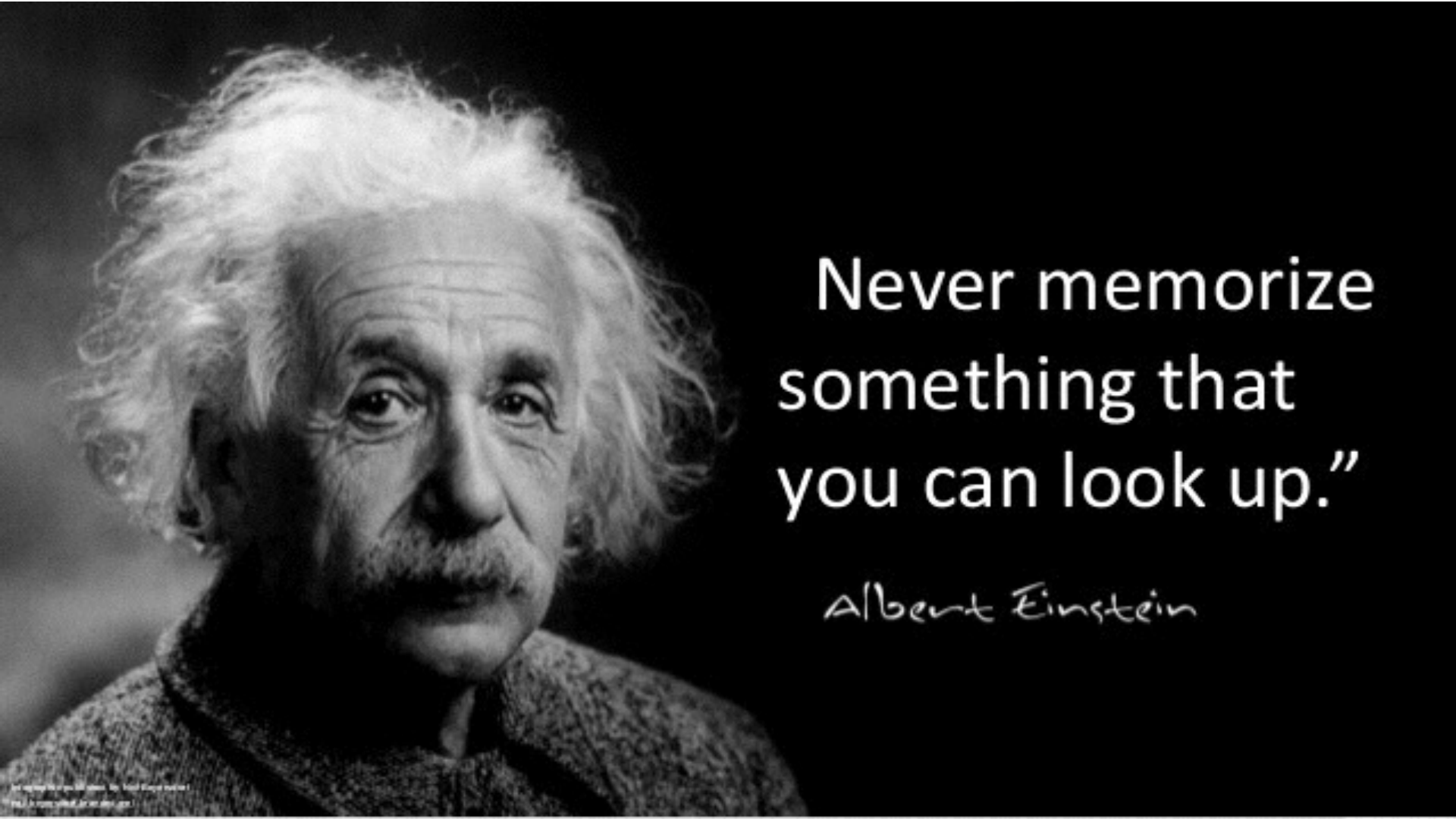
Workshop 1:

Single Pathway Observations

Disclosure:

Relationship with commercial interests - None
Disclosure of commercial support - None
Conflict of interest - None


Never memorize
something that
you can look up.”
Albert Einstein

Errors

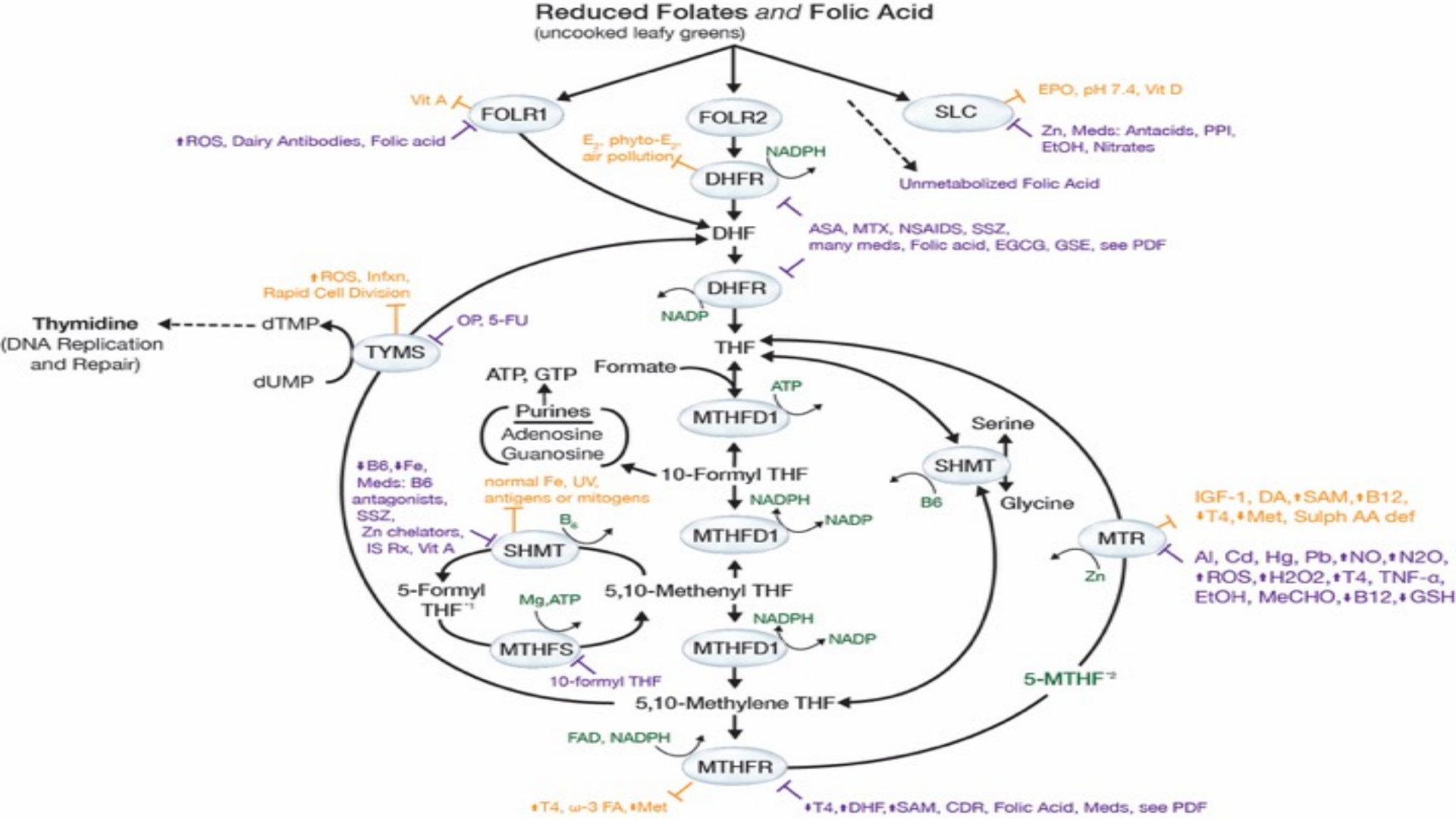
PAPSS1 and 2: GSH supports it

GNMT: high MTHF inhibits. Low speeds

ASMT: N-acetylserotonin supports – not inhibits

Start Digging

Let's Solve This: 4 + ___ = 10


Reduced Folates and Folic Acid
(uncooked leafy greens)
Vit A
FOLR1
↑ROS, Dairy Antibodies, Folic acid
FOLR2
E2, phyto-E2, air pollution
NADPH
DHFR
SLC
EPO, pH 7.4, Vit D
Zn, Meds: Antacids, PPI, EtOH, Nitrates
Unmetabolized Folic Acid
DHF
ASA, MTX, NSAIDS, SSZ, many meds, Folic acid, EGCG, GSE, see PDF
DHFR
NADP
THF
↑ROS, Infxn, Rapid Cell Division
Thymidine
(DNA Replication and Repair)
dTMP
dUMP
TYMS
OP, 5-FU
ATP, GTP
Formate
Purines
Adenosine
Guanosine
ATP
MTHFD1
Serine
SHMT
Glycine
B6
10-Formyl THF
↓B6, ↓Fe, Meds: B6 antagonists, SSZ, Zn chelators, IS Rx, Vit A
normal Fe, UV, antigens or mitogens
B6
SHMT
NADPH
NADP
MTHFD1
IGF-1, DA, ↑SAM, ↑B12, ↓T4, ↓Met, Sulph AA def
MTR
Zn
Al, Cd, Hg, Pb, ↑NO, ↑N2O, ↑ROS, ↑H2O2, ↑T4, TNF-α, EtOH, MeCHO, ↓B12, ↓GSH
5-Formyl THF-1
Mg,ATP
5,10-Methenyl THF
MTHFS
NADPH
NADP
MTHFD1
10-formyl THF
5-MTHF-2
5,10-Methylene THF
FAD, NADPH
MTHFR
↑T4, ω-3 FA, ↑Met
↑T4, ↑DHF, ↑SAM, CDR, Folic Acid, Meds, see PDF

Folate

Your patient is taking folic acid.

What are three things you should tell them?

1. Blocks folate transport
2. Blocks folate receptors
3. Contributes to MTHF deficiency
   Slows DHFR

Folate

Is folic acid found in leafy green vegetables?

No.

Folate

The lab you work with has ‘serum folic acid’ on their website.

You also work with another lab that measures ‘serum folate’.

What are they both really measuring?

All types of folate – folic acid, MTHF, Folinic acid

Folate

Patient gets a high serum folate test back.

What does it tell you about folate?

Tells you it is high, but you don’t know which form.

Folate

Patient has high serum folate, high MCV/high MCH.

What could be a reason?

Low B12

Folate

Patient has low platelets, low energy, memory issues and hair loss.

What type of folate does she most likely need?

Folinic acid

Folate

Patient has high homocysteine.

What type of folate does she most likely need?

MTHF

Folate

Patient was prescribed methotrexate.

Doctor said to take folic acid because they noticed low platelets.

What do you tell the prescribing doctor?

Need folinic acid

Folate

During times of oxidative stress and infections, does your patient burn through more or less folate?

Which type specifically?

More

Folinic acid

Folate

Patient is taking 15 mg of Deplin and feeling no difference at all.

What could be a reason?

There are a few.

Name four.

1. Folate receptor antibodies.
2. Low B12.
3. Still taking folic acid
4. Blocked receptors.
7. Blocked MTR
8. High ROS
9. Antacids

Folate

Your pediatric 9 yr old patient struggling with attention and low cognitive ability is consuming non-organic apples and apple juice.

