counteract the infection, thus prolonging the pathogenic effects of *C. difficile* toxins.

Calderón GM, Torres-López J, Lin TJ et. al. Effects of toxin A from Clostridium difficile on mast cell activation and survival. Infect Immun. 1998 Jun;66(6):2755-61. doi: 10.1128/IAI.66.6.2755-2761.1998. PMID: 9596744; PMCID: PMC108266.

M. SCHINK[1], P.C. KONTUREK[2], E. TIETZ[1], W. DIETERICH[1], T.C. PINZER[3], S. WIRTZ[3], M.F. NEURATH[3], Y. ZOPF[1]

MICROBIAL PATTERNS IN PATIENTS WITH HISTAMINE INTOLERANCE

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We concluded that the altered occurrence of Proteobacteria (elevated) and Bifidobacteriaceae (greatly reduced), reduced alpha-diversity as well as elevated stool zonulin levels suggest a dysbiosis and intestinal barrier dysfunction in histamine intolerant patients, which in turn may play an important role in driving disease pathogenesis.

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Bifidobacteriaceae, reduced alpha-diversity as well as elevated stool zonulin levels suggest a dysbiosis and intestinal barrier dysfunction in histamine intolerant patients, which in turn may play an important role in driving disease pathogenesis.

Key words: *dysbiosis, food* ... *tinal barrier, diamine oxidase, lactic acid bacteria*

Schink M, Konturek PC, Tietz E et. al. Microbial patterns in patients with histamine intolerance. J Physiol Pharmacol. 2018 Aug;69(4). doi: 10.26402/jpp.2018.4.09. Epub 2018 Dec 9. PMID: 30552302.

nutrients

MDPI

Article

Intestinal Dysbiosis in Patients with Histamine Intolerance

Sònia Sánchez-Pérez [1,2,3], Oriol Comas-Basté [1,2,3], Adriana Duelo [1,2,3], M. Teresa Veciana-Nogués [1,2,3], Mercedes Berlanga [4], M. Luz Latorre-Moratalla [1,2,3,†] and M. Carmen Vidal-Carou [1,2,3,*,†]

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Dysbiosis of the gut microbiota was observed in the histamine intolerance group who, in comparison with the healthy individuals, had a significantly lower proportion of Prevotellaceae, Ruminococcus, Faecalibacterium and Faecablibacterium prausnitzii, which are bacteria related to gut health. They also had a significantly higher abundance of histamine secreting bacteria, including the genera Staphylococcus and Proteus, several unidentified genera belonging to the family Enterobacteriaceae and the species Clostridium perfringens and Enterococcus faecalis.

Citation: Sánchez-Pérez, S.; Comas-Basté, O.; Duelo, A.; Veciana-Nogués, M.T.; Berlanga, M.; Latorre-Moratalla, M.L.; Vidal-Carou, M.C. Intestinal Dysbiosis in Patients with Histamine Intolerance. *Nutrients* **2022**, *14*, 1774. https://doi.org/10.3390/nu14091774