What compound are you concerned about which is impacting their folate pathway?

Organophosphates

Folate

What is a potential benefit of having the MTHFR polymorphism?

Think within the Folate pathway only.

Conserves folate for DNA repair and Purines.

Folate

If someone is exposed to the sun, what type of folate are they going to
burn through and why?

Folinic acid. Skin cell repair and regeneration.

Folate

Why is high dose EGCG useful in cancer treatments?

Think folate pathway.

Blocks DHFR.

Folate

You know that pregnant women shouldn’t take folic acid.

What type of folate do you recommend for pregnancy and why?

Folinic acid and MTHF.

Support DNA synthesis and methylation.

Folate

Some people say we have to take folic acid in order to provide other forms of folate like THF.

Is this true or false?

Why?

False.

Two way reactions.

Folate

Your 40 yr old female patient found out they have MTHFR C677T and is freaking out a bit. They have no health issues at all, are eating a solid healthy diet with considerable leafy green vegetables every day. Fasting serum homocysteine level is 8.

How much MTHF do you recommend they take every day?

None. Take as needed only.

Folate

When you prescribe MTHF, what do you tell your patient could happen and if it does, what do they do to reverse it?

Side effects.

Stop and take niacin.

B12 Focus

What does a ‘serum B12 test’ tell you in terms of vitamin B12 – specifically?

Nothing really. Just a bunch of B12.

B12 Focus

Patient’s MCV/MCH is high. You give methylcobalamin. Month later you recheck. No change.

How could this be?

Low folinic acid.

B12 Focus

Your patient is not supplementing with B12 at all yet their B12 levels are sky high.

What could cause this?

Name two reasons.

1. SIBO
2. Low folate
3. Blocked MTR
4. Low Glutathione
5. Cancer

B12 Focus

Your patient comes back with elevated urinary methylmalonic acid.

Which form of B12 are you going to use?

Adenosylcobalamin

B12 Focus

You give your patient methylcobalamin. They get worse.

What could be one mechanism why this happens?

Focus on B12 recycling.

1. High ROS
2. Low glutathione
3. Low FAD, NAD, SAM

Methylation Cycle

Your patient's homocysteine level is 41.

You've tried high dose MTHF and methylcobalamin.

What else could you try?

1. TMG
2. B6
3. Zinc
4. GSH

Methylation Cycle

What does high ROS do to the Methylation cycle?

Why would it do this?

1. Shifts homocysteine to GSH
2. To protect the system against pathogens

Methylation Cycle

What is a useful intervention to reduce SAH which requires no supplements or meds?

Fasting

Methylation Cycle

How do you slow down homocysteine from going to SAH and MARS?

1. B6
2. Fasting
3. MTHF / B12
4. MTR restoration

Methylation Cycle

What else besides low SAM will slow PEMT?

What are possible consequences for this in women?

1. Low estrogen.

Fatty liver.

Weak cell membranes.

Low choline.

Methylation Cycle

What medication breaks down homocysteine thiolactone?

Valtrex

Methylation Cycle

If homocysteine is elevated in your patient, where is it going?

Name two places.

1. SAH
2. MARS (haha)

Methylation Cycle

You don’t want to use methyl donors on your patient this early in the treatment but you want to support their methylation right away.

What two nutrients do you consider using and why?

1. PC
2. Creatine

Methylation Cycle

Who uses more methylation by weight – a 10 yr old child average healthy kid or an average non stressed non drinking middle aged man?

10 year old kid. Growing.

Methylation Cycle

Who uses more methylation – a pregnant woman or someone who is stressed out and drinks alcohol?

Both using a lot.

Methylation Cycle

Who uses more methylation – a middle aged man on vacation or a middle aged man stressed out at work?

Stressed out guy.

Methylation Cycle

Patient is going into the doctor and they have to use nitrous oxide.

What nutrients do you provide the patient before and after? Why?

1. Liposomal glutathione
2. Methylcobalamin
3. Protein meal night before and after with salad.

Why? Because nitrous ruins B12 and MTR gets blocked.

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Methylation Cycle

Thirty-five yr old woman's homocysteine is 4.5. She wants to get pregnant. Her doctor said her homocysteine is great.

What do you see that's wrong here and what do you tell her?

1. Too low

2. Need more protein. Low Hcy means low GSH and low methylation production.

Methylation Cycle

Your patient is a vegan.

What key nutrients are you concerned about being deficient?

1. Choline
2. B12
3. Folate if not healthy diet.

Methylation Cycle

Your patient is a vegan. They are complaining of constipation and their HDL and triglyceride levels are low.

What immediately comes to mind?

Fatty liver

Methylation Cycle

Name one reason why some people react to protein – specifically methionine.

High ROS

Table 1
Proteins and peptides with activity altered by methionine oxidation

Adrenocorticotropic hormone[a] (*38*)
α-1-antitrypsin (*39–41*)
α-2-antiplasmin (*42, 43*)
α-2-macroglobulin (*14, 44*)
Amyloid beta peptide (*45, 46*)
Antiflammin (*47*)
Antithrombin III (*42*)
Apolipoprotein (*48, 49*)
Bombesin (*50*)
Bugarotoxin (*51*)
Calcitonin[a] (*52*)
Calmodulin[b] (*30, 53*)
Chemotactic peptide f-Met-Leu-Phe[b] (*54, 55*)
Cholecystokinin (*56*)
Chorionic somatomammotropin (*57*)
Chymotrypsin[b] (*58, 59*)
Complement C5[b] (*54, 60*)
Cytochrome *c* peroxidase (61)
Cytochrome *c*[a] (*62*)
Echistatin (*63*)
Enkephalin[a] (*64*)
Factor VII (*65*)
Fibronectin (*66*)
Flagellin[a] (*67*)
inhibitor (*86*)
Glucagon (*68*)
Glutamine synthetase (*1*)
Growth hormone (69–71)
Hemoglobin (*72*)
HIV-2 protease (*73*)
Interferon α-2b (*74*)
Interferon γ (*16*)
Interleukin 6 (*75*)
Keratinocyte growth hormone (*76*)
Lipoxygenase (*18*)
Lutropin (*77*)
Lysozyme[b] (*78*)
Mucus proteinase inhibitor (*79, 80*)
Neuropeptide Y (*81*)
Ovoinhibitor[a] (*82*)
Parathyroid hormone[a] (*83, 84*)
Pepsin[b] (*85*)
Phosphoglucomutase[b] (*58*)
Plasminogen activator inhibitor (*86*)
Potassium channel (*26, 87*)
Prolactin (*88*)
Ribonuclease[b] (*58*)
Ribosomal protein L12[b] (*89, 90*)
Secretory leukocyte proteinase inhibitor (*91*)
Small heat shock protein (*92*)
Snake venom cardiotoxin[b] (*93*)
Stem cell factor (*94*)
Subtilisin[a] (*95*)
Thrombomodulin (*96*)
Tissue plasminogen activator (*16*)
Tryptophanase (*97*)
Vasoactive intestinal peptide (*56*)

Oxidation of Methionine in Proteins: Roles in Antioxidant Defense and Cellular Regulation

Phosphofructokinase is a key enzyme in sugar metabolism; Kemp and colleagues pointed out that an active site methionine residue is conserved in all phosphofructokinases examined (*28*). Substitution of the conserved methionine by leucine caused a substantial decrease in catalytic efficiency. Oxidation of that methionine would likely have a similar effect, although this has not yet been investigated.

References

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References may be found here:
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Workshop 2:

Single Pathway Observations (cont'd)

Disclosure:

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Disclosure of commercial support - None
Conflict of interest - None

Transulfuration Cycle

Your patient has a low homocysteine level – 4.

What are two reasons for a low homocysteine?

1. Poor absorption
2. Low protein intake
3. High need for glutathione
4. High need for methylation

Transulfuration Cycle

Your patient did not respond to B12, MTHF or TMG to reduce their homocysteine. But they did with B6.

Why?

Supported CBS and glutathione production which opened up MTR.

Transulfuration Cycle

You gave your inflamed patient glutathione. They felt worse from it.

Name two reasons why.

1. Negative feedback to GCLC and increased cysteine which pushed it to cystine.

2. They increased their levels of GSSG because they were low in B2.

3. They increased their levels of glutamate because less got used to make GSH and they already have NMDA activation.

Transulfuration Cycle

You gave your inflamed patient something which blunted inflammation and lowered TNFa. You gave them glutathione again with vitamin B2. Still reacting.

Name 1 reason why.

1. High arsenic.

Arsenic elimination: GSH + SAMe + Avoidance (filtration, organic)

Transulfuration Cycle

Glutathione gets exported from the cell for various protective reasons – such as supporting cell membrane integrity, nutrient transport and apoptosis.

What happens to the exported glutathione during times of high ROS?

What lab marker demonstrates this happening?

Broken down GGT

Transulfuration Cycle

One of your patients does exceptional on NAC and it raises their glutathione levels well. Yet another one, the NAC does nothing at all. Glutathione levels stay low.

What do you suspect?

1. Mold

2. Infections

Transulfuration Cycle

Why is inflammation good in the transsulfuration pathway?

Makes GSH

Transulfuration Cycle

Why is inflammation bad in the transsulfuration pathway?

1. Blocks CDO1 and if GSH is high, then can make cystine.

2. Slows G6PD and can’t recycle GSSG to GSH.

Transulfuration Cycle

Patient is on a low sulfur diet because they feel better on it. When they eat sulfur, they get pain, gas and irritable.

Name two reasons why they feel better.

1. Lower cystine

2. Lower sulfites

Transulfuration Cycle

This patient continues on the low sulfur diet and is frustrated by it.

What nutrient(s) could you recommend so they likely could introduce some sulfur back into their diet?

1. PQQ
2. Molybdenum
3. B2
4. Anti-microbials
5. Hydroxocobalamin
6. Calcium D Glucarate
(careful with hypothyroid and low estrogen)

Transulfuration Cycle

The patient continues to be low sulfur but you get a call from her saying that her chest is tight and having some difficulties breathing. Her other PCP says it's not asthma and doesn't know what to do.

What is happening?

1. Low H2S
2. Low GSH

Transulfuration Cycle

What do you do for the patient?

1. Stop low sulfur diet.
2. Introduce NAC slowly. Pulse.

Transulfuration Cycle

Your patient was low sulfur for so long, she's a bit constipated and worse from fatty foods. She didn't used to have this problem.

What may have happened?

Low taurine synthesis.

Transulfuration Cycle

Your patient comes to you and tells you their urine wreaks of sulfur.

What do you tell them to do?

1. Slow down on sulfur.
2. Take molybdenum until smell goes away.
3. Consider CDSA or urinalysis

Transulfuration Cycle

You gave your patient Mn to support their SOD2. It actually made them worse.

Why?

1. Increased H202 and they are low in GSH, high in GSSG

2. They are fighting an infection and O2- is needed to fight the infection .

3. Mn is a cofactor for other enzymes and high is associated with neurological issues

4. Bile is sluggish. Mn elimination is via bile.

Transulfuration Cycle

What are potential consequences of giving too much molybdenum?

Give two reasons.

1. High uric acid
2. High superoxide
3. Low PAPS

Transulfuration Cycle

Your patient feels better. You forgot to tell them – don't exercise yet. They exercise. They feel worse and takes them weeks to recover. What is one reason for this – based on oxidative stress.

What happened and how can you fix it?

High production of H202 due to low GSH

1. Antioxidants – liposomal glutathione or PQQ.
2. Don't exercise so hard.
3. Consider D-Ribose, electrolytes, creatine

Transulfuration Cycle

Your patient swims in pools often. What are you concerned about?

PAPS synthesis

Dopamine / Norepinephrine

Your patient took SAMe before bed and for the first time, got knocked out and had a fantastic sleep.

Why? What happened?

Cleared catecholamines

Dopamine / Norepinephrine

You had such success with this patient, now you gave it to another and you received an angry message the next day, “Man! What did you give me!? I couldn’t fall asleep at all and actually found myself to be more irritable. I’m scared I wont be able to sleep again tonight!”

What happened?

Their catecholamine pathway is blocked due to high SAH.

SAMe Test → Call it this so they are ready for consequences.

Dopamine / Norepinephrine

What could you have done immediately to reduce the potential insomnia from SAMe?

Tell them to take niacin 50 mg – 150 mg.

Dopamine / Norepinephrine

Your patient with COMT V158M ++ is terrified to take SAMe as it is a methyl donor.

What do you tell them?

It’s the cofactor. You need it.

Dopamine / Norepinephrine

Your patient who had tremendous success falling asleep came back. “Doc. I find myself sleeping all the time. I’m teary, crying all the time and have no urge to do anything.”

What do you ask?

What do you then do about it?

Are you still taking SAMe? Ie. Catecholamine deficiency.

1. Pulse SAMe.
2. Give Tyrosine.
3. Increase protein.

Dopamine / Norepinephrine

Parent comes in. “Doc. My kid was doing so well on the GAPS diet. Now he’s irritable, can’t sleep and his body odor is something else. We’re still doing GAPS but I am not sure it is right for him anymore.”

What do you say is happening?

Name three major things.

1. Sulfites
2. Ammonia
3. Tyrosine
4. Low B6
5. Methionine Sulfoxide
6. Cystine
7. Hydrogen Sulfide

Dopamine / Norepinephrine

Who is more likely to burn through serotonin? Men or women?

Women. X linked.

Dopamine / Norepinephrine

Your patient is taking Ritalin to increase dopamine levels.

What compound are you concerned about harming their brain?

Quinone.

Dopamine / Norepinephrine

“Doc, my kid and I can’t think. We’re just classic ADHD.”

What nutrient do you try first right in your clinic to see if it helps?

Tyrosine

Dopamine / Norepinephrine

You find that it helps them.

What dietary change do you tell them to do?

1. Increase protein.
2. Decrease carbs.

Dopamine / Norepinephrine

What SNPs do you think the kid with ADHD has? Why?

1. Fast COMT
2. Wild type MTHFR
3. Fast MAOB / MAOA

Dopamine / Norepinephrine

You recommend your next patient to eat a high protein meal before bed. They do it. They report back that they have more energy and can't fall asleep now.

What SNPs do you suspect?

1. Slow COMT
2. Slow MAOA / Slow MAOB

Dopamine / Norepinephrine

You recommend your patient to eat a high protein meal before bed. They do it. They report back that they have more energy and can't fall asleep now.

What do you tell them to do? Why?

1. Lower protein. Have a low protein dinner.
2. Protein is high in tyrosine and supporting dopamine.
3. Consider SAMe Test

Dopamine / Norepinephrine

Patient is also taking quercetin by the bucket load for their allergies. They've noticed increased irritability.

Why?

1. MAOA inhibitor.
2. COMT inhibitor.

Dopamine / Norepinephrine

What do you tell them to try instead?

1. Neti pot
2. SAMe
3. Fish Oil
4. Air purifier
5. Probiotics

Dopamine / Norepinephrine

Every month, like clockwork, your patient struggles with horrendous moods just before menses.

Why?

1. High estrogen spike

2. Increased catecholamines

Dopamine / Norepinephrine

Every month, like clockwork, your patient struggles with horrendous moods just before menses.

What SNPs do you suspect?

1. Slow MTHFR
2. Slow COMT
3. Slow MAOA / MAOB

Serotonin / Melatonin

Your patient took SAMe before bed and for the first time, got knocked out and had a fantastic sleep.

Why? What happened?

Made melatonin from serotonin.

Cleared catecholamines.

Serotonin / Melatonin

Patient can’t fall asleep.

What lifestyle habit are you asking about?

1. Light
2. Electronics.

Serotonin / Melatonin

You give your patient 5-HTP and she feels great from it. Another one takes it and feels absolutely nothing.

What is your next step for the one who doesn't feel anything?

Vitamin B6

Serotonin / Melatonin

Your patient is super stressed out and can't fall asleep.

What do you tell her?

1. Stress increases tryptophan loss and lowers serotonin and thus melatonin.

2. Stress uses up vitamin B5. Need to support this during the day.

Serotonin / Melatonin

Your patient was sulfur intolerant and took molybdenum. They got a bit more irritable than usual they tell you.

Why?

Low PAPS

Increased ROS

Serotonin / Melatonin

The 5-HTP initially helped your patient's mood significantly. Now, however, two weeks later, she is feeling more irritable than ever.

Why? Two reasons.

Serotonin slows COMT

Saturated MAOA genes and reduced cofactors downstream

Serotonin / Melatonin

Stressed out patient noticed he is getting more gray hairs.

You explain how this happens.

Increased H202

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Workshop 3:

Intermediate Reasoning

Disclosure:

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Disclosure of commercial support - None
Conflict of interest - None

Folate

Patient just got their MTHFR results back. MTHFR C677T homozygous. They are tired, irritable and struggling with insomnia.

Do you prescribe MTHF on day one or do something else first?

Explain.
No.

Open neurotransmitter pathways first to prevent excess.

Evaluate lifestyle, diet, sleep, environment, meds, supplements first.
Electrolytes

Folate

Your patient is taking 4 mg of folic acid. She asks you how much additional MTHF she should take for her pregnancy.

What do you tell her?

Stop Folic acid.

Use natural folates – folinic acid and MTHF

Folate

How is folate connected to the Biopterin synthesis and recycling pathway?

Name three reasons.

1. GTP
2. homocysteine/ADMA
3. glutathione production via SAMe
4. DHFR recycling BH2-> BH4

B12 Focus

Name the three types of vitamin B12 that are available and what each one does. (Cyanocobalamin is not one).

Hydroxocobalamin → reduces NO, H2s and homocysteine reduction
Methylcobalamin → supports methylation and homocysteine reduction
Adenosylcobalamin → reduce MMA and supports mitochondria

B12 Focus

You know that hydroxocobalamin reduces hydrogen sulfide levels.

Describe a couple scenarios where you suspect your patient is struggling with elevations in hydrogen sulfide.

Asthma

Inflammatory bowel disorders

Persistent diarrhea which smells of sulfur

Migraines / headaches (vasodilation type)

B12 Focus

You know that hydroxocobalamin reduces nitric oxide levels.

Describe a couple scenarios where you suspect your patient is struggling with elevations in nitric oxide.

Infections

Asthma

Inflammation

MTHF side effects

Migraines / headaches (vasodilation type)

B12 Focus

Your patient was doing really well with hydroxocobalamin but now they are telling you they have tightness in their chest.

Do you think it could be causing this issue? Why or why not?

Low hydrogen sulfide

B12 Focus

Your patient was doing really well with hydroxocobalamin but now they are telling you they have tightness in their chest.

How do you fix it?

MSM

NAC

Stop Hydroxocobalamin

B12 Focus

Your patient was doing really well with hydroxocobalamin but now they are telling you they have higher blood pressure.

Do you think it could be causing this issue? Why or why not?

Low nitric oxide

B12 Focus

Your patient was doing really well with hydroxocobalamin but now they are telling you they have higher blood pressure.

What do you give them to restore healthy blood pressure?

Stop hydroxocobalamin

MTHF

Methylcobalamin

PQQ

Liposomal glutathione

B12 Focus

Two patients who have MTHFR C677T +/+ COMT V158M +/+ are patients of yours. One does really well with methylcobalamin and another one doesn't at all.

Name two reasons why this could be.

1. ROS status
2. Electrolyte status
3. ?

B12 Focus

Your patient is COMT V158M +/+. What form of B12 do you use and why?

Depends on their situation.

Histamine

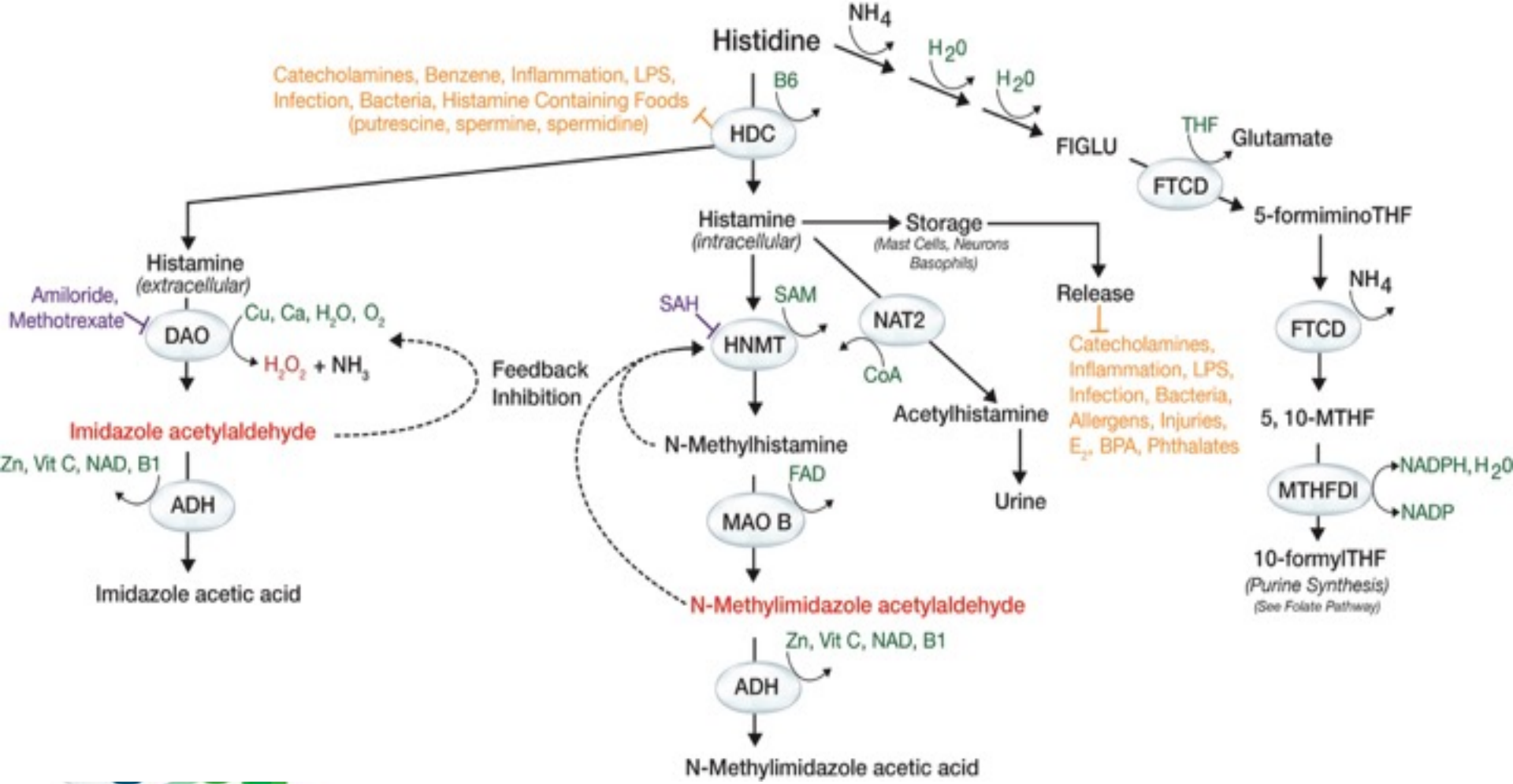
Your patient has gut dysbiosis and taking methotrexate. What gene do you think is dirty?