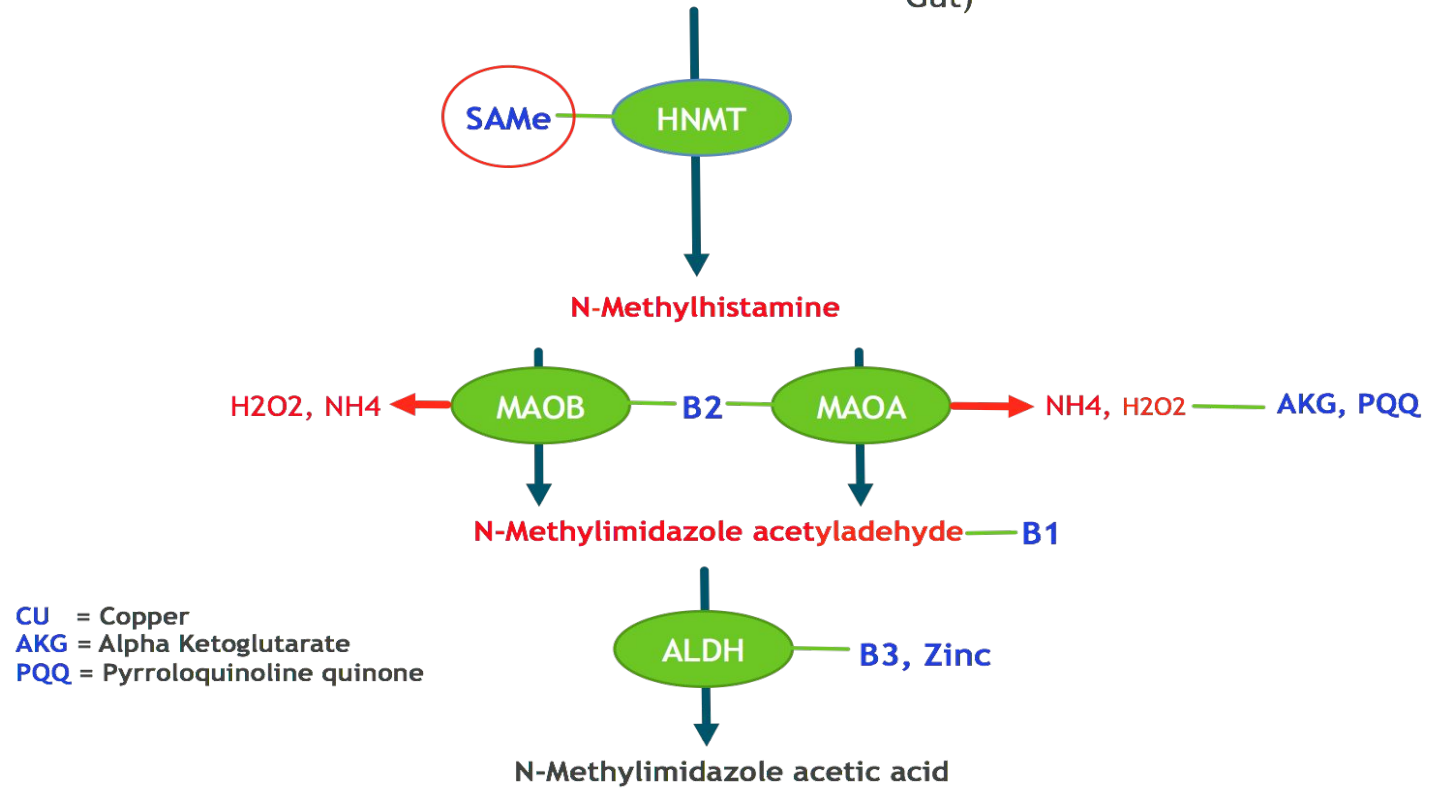
Academic Ed

microbiota of patients with histamine intolerance symptoms and compare it with that of healthy individuals. The study was performed by sequencing bacterial 16S rRNA genes (V3-V4 region) and analyzing the data using the EzBioCloud Database. Dysbiosis of the gut microbiota was observed in the histamine intolerance group who, in comparison with the healthy individuals, had a significantly lower proportion of *Prevotellaceae*, *Ruminococcus*, *Faecalibacterium* and *Faecablibacterium prausnitzii*, which are bacteria related to gut health. They also had a significantly higher abundance of histamine-secreting bacteria, including the genera *Staphylococcus* and *Proteus*, several unidentified genera belonging to the family *Enterobacteriaceae* and the species *Clostridium perfringens* and *Enterococcus faecalis*. A greater abundance of histaminogenic bacteria would favor the accumulation of high levels of adverse effects,

Sánchez-Pérez S, Comas-Basté O, Duelo A et. al. Intestinal Dysbiosis in Patients with Histamine Intolerance. *Nutrients*. 2022; 14(9):1774. https://doi.org/10.3390/nu14091774

Histamine

(From Inside the Body- Mast Cells, Basophils, Absorbed from Gut)



CU = Copper
AKG = Alpha Ketoglutarate
PQQ = Pyrroloquinoline quinone

Actions for 70 Yr Female

1. REDUCE the IRRITANTS in the gut.
    a. Lessens histamine burden from foods.
        i. LOW-Histamine Diet Plan
            1. Lower alcohol
    b. Elimination Diet (esp. gluten and dairy)
            1. Lessens mast cell and basophil activation which reduces histamine.
    c. Balance Gut Microbes
        i. Probiota HistaminX
        ii. FloraStor
        iii. Culturelle

Actions for 70 Yr Old Female

1. Nourish the Pathways the metabolize Histamine
    a. Increase Cofactors and Coenzymes and DAO
        i. HomocysteX Plus
            1. B12 1000mcg mixture adenosyl- and methylcobalamin
            2. 5-MTHF 800 mcg DFE
            3. Trimethylglycine (TMG) 700mg
            4. Riboflavin-5'-Phosphate (B2) 25mg
            5. Pyridoxal-5'-Phosphate (B6) 15mg
        ii. Histamine Block
            1. Diamine Oxidase (DAO) 4.2mg (10,000HDU) at each meal

RESULTS

1. Complete resolution of headaches
2. Bowels have normalized
3. Has not had eczema or “burning lips”
4. Did not complain of mood initially but…noticed mood and energy increased tremendously