DAO

Histamine

Your patient heard that SAMe clears histamine. They take it. Feel actually a bit worse. Why?

Feedback inhibition – downstream MAOB and ALD plugged


Histidine
NH_4
H_2O
H_2O
B6
HDC
Catecholamines, Benzene, Inflammation, LPS, Infection, Bacteria, Histamine Containing Foods (putrescine, spermine, spermidine)
FIGLU
THF
Glutamate
FTCD
5-formiminoTHF
NH_4
FTCD
5, 10-MTHF
MTHFDI
$NADPH, H_2O$
$NADP$
10-formylTHF
(Purine Synthesis)
(See Folate Pathway)
Histamine (intracellular)
Storage
(Mast Cells, Neurons Basophils)
Release
Catecholamines, Inflammation, LPS, Infection, Bacteria, Allergens, Injuries, E_2, BPA, Phthalates
Histamine (extracellular)
Amiloride, Methotrexate
DAO
Cu, Ca, H_2O, O_2
H_2O_2 + NH_3
Imidazole acetylaldehyde
Zn, Vit C, NAD, B1
ADH
Imidazole acetic acid
Feedback Inhibition
SAH
SAM
HNMT
NAT2
CoA
Acetylhistamine
Urine
N-Methylhistamine
FAD
MAO B
N-Methylimidazole acetylaldehyde
Zn, Vit C, NAD, B1
ADH
N-Methylimidazole acetic acid

Histamine

Your patient tells you that they are quite positive their histamine related issues are linked to stress. What do you tell them?

Absolutely. Stimulation of HDC and release of histamine.

Histamine

Every month, like clockwork, your patient gets worse asthma and allergies just before menses. Why?

Estrogen stimulates histamine release

Histamine

You really want to check for bacterial infections as you suspect they are contributing to histamine issues in your patient. What marker do you test?

LPS

Histamine

Your patient's homocysteine is elevated at 16. Does this affect their histamine metabolism? Why or why not?

Yes, because SAM is cofactor for HNMT

Histamine

Your patient gets exercise induced asthma. They heard if they support their methylation before exercise, they may not react.

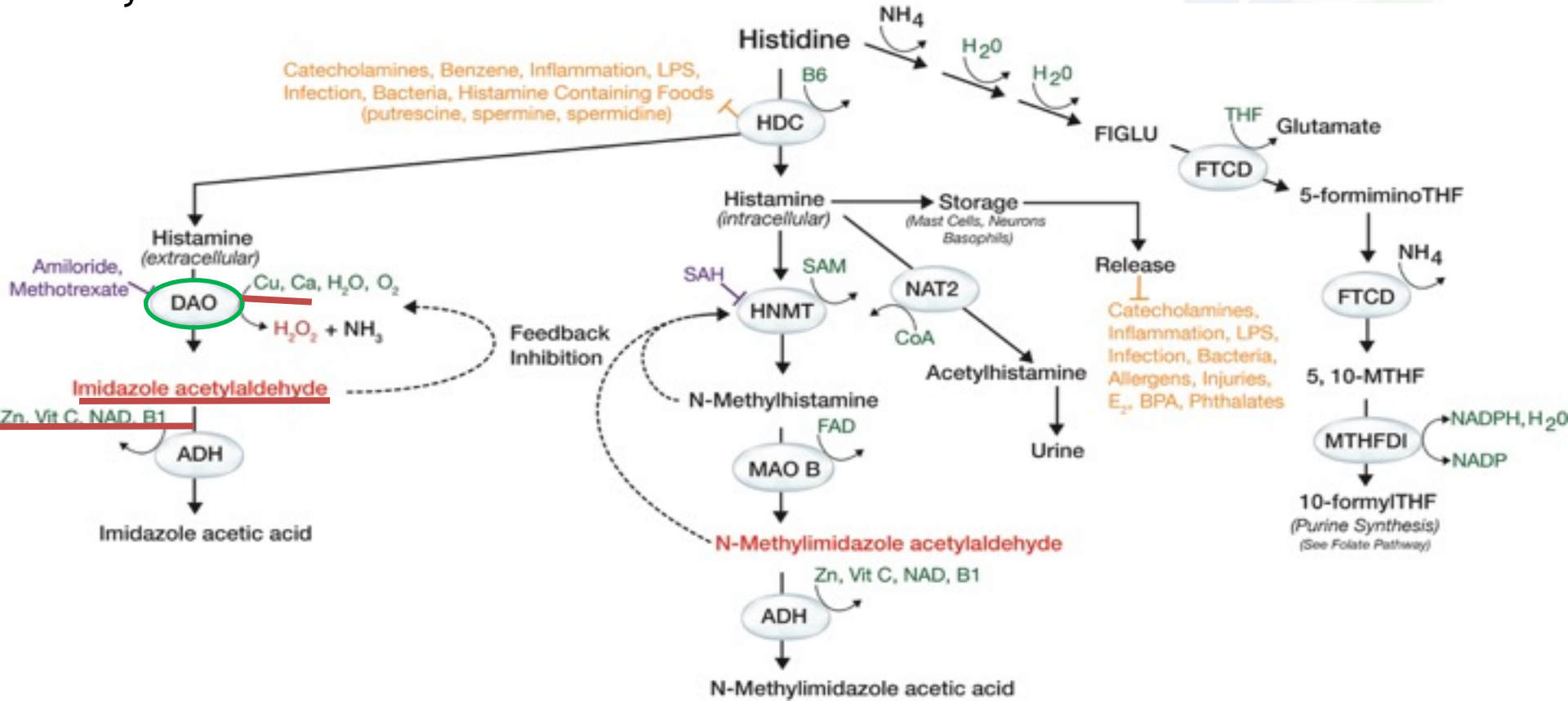
What's a great way to support their methylation prior to exercise? Why?

MTHF and MethylB12

Creatine

Supports methylation cycle and conserves methyl donors

Your patient's struggling from fermented foods and lactobacillus bulgaricus probiotic. They don't get why as their DAO is fine. What do you tell them?



Arginine

Your patient is a vegan and has no idea why they just had a heart attack.

What lab can you order to see their cardiovascular risk?

ADMA

hsCRP

Neopterin

Homocysteine

Fasting insulin

Lipid peroxidation

RBC glutathione

Arginine

Your patient has low arginine. Other amino acids are fine. They eat a ton of protein and don't exercise.

Where is it going? How can you check to see if you're right?

Infections

LPS, vitamin D ratio, neopterin, hsCRP, TNFa

Arginine

An athlete comes in and is taking high amounts of arginine. They are feeling tired from it.

What is going on?

What can you recommend to them to take instead for similar effect?

NOS uncoupling → reactive NO

Creatine, ornithine, beet root powder

Arginine

An athlete comes in and is taking high amounts of arginine. They are feeling tired from it.

How can you improve their ability to take arginine?

Support with liposomal glutathione and PQQ

Arginine

Your patient has COMT V158M ++ and took hydroxocobalamin because they had to since they cannot take methyl donors.

Ever since they feel worse. Cold hands/feet and headaches.

Why?

What do you tell them to do?

They lowered their nitric oxide levels too much.

Stop taking hydroxocobalamin and consider creatine.

Consider the SAMe Test

Arginine

Your pediatric patient has low glutathione, low muscle tone and speech delay.

What nutrient do you consider to support them safely?

Why?

Creatine.

Conserves methylation, supports muscle mass and supports speech.

Arginine

Name all the major genes which consume arginine.

Which ones consume the most during inflammation?

During infections?

During growth and building muscle mass?

iNOS. GAMT

iNOS

Arginine

Name one reason why women have increased CVD after menopause.

Lower estrogen reduces eNOS expression

Arginine

Why happens to iNOS and eNOS if your patient is taking folic acid?

They have reduced expression because of lack of BH4

Arginine

If your patient is deficient in folinic acid, does it affect their eNOS and iNOS?

Why or why not?

Yes because folinic acid supports GTP synthesis and BH4 formation

Arginine

What compound can increase glutamate in the brain?

Why?

Sulfites

Slows expression of GDH

Arginine

On a lab test, what will tell you if ammonia is high in the brain?

Glutamine

Arginine

What helps reduce ammonia in the brain?

What nutrient is really helpful to reduce ammonia?

Mitochondria

Acetyl-L-Carnitine

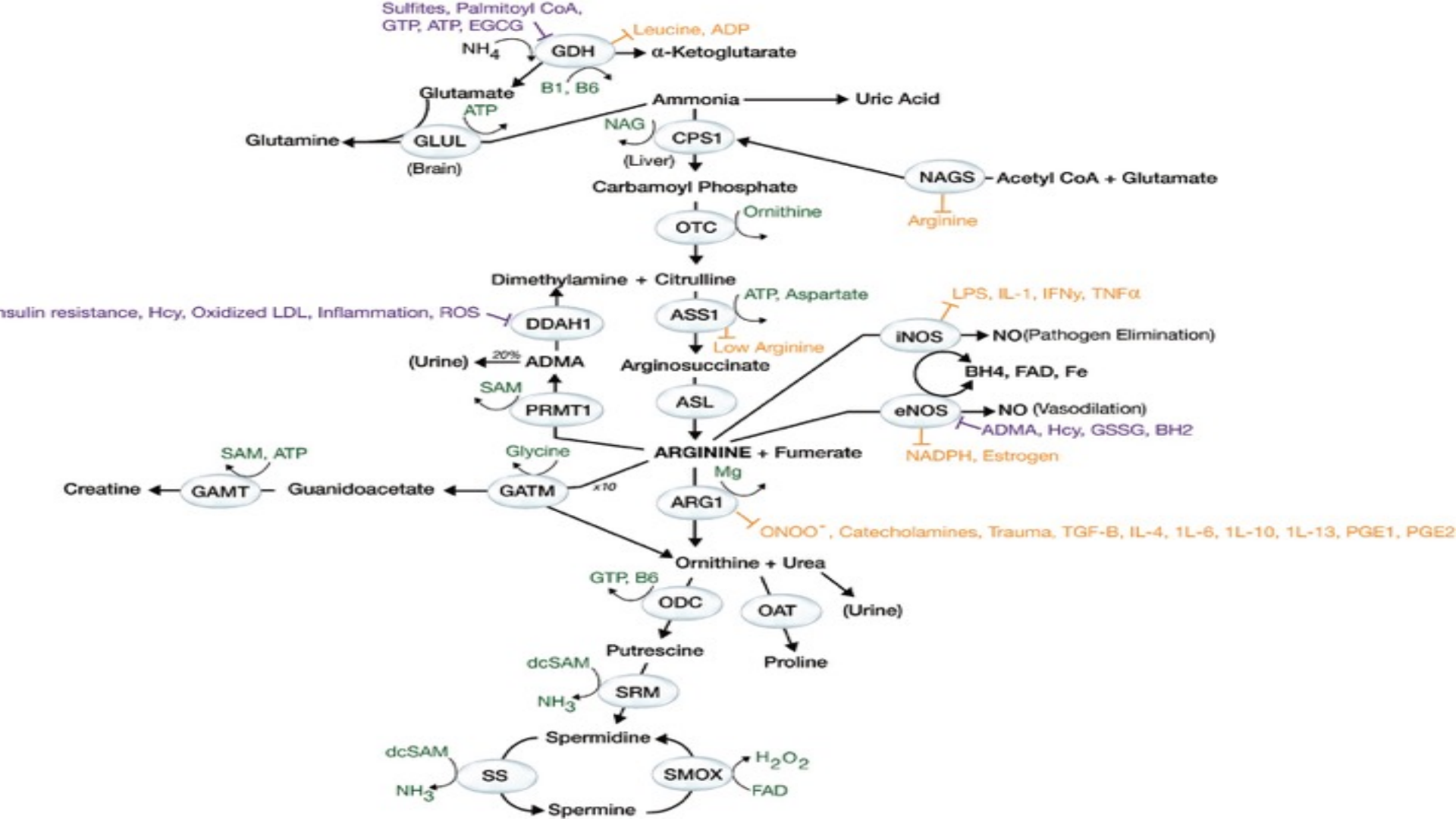
Arginine

Why would folinic acid be something that may contribute to higher glutamate levels in the brain?

What should be done prior to giving folinic acid to stimulate GTP?

Inhibits GDH due to higher production of GTP

Electrolytes, carnitine, B1, B6, molybdenum, watch ECGC and consider intermittent fasting or prolonged fasting or mild exercise (to lower ATP)


Sulfites, Palmitoyl CoA,
GTP, ATP, EGCG
Leucine, ADP
NH4
GDH
α-Ketoglutarate
B1, B6
Glutamate
Ammonia
Uric Acid
ATP
NAG
Glutamine
GLUL
CPS1
(Brain)
(Liver)
Carbamoyl Phosphate
NAGS
Acetyl CoA + Glutamate
Arginine
OTC
Ornithine
Dimethylamine + Citrulline
ATP, Aspartate
LPS, IL-1, IFNγ, TNFα
nsulin resistance, Hcy, Oxidized LDL, Inflammation, ROS
DDAH1
ASS1
iNOS
NO(Pathogen Elimination)
Low Arginine
(Urine)
20%
ADMA
Arginosuccinate
BH4, FAD, Fe
SAM
PRMT1
ASL
eNOS
NO (Vasodilation)
ADMA, Hcy, GSSG, BH2
SAM, ATP
Glycine
ARGININE + Fumerate
NADPH, Estrogen
Creatine
GAMT
Guanidoacetate
GATM
x10
Mg
ARG1
ONOO⁻, Catecholamines, Trauma, TGF-B, IL-4, 1L-6, 1L-10, 1L-13, PGE1, PGE2
Ornithine + Urea
GTP, B6
ODC
OAT
(Urine)
Putrescine
Proline
dcSAM
NH3
SRM
Spermidine
dcSAM
SS
SMOX
H2O2
NH3
FAD
Spermine

Methylation Cycle

What important nutrients are necessary to consider before supporting the methylation cycle?

Why?

Electrolytes
Antioxidants
Antimicrobials
Downstream nutrients
Molybdenum
Adaptogens

Methylation Cycle

Patient is not eating much protein. You measure their lipid peroxidation -> high. SAM:SAH ratio is fine. Glutathione levels are low.

How is it that their homocysteine is normal at 8?

Homocysteine pulled down to make GSH

Methylation Cycle

Another patient comes in not eating much protein, high lipid peroxidation, low GSH yet their homocysteine is 30 and their SAM:SAH is favoring SAH.

Why?

Blocked MTR

Blocked CBS

References

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All diagrams shown have references organized by pathway and gene.

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Workshop 4:

Intermediate Reasoning

Disclosure:

Relationship with commercial interests - None
Disclosure of commercial support - None
Conflict of interest - None

Every month, like clockwork, your obese patient experiences PMS, insomnia and her allergies flare making her asthma worse. Quercetin does not help.

What primary pathway do you suspect is slowed?

Dopamine / Norepinephrine → COMT slowed

How could liposomal or IV glutathione worsen your patient?

Huge headache, difficulty breathing. Sulfites. High glutamate.
High cysteine -> reactive with heavy metals / superoxide.

You knew to support methylation indirectly by giving creatine and phosphatidylcholine. Your patient improved a lot. Now they are showing signs of depression.

What do you do and why?

What could be going on?

Conserving methyl groups -> increasing SAMe -> clearing out catecholamines.

Uridine needed too -> PC -> AC -> high AC -> depression.

With your understanding of all pathways, what primary actions do you need to consider first with your patient before anything else?

1. Basics: stress, sleep, lifestyle, diet, breathing, hobbies, community, movement
2. Infections
3. Glutathione / ROS
4. Electrolytes
5. Heavy metals
6. Gut function / absorption / elimination

Name the Dirty Gene

Carbs. CARRBS! Man get me some of those! My grocery cart looks like I work for the grain and chocolate industry! I feel soo great eating them but I know I shouldn't. When I don't eat them, I get blue and depressed. The problem is I eat these carbs and they pick me up for a moment and then I crash. So what do I do? I eat more of them. I know I can't do this. My friends know as well. I try diets but they just make me feel depressed. I'm sick of gaining weight but I'm stuck! I don't want to be on antidepressants but I certainly know I can't keep on doing this. I fall asleep but I certainly have issues staying asleep.

MAOA fast

How to support a fast MAOA?

Solid protein breakfast – balanced meals

5-HTP as needed

Liposomal glutathione as needed

Inositol as needed

Name the Dirty Gene

I’m freaking out. My dad, uncle, grandma, grandpa all have had significant heart problems at around 50 yrs old. I’m getting there. I don’t want that. My doc checks my heart stuff and all looks ‘ok’ but are they checking what they need to check or are they missing things? I’m needing answers! I love life and this is really weighing on me. Oh – and I have cold hands and feet. This is embarrassing but I’m noticing that I’m starting to have erectile dysfunction.

NOS3

How to support NOS3?

Watch homocysteine

Support healthy glutathione levels

Support arginine levels – ornithine, citrulline, beet root powder

Exercise

Breathing

Name the Dirty Gene

It’s pretty easy to get you startled, anxious or irritated. When irritated, you can get pretty aggressive even though afterwards you feel badly about it. You just can’t help it. Headaches seem to happen especially if eating things like cheese, wine and chocolate. Falling asleep at night is pretty tough but once you do, you sleep pretty soundly through the night.

MAOA slow

How to support a slow MAOA?

Solid protein breakfast – balanced meals

Riboflavin as needed. Limit 5-HTP.

Lithium as needed

Adaptogens as needed

Name the Dirty Gene

Look at that blinking light! Did you see that dog over there?! Man I wish I could read a book but it's just not possible to focus. Multitasking is what I do best but in reality I don't really get much done. Focusing is a bear. Some say I have ADHD. You are definitely an attention seeker – love being the class clown and some say you're addicted to shopping. Hugs are welcomed!

Fast COMT

How to support fast COMT?

Healthy balanced meals – especially with enough protein

Tyrosine as needed

Find activities which you enjoy and are stimulating to you

Understand you may lose focus so give it 20 minutes solid before switching
Keep an eye on addictive behavior – gaming, shopping, drinking, smoking

Name the Dirty Gene

I am so tired of not knowing what I can or can't eat. One meal I'm good and the next I feel awful. Headaches, irritable, sweaty, heart racing, itchy skin, nose bleeds. What the heck! I finally spend a ton of money on food allergy testing and it showed nothing! So frustrated. I keep limiting my foods one by one in hopes that I find out the culprit but it's just a never ending battle.

DAO

How to support DAO?

Limit high histamine foods and drinks

Treat gut infections

Support stomach acid and digestive enzymes and bile acids

Support microbiome with histamine reducing bacteria – bifido / rhamnosis
Adaptogens

Main Symptoms?

Slow COMT with slow MAOA.

High focus and attention

Not a risk taker

Insomnia

Quickly irritated and slow to calm down

Workaholic. Highly productive – when not stressed

Needs a lot of time to recharge – long vacations

Would you want to make them mad?

Slow COMT, MTHFR 677TT with slow MAOA.

No

Who is most susceptible to addiction?

Slow COMT, MTHFR 677TT with slow MAOA.

Slow COMT, MTHFR 677CC with slow MAOA.

Fast COMT, MTHFR 677CC with fast MAOA.

Fast COMT, MTHFR 677TT with fast MAOA.

Fast COMT, MTHFR 677CC with fast MAOA

Who is most susceptible to depression?

NOS3 ++, MTHFR 677CC, slow MAOA

Fast COMT, NOS3 ++, slow MAOA

NOS3++, MTHFR 677CC, fast COMT

NOS3 --, slow COMT, fast MAOA

NOS3++, MTHFR 677CC, fast COMT

Who may struggle with histamine-related issues most?

MTHFR 677CC, DAO ++, slow MAOA

MTHFR 677TT, DAO ++, slow MAOB

MTHFR 677TT, DAO--, slow COMT

Slow COMT, DAO ++, MTHFR 677TT

MTHFR 677TT, DAO++, slow MAOB and Slow COMT, DAO++, MTHFR 677TT

Who is most susceptible to ED?

NOS3++, MTHFR 677TT, Fast MAOA

NOS3--, MTHFR 677CC, GPX ++

NOS3++, MTHFR 677TT, GPX ++

NOS3++, MTHFR 677TT, Slow COMT

NOS3++, MTHFR 677TT, GPX ++ and NOS3++, MTHFR 677TT, Slow COMT

Who is most likely going to focus longer?

Slow MAOA, Fast COMT, MTHFR 677TT

Slow MAOA, Slow COMT, MTHFR 677CC

Fast MAOA, Slow COMT, MTHFR 677TT

Slow MAOA, Slow COMT, MTHFR 677TT

Slow MAOA, Slow COMT, MTHFR 677TT

Who is most susceptible to child w NTD?

NOS3 ++, MTHFD1 ++, MTHFR 677TT

PEMT ++. MTHFR 677TT, MTR ++

GST ++, DAO ++, MTHFD1 ++

NOS3++, MTHFD1++, MTHFR 677TT

All are quite susceptible

Who is most susceptible to Fatty Liver?

MTHFR 677TT, NOS3++, Fast MAO

MTHFR 677TT, MTHFD1 ++, PEMT ++

PEMT ++, MTHFD1 --, MTHFR 677CC

PEMT --, MTHFD1 ++, MTHFR 677CC

MTHFR 677TT, MTHFD1 ++, PEMT ++

Who is most susceptible to mood disorders?

NOS3++, MTHFR 677TT, GST ++

Slow COMT, slow MAOA, NOS3 ++

MTHFD1 ++, MTHFR 677TT, Slow COMT

Fast COMT, Fast MAOA, GPX ++

All are susceptible

Who is most susceptible to Fatty Liver?

MTHFR 677TT, NOS3++, Fast MAO

MTHFR 677TT, MTHFD1 ++, PEMT ++

PEMT ++, MTHFD1 --, MTHFR 677CC

PEMT --, MTHFD1 ++, MTHFR 677CC

MTHFR 677TT, MTHFD1 ++, PEMT ++

Who is most susceptible to SIBO?

FUT2 ++, DAO ++, MTHFD1 ++

PEMT ++, Slow COMT, DAO ++

FUT2 ++,

PEMT --, MTHFD1 ++, MTHFR 677CC

MTHFR 677TT, MTHFD1 ++, PEMT ++

Name the Dirty Gene

Man, you're on fire! ADHD not in this house. You're cranking away on projects and eager for the next one. As you lay down going to bed, you're still cranking away on them. Tossing and turning, you finally doze off dreaming of what else you're going to be doing the next day. Next day arrives. Coffee is needed. Once that hits and you start on your project again, you're off and running. You put pressure on yourself and if you're not accomplishing what you need to, anxiety sets in so you focus harder to get it done. You get it done. Your colleague makes fun of you for working overtime on a project and you let them have it. You know you can be quick to being irritated. Oh – and what a wuss you are when something hurts you. So sensitive to pain. Headaches are also possible especially during menses.

Slow COMT

How to support slow COMT?

Watch estrogens - Support liver detoxification and gut microbiome

Limit exposure to xenoestrogens

Optimize weight

Vacations / Time to recharge – work hard / play hard

Adaptogens as needed

SAMe as needed with magnesium

Watch protein intake – especially at dinner

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Workshop 5:

Multidimensional Reasoning

Disclosure:

Relationship with commercial interests - None
Disclosure of commercial support - None
Conflict of interest - None

Boy with Frequent Eye Blinking

8 yr old boy, struggling with FEB.

Healthy diet but slightly slanted towards more carbohydrate

Stressed easily and hard to calm down

Sleeps well and on schedule

Active and healthy

Supplemented with non-methylated multi, copper / iron free, adaptogens

Gene	Variation	Result
SLC19a1	G80A	+/-
MTHFD1	G1958A	+/+
MTHFR	A1298C	+/+
MTHFR	C677T	-/-
MTRR	A66G	+/-
MTRR	C524T	+/-
MAT1A	R264H	-/-
CBS	D444N	-/-
CBS	C19150T	+/-
CBS	T833C	-/-
CBS	C699T	+/-
SOD2	A16V	+/-
SOD3	Ex3-631C>G	-/-
GSTP1	Ile105Val	-/-
GSTP1	A114V	-/-
G6PD	G202A	-/-
G6PD	A376G	-/-
G6PD	C563T (Medit.)	-/-
GPX1	Pro199Leu	-/-
NOS3/eNOS	-1495A>T	-/-
NOS3/eNOS	A(-922)G	NC
SULT1A1	638G>A	NA
MAOA	T941G	-/-
MAOA	1410T>C	-/-
MAOB		+/+*
COMT	V158M	-/-
COMT	H62H	-/-
AOC1/ABP1	Thr16Met	+/-

Susceptibility ?

1 Lab to order?

Gene	Variation	Result
BCO1	R267S	+/-
BCO1	A379V	-/-
BCO1 (PKD1L2)	C754T	+/+
BCO1		+/+
BCO1		+/+
FUT2		+/-
NQO1		-/-
HFE	C282Y	-/-
HFE	H63D	+/-
HFE	Ser65Cys	-/-
PEMT	5465G>A	+/-
FADS1		-/-
FADS1		+/-
FADS2		+/+
TNF-alpha		+/-
LRRK2	2109S	-/-
VDR	Fok1	NA
VDR	Taq1	-/-
VDR	Bsm1	-/-
APOE	Arg176Cys	+/+
APOE		+/+

WHAT DO YOU DO NOW?

B-Complex Vitamin Markers			
b-Hydroxyisovalerate	↑	Biotin, B2	Impaired Isoleucine metabolism
Methylation Cofactor Markers			
Formiminoglutamate	↑	Folic acid	Tetrahydrofolate insufficiency
Neurotransmitter Metabolism Markers			
Picolinate	↑	Add n-3 PUFA, limit protein intake	Inflammatory cytokine stimulation
Oxidative Damage and Antioxidant Markers			
8-Hydroxy-2-deoxyguanosine	↑	Vitamin C, Vitamin E	DNA oxidation product
Detoxification Indicators	No Abnormality Found		
Bacterial - General			
p-Hydroxyphenylacetate	↑	Probiotics	Intestinal Bacterial Overgrowth

Methylation Cofactor Markers
(B12, Folate)

WHAT MARKERS ARE TELLING?

20.	Methylmalonate	2.0		2.4	<= 3.3
21.	Formiminoglutamate	4.6	H	1.9	<= 3.2

Cell Regulation Markers

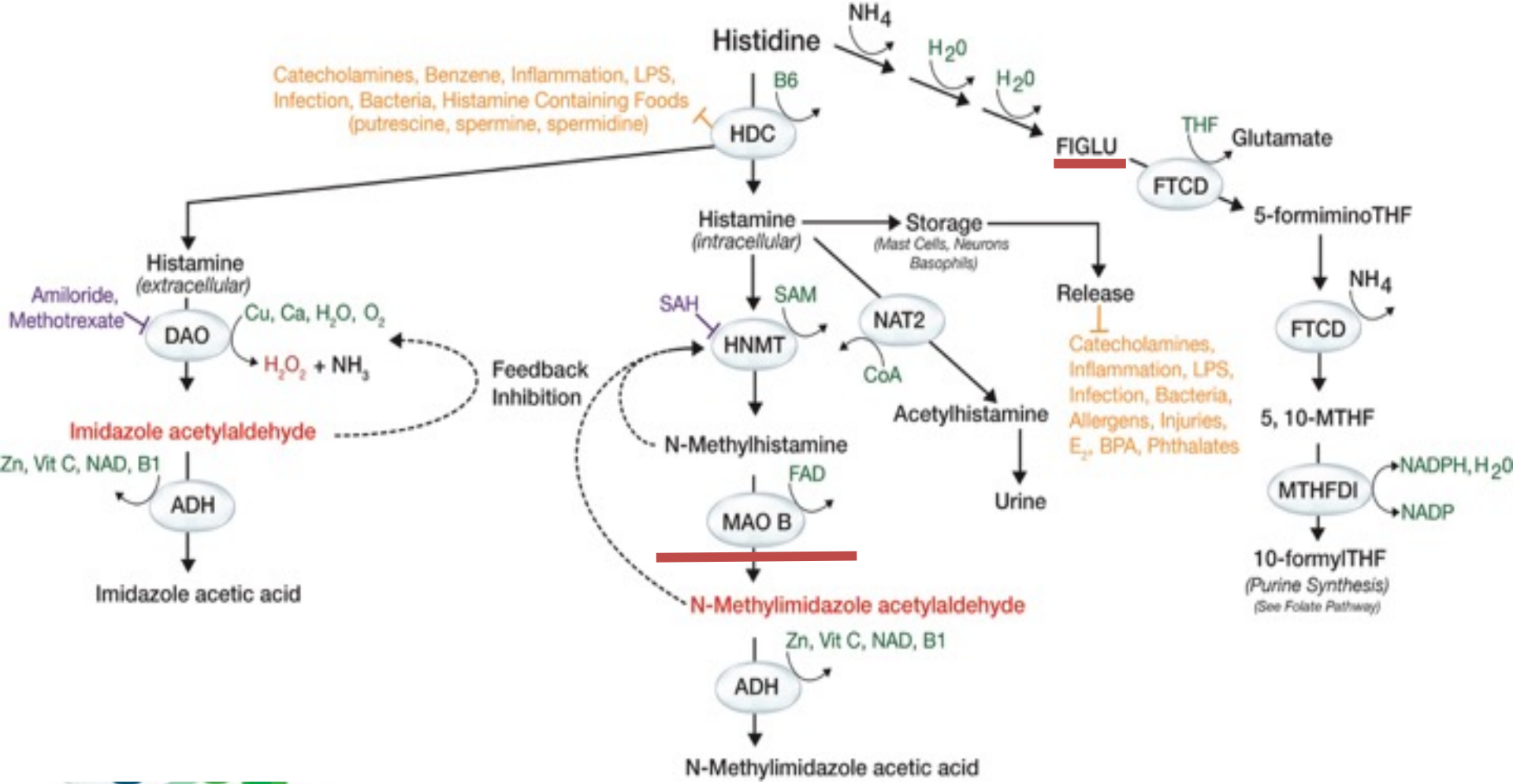
Neurotransmitter Metabolism Markers
(Tyrosine, Tryptophan, B6, Antioxidants)

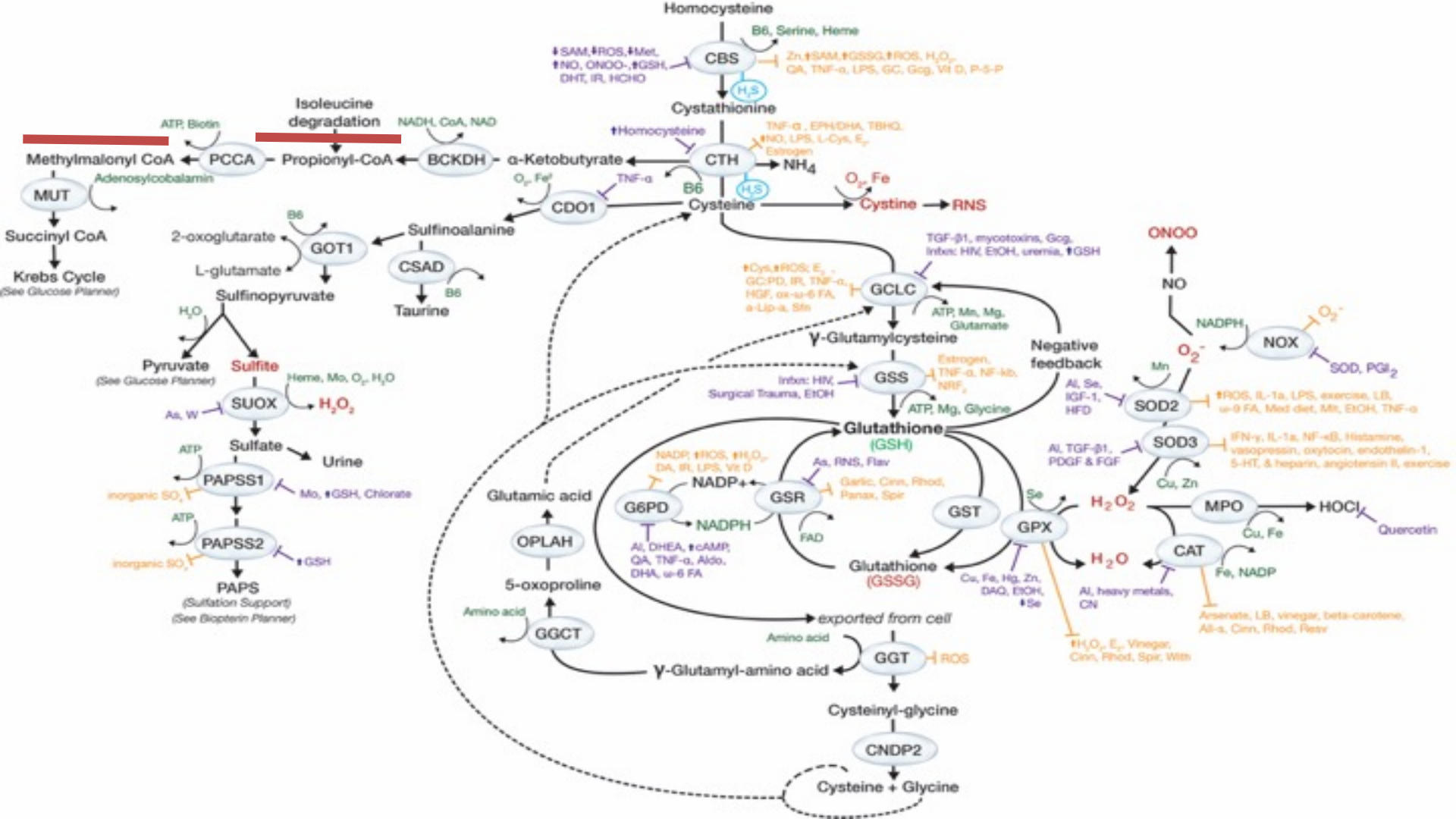
22.	Vanilmandelate	3.2		2.9 – 6.4	2.0 - 8.2
23.	Homovanillate	10.0		3.3 – 11.3	2.4 - 16.7
24.	5-Hydroxyindoleacetate	6.9		3.7 – 11.9	2.6 - 22.2
25.	Kynurenate	0.7		1.4	<= 2.3
26.	Quinolinate	5.7		8.0	<= 12.3
27.	Picolinate	19.3		16.3	4.8 - 28.7

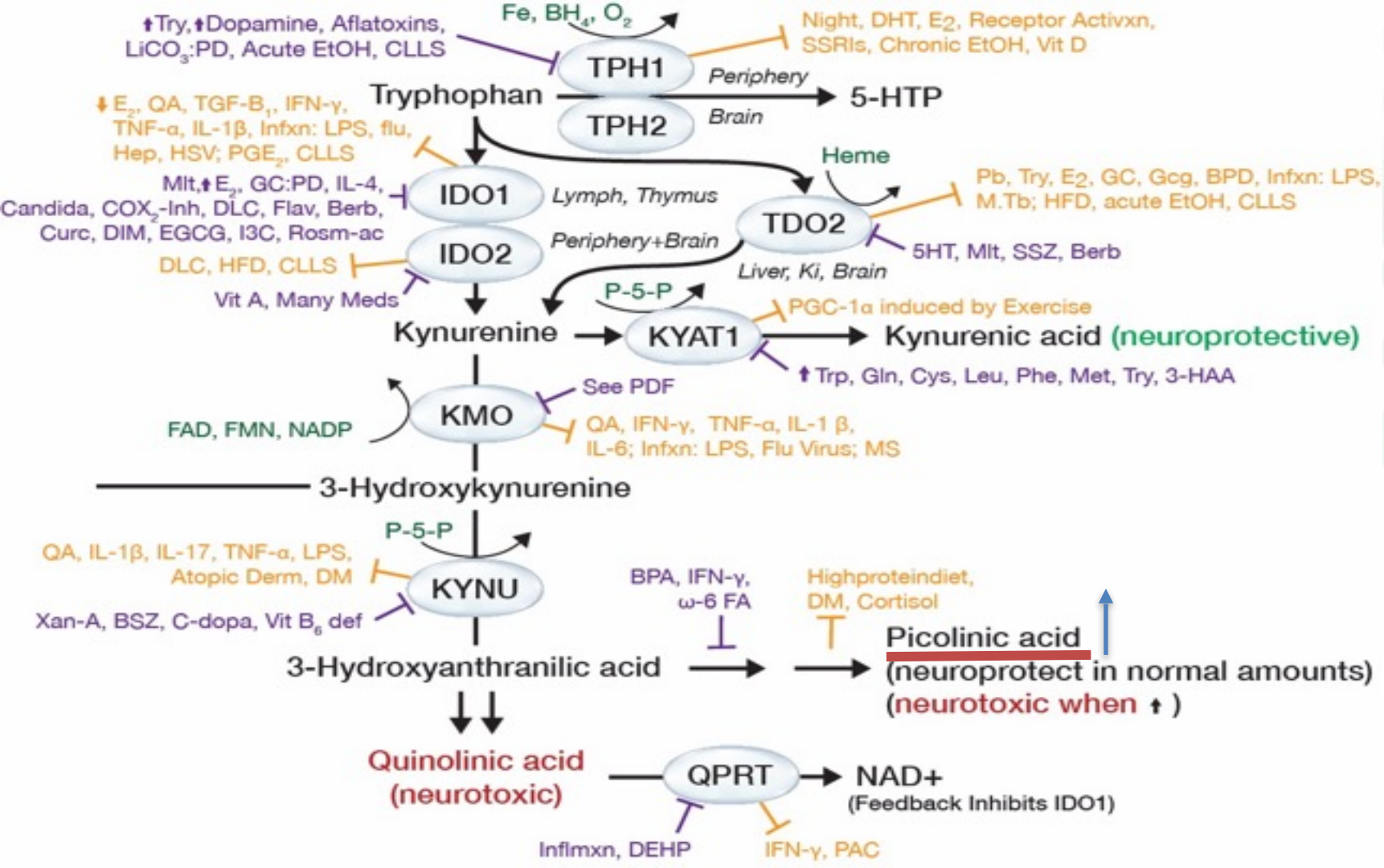
Oxidative Damage and Antioxidant Markers
(Vitamin C and Other Antioxidants)

28.	p-Hydroxyphenyllactate	0.05		0.27	<= 0.67
29.	8-Hydroxy-2-deoxyguanosine	6.9		5.9	<= 8.7

(Units for 8-hydroxy-2-dexoyguanosine are ng/mg creatinine)

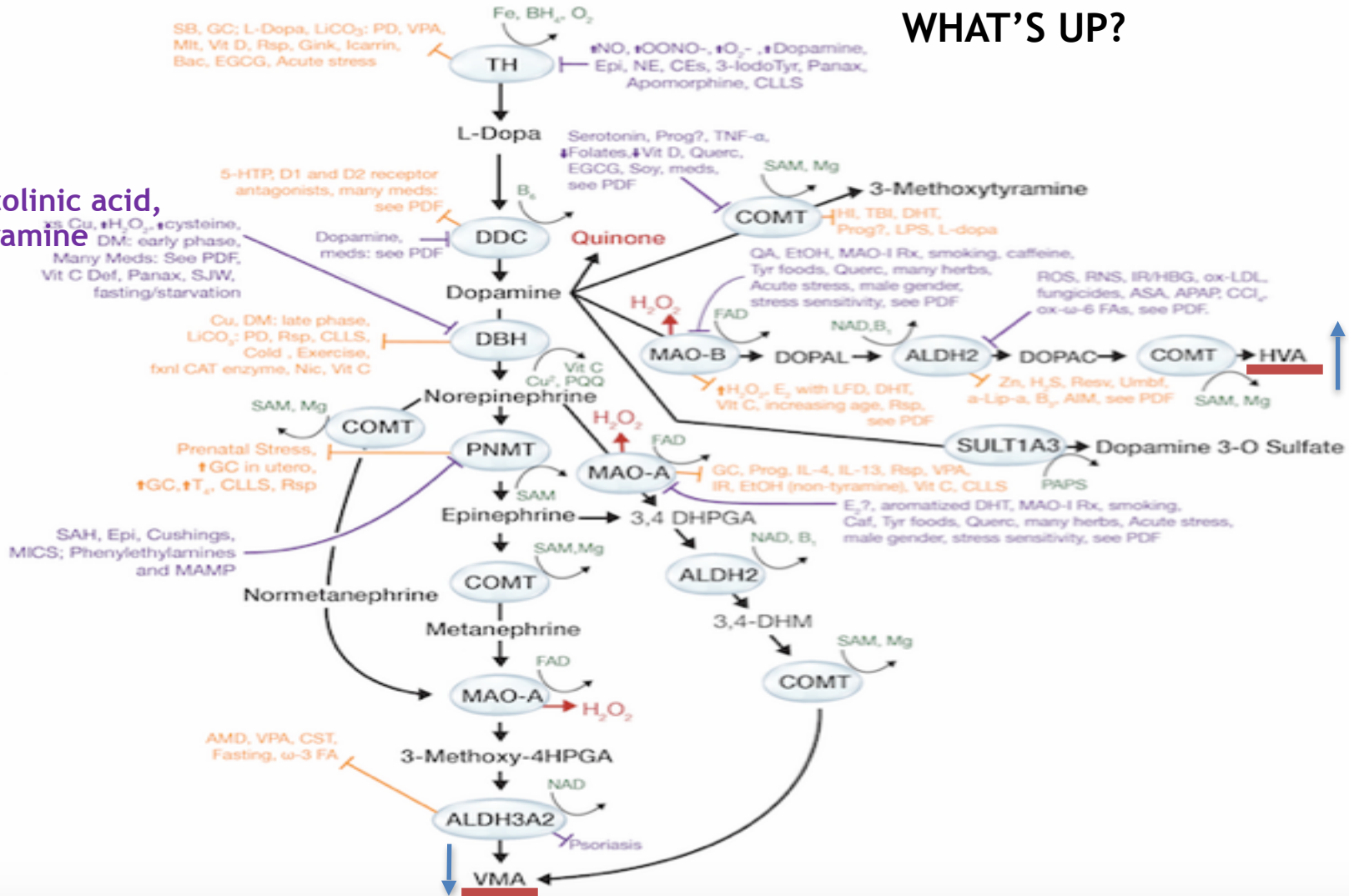

Histidine
NH_4
H_2O
H_2O
B6
HDC
Catecholamines, Benzene, Inflammation, LPS, Infection, Bacteria, Histamine Containing Foods (putrescine, spermine, spermidine)
FIGLU
THF
Glutamate
FTCD
5-formiminoTHF
NH_4
FTCD
5, 10-MTHF
MTHFDI
$NADPH, H_2O$
$NADP$
10-formylTHF
(Purine Synthesis)
(See Folate Pathway)
Histamine (intracellular)
Storage
(Mast Cells, Neurons Basophils)
Release
Catecholamines, Inflammation, LPS, Infection, Bacteria, Allergens, Injuries, E_2, BPA, Phthalates
Histamine (extracellular)
Amiloride, Methotrexate
DAO
Cu, Ca, H_2O, O_2
H_2O_2 + NH_3
Imidazole acetylaldehyde
Zn, Vit C, NAD, B1
ADH
Imidazole acetic acid
Feedback Inhibition
SAH
SAM
HNMT
NAT2
CoA
Acetylhistamine
Urine
N-Methylhistamine
FAD
MAO B
N-Methylimidazole acetylaldehyde
Zn, Vit C, NAD, B1
ADH
N-Methylimidazole acetic acid


Homocysteine
B6, Serine, Heme
↓SAM,↓ROS,↓Met, ↑NO, ONOO-,↑GSH, DHT, IR, HCHO
CBS
Zn,↑SAM,↑GSSG,↑ROS, H_2O_2, QA, TNF-α, LPS, GC, Gcg, Vit D, P-5-P
H_2S
Cystathionine
Isoleucine degradation
ATP, Biotin
NADH, CoA, NAD
Methylmalonyl CoA
PCCA
Propionyl-CoA
BCKDH
α-Ketobutyrate
↑Homocysteine
TNF-α , EPH/DHA, TBHQ, ↑NO, LPS, L-Cys, E_2, Estrogen
CTH
NH_4
Adenosylcobalamin
MUT
Succinyl CoA
Krebs Cycle
(See Glucose Planner)
O_2, Fe^{2}
TNF-α
B6
H_2S
CDO1
Cysteine
O_2, Fe
Cystine
RNS
B6
2-oxoglutarate
GOT1
L-glutamate
Sulfinoalanine
CSAD
B6
Taurine
Sulfinopyruvate
H_2O
Pyruvate
(See Glucose Planner)
Sulfite
Heme, Mo, O_2, H_2O
As, W
SUOX
H_2O_2
Sulfate
Urine
ATP
PAPSS1
inorganic SO_3
Mo, ↑GSH, Chlorate
ATP
PAPSS2
inorganic SO_3
↑GSH
PAPS
(Sulfation Support)
(See Biopterin Planner)
TGF-β1, mycotoxins, Gcg, Infxn: HIV, EtOH, uremia, ↑GSH
↑Cys,↓ROS; E_2, GCPD, IR, TNF-α, HGF, α-ω-6 FA, a-Lip-a, Sfn
GCLC
ATP, Mn, Mg, Glutamate
γ-Glutamylcysteine
Negative feedback
Infxn: HIV, Surgical Trauma, EtOH
GSS
Estrogen, TNF-α, NF-kb, NRF_2
ATP, Mg, Glycine
Glutathione (GSH)
NADP, ↑ROS, ↑H_2O_2, DA, IR, LPS, Vit D
NADP+
G6PD
NADPH
Al, DHEA, ↑cAMP, QA, TNF-α, Aldo, DHA, ω-6 FA
As, RNS, Flav
GSR
Garlic, Cinn, Rhod, Panax, Spir
FAD
Glutathione (GSSG)
GST
GPX
Se
Cu, Fe, Hg, Zn, DAQ, EtOH, ↓Se
↑H_2O_2, E, Vinegar, Cinn, Rhod, Spir, With
H_2O
Al, heavy metals, CN
Glutamic acid
OPLAH
5-oxoproline
GGCT
Amino acid
exported from cell
Amino acid
GGT
ROS
γ-Glutamyl-amino acid
Cysteinyl-glycine
CNDP2
Cysteine + Glycine
ONOO
NO
NADPH
NOX
O_2^-
SOD, PGI_2
Mn
O_2^-
SOD2
Al, Se, IGF-1, HFD
↑ROS, IL-1a, LPS, exercise, LB, ω-9 FA, Med diet, Mit, EtOH, TNF-α
SOD3
Al, TGF-β1, PDGF & FGF
IFN-γ, IL-1a, NF-κB, Histamine, vasopressin, oxytocin, endothelin-1, 5-HT, & heparin, angiotensin II, exercise
Cu, Zn
H_2O_2
MPO
HOCl
Quercetin
Cu, Fe
CAT
Fe, NADP
Arsenate, LB, vinegar, beta-carotene, All-s, Cinn, Rhod, Resv


↑Try, ↑Dopamine, Aflatoxins, LiCO3:PD, Acute EtOH, CLLS
Fe, BH4, O2
TPH1
Night, DHT, E2, Receptor Activxn, SSRIs, Chronic EtOH, Vit D
Periphery
Tryphophan
5-HTP
TPH2
Brain
↓E2, QA, TGF-B1, IFN-γ, TNF-α, IL-1β, Infxn: LPS, flu, Hep, HSV; PGE2, CLLS
Heme
Mlt, ↑E2, GC:PD, IL-4, Candida, COX2-Inh, DLC, Flav, Berb, Curc, DIM, EGCG, I3C, Rosm-ac
IDO1
Lymph, Thymus
Pb, Try, E2, GC, Gcg, BPD, Infxn: LPS, M.Tb; HFD, acute EtOH, CLLS
TDO2
IDO2
Periphery+Brain
5HT, Mlt, SSZ, Berb
DLC, HFD, CLLS
Liver, Ki, Brain
Vit A, Many Meds
P-5-P
PGC-1α induced by Exercise
Kynurenine
KYAT1
Kynurenic acid (neuroprotective)
↑Trp, Gln, Cys, Leu, Phe, Met, Try, 3-HAA
See PDF
KMO
FAD, FMN, NADP
QA, IFN-γ, TNF-α, IL-1 β, IL-6; Infxn: LPS, Flu Virus; MS
3-Hydroxykynurenine
P-5-P
QA, IL-1β, IL-17, TNF-α, LPS, Atopic Derm, DM
KYNU
BPA, IFN-γ, ω-6 FA
Highproteindiet, DM, Cortisol
Xan-A, BSZ, C-dopa, Vit B6 def
Picolinic acid
(neuroprotect in normal amounts)
(neurotoxic when ↑)
3-Hydroxyanthranilic acid
Quinolinic acid (neurotoxic)
QPRT
NAD+
(Feedback Inhibits IDO1)
Inflmxn, DEHP
IFN-γ, PAC

WHAT'S UP?

Picolinic acid, tyramine



Inhibition of dopamine beta-hydroxylase in blood vessels by picolinic acid derivatives in vivo and their anthypertensive effects.

Hidaka H, Shoka F, Hashizume Y, Takemoto N, Yamamoto M.

Abstract

The effect of picolinic acid derivatives, 5-butylpicolinic (fusaric) acid (FA), 5-(3',4'-DIBROMOBUTYL)PICOLINIC ACID(BPR2FA)and 50(N'N-dimethyldithiocarbamoilmethyl)picolinic acid (YP-279) on dopamine beta-hydroxylase in blood vessels in vivo was studied. Maximum inhibition of the conversion of 14C-dopamine (14C-DA) to 14C-norepinephrine (14C-ne) in rat aorta, mesenteric artery and renal artery was detected 30 min after FA and Br2FA (75 mg/kg) and 60 min after YP-279 (75 MG/KG). NE synthesis from 14C-DA returned to near control values by 6 hr in the blood vessels. NE levels of the aorta and mesenteric artery were sigkificantly reduced by 30 to 50% at 4 hr after Br2FA or FA (75 mg/kg). Dopamine beta-hydroxylase (DBH) activity, using tyramine as substrate, in heart, aorta, mesenteric artery and renal artery was markedly reduced. The concentrations of FA, Br2FA and YP-279 in rat blood following a single i.p, injection of each drug increase rapidly, reaching highest values in 0 to 30 min and decreasing slowly to 0 after 6 hr. These compounds did not affect the uptake of 3H-NE into the rat heart. These three compounds were found to lower blood pressure effectively in normal Wistar rats (above 25 mg/kg).

Case of Can't Focus to Crazy

14 yr old boy fit, thin, toned, healthy and struggling with ADHD.
-Loves carbohydrates
-Can't wake up in morning
-Athlete and wants to get more muscle tone
-Generally respectful
-Quite 'huggy' even as a teenager
-Constantly on electronics – phone, video games
-Genetics: COMT V158M -/+, MTHFR 677CT -/+, MAOA -/-, MAOB +/+, FADS2 +/+, MTHFD1 +/+, SLC19a1 +/-

What do the genetics tell you – alone?

What do you tell him about carbohydrates?

What do you tell him about lifting weights?

Why do you think he loves hugs?

What simple recommendation do you give a teenage boy for dietary change?

What single nutrient do you recommend? Why?

When do you ask for follow up?

Case of Can't Focus to Crazy

2nd Visit:

Significantly better. "I feel like I can actually think."

What do you tell him about supplementation?

Next visit?

Surprise:

Parents report increased irritability. Just lashing out.

What do you do?

What do you suspect?

Next visit?

Follow Up: Feel great!

What do you warn him and his parents about for future based on history and genes?

References

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All diagrams shown have references organized by pathway and gene.

References may be found here:
https://seekinghealth.org/bibliography/

Workshop 6:

Multidimensional Reasoning

Disclosure:

Relationship with commercial interests - None
Disclosure of commercial support - None
Conflict of interest - None

Case of Can't Sleep to Can't Wake Up: Not Aligned

43 yr old actress. Can't fall asleep, anxious, irritable.
-On estrogen hormone. PMS intense
-Thin
-Not eating well – too concerned about weight
-Knows she is a rapid breather
-Stress in family significant
-She is not very compliant. She travels all the time. Oh – and she smokes. She wants pills.

What pathways do you think are mainly 'plugged' up?

What neurotransmitters do you suspect are elevated?

What supplements do you recommend? Why?

What do you say about the supplements?

When is next visit?

You try the lifestyle approach. You even discover she has mold in the home but never remediated.

No genetic reports.

Wont do any lab testing.

Case of Can't Sleep to Can't Wake Up

Next visit – 2 weeks later:
Sleeping well. Still stressed. Would like to increase sleep a bit more and reduce stress.

Supplement changes?

When next visit?

Month later:
Crying. Can't wake up. Sleeping all the time.

Why?

What happened?

What do you do?

What do you tell her about the supplements?

Next visit:
-Much better – getting up and moving about and still sleeping

Still stressed. Goes off to another doctor

Case of Cold, Can't Sleep, Pain and Depressed

You have 30 minutes. Patient aged 40, Caucasian, slightly overweight, complexion slight acne.

-Cardiovascular risk runs in her family. Stroke, MI in mom and dad already
-She is depressed and has been for some time – and it's accompanied by anxiety. 7/10
-Eats SAD. Lot of carbs. No protein with breakfast. Snacks all day. Eats late and largest meal is
dinner. Red wine x 2 glasses in evening to relax. Stress 7/10
-Generalized muscle aches and pains. Worse w exercise. Wonders if it is fibromyalgia. 6/10
-Has cold hands and feet for as long as she can remember. 7/10
-She has no labs.
-Her menses are light. Moods slightly better but sleep worse.
-When she drinks water, it goes right through her. Has to pee.
-Her main complaint is fatigue
-Digestion is 'fine' according to her. She can't talk about it.

She wants to go over her genetic testing right away. That's why she came to see you.

Case of Cold, Can't Sleep, Pain and Depressed

Metrics: Cold hands/feet 7/10, Pain 6/10, Insomnia 8/10, Depression/Anxiety 7/10, Fatigue, 8/10, Stress 7/10

What do you tell her about genetic testing and the information it provides?

What do you tell her about how you work with patients?

What is your next question? What is your goal for today?

"I want to know how to fix my SNPs. Now. That's why I am here. Tell me what I should take"

What do you say to her now?

She's BACK! Cold, Can't Sleep, Pain and Depressed

You have 30 minutes. Patient aged 40, Caucasian, slightly overweight, complexion slight acne.

-Cardiovascular risk runs in her family. Stroke, MI in mom and dad already
-She is depressed and has been for some time – and it's accompanied by anxiety. 7/10
-Eats SAD. Lot of carbs. No protein with breakfast. Snacks all day. Eats late and largest meal is
dinner. Red wine x 2 glasses in evening to relax. Stress 7/10
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-Has cold hands and feet for as long as she can remember. 7/10
-She has no labs.
-Her menses are light. Moods slightly better but sleep worse.
-When she drinks water, it goes right through her. Has to pee.
-Her main complaint is insomnia/overfatigued
-Digestion is 'fine' according to her. Doesn't talk about it

She wants to go over her genetic testing soon but she knows she has to do the basics. She's ready.

Cold, Can't Sleep, Pain and Depressed

Metrics: Cold hands/feet 7/10, Pain 6/10, Insomnia 8/10, Depression/Anxiety 7/10, Fatigue, 8/10, Stress 7/10

What physical signs are you looking for right now with her?

Breathing rate and style.

You notice breathing rate is fast and shallow. What do you do?

You have three main recommendations for her to implement until you see her again. What are they?.

1. SAD dietary changes and tracking 2. Breathing 3. Night time routine

What do you tell her about dietary changes? What key basics to implement?

What do you tell her about night routine?

What do you tell her about breathing?

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