Module 14

Allergy, Hypersensitivity and Toxicity

The **Applied Kinesiology** approach to allergy and hypersensitivity is to identify items to which the patient is allergic or sensitive by how the nervous system reacts as observed by its control of muscles evaluated by manual muscle testing.*

*Applied Kinesiology Synopsis 2nd Edition by David Walther DC page 532

Ideally by this method of testing one finds why the autoimmune system is incapable of coping with the noxious substance. This is accomplished by combining the reactive substance test with another factor such as therapy localisation, nutrition etc.*

*Applied Kinesiology Synopsis 2nd Edition by David Walther DC page 532

Genetic allergy. Pottinger's cats with 3 generations of allergy and hypersensitivity.

AK testing is done by stimulating the gustatory, olfactory and sometimes the cutaneous nerves with the substance testing from strength to weakness.*

*Applied Kinesiology Synopsis 2nd Edition by David Walther DC page 533

Allergy tests

Scratch test

IgE (RAST test)

IgG (RAST)

IgE immune complexes

IgG immune complexes

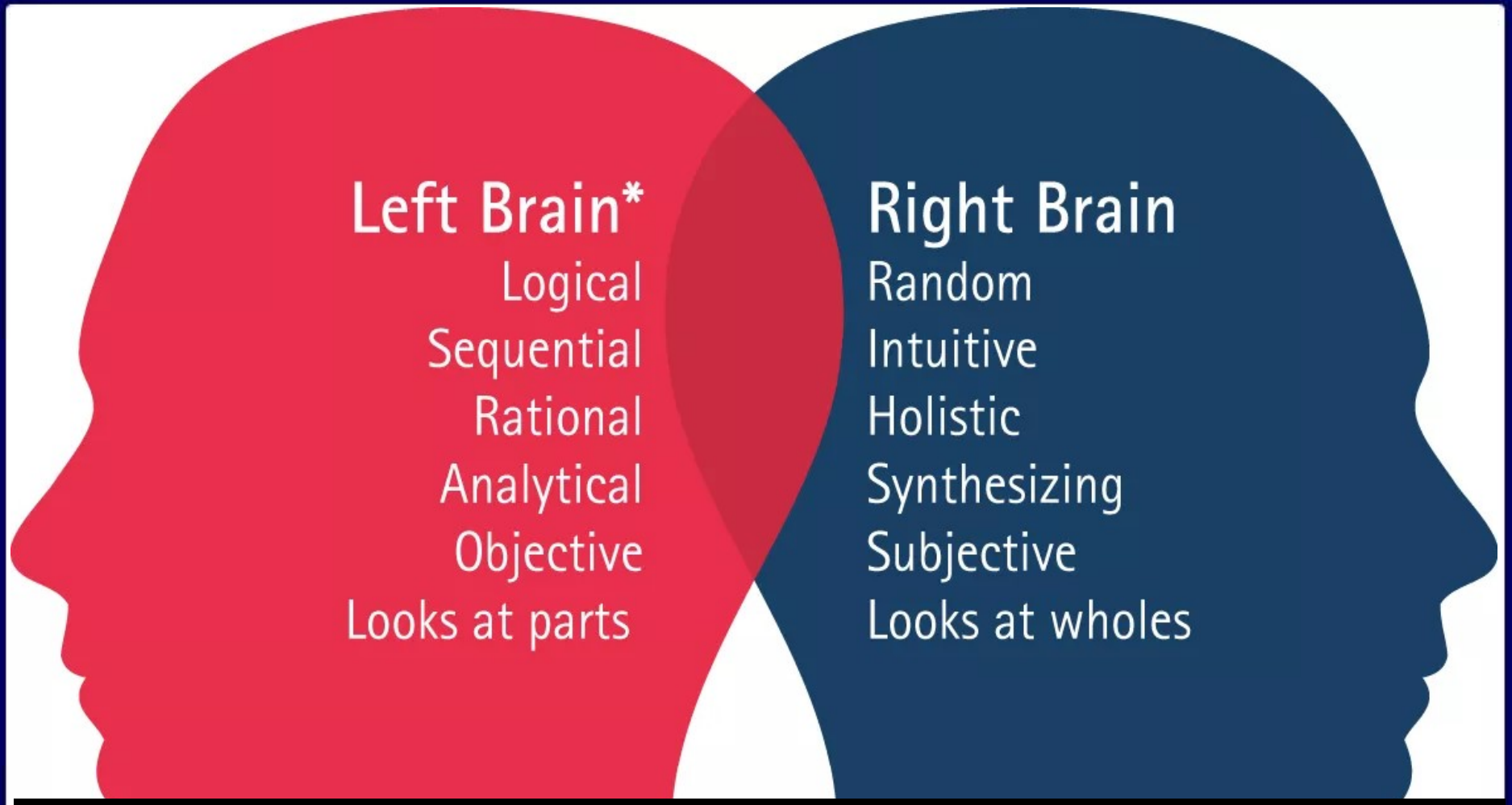
Coca's pulse test

Philpot type fast

Callahan – psychological reversal

*Applied Kinesiology Synopsis 2nd Edition by David Walther DC page 533

Left and Right Brain Dominance



Firstly challenge for Left Brain – Right Brain dominance

*Source: Funderstanding.com, Inc., New Jersey

1. Left brain eyes left
   Right brain eyes right

Side that weakens is the less dominant brain.

Dilts, R., Grinder, J., Delozier, J., and Bandler, R. (1980). Neuro-Linguistic Programming: Volume I: The Study of the Structure of Subjective Experience. Cupertino, CA: Meta Publications. p. 2. ISBN 978-0-916990-07-7.

Toxicity

Probably 90% of detoxification involves the metabolism of the endogenously produced chemicals.

Functional Medicine Update 2004 Bruce Ames

Principles of Functional Biochemistry


ENZYMES

Enzymes are protein catalysts that regulate the rates at which physiological processes take place. **They are encoded by specific genes which in turn are stimulated by hormones and various ligands.**

There are 7000+ enzymes catalogued in the **ENZYME DATABASE.**

https://www.brenda-enzymes.org/enzyme.

There are two types

1) those that require a coenzyme such as the oxido-reductases. 22% of known enzymes require coenzymes to function.

2) those that do not require a coenzyme such as the digestive enzymes.

Four parts

1.The **apoenzyme** is the protein part of an enzyme.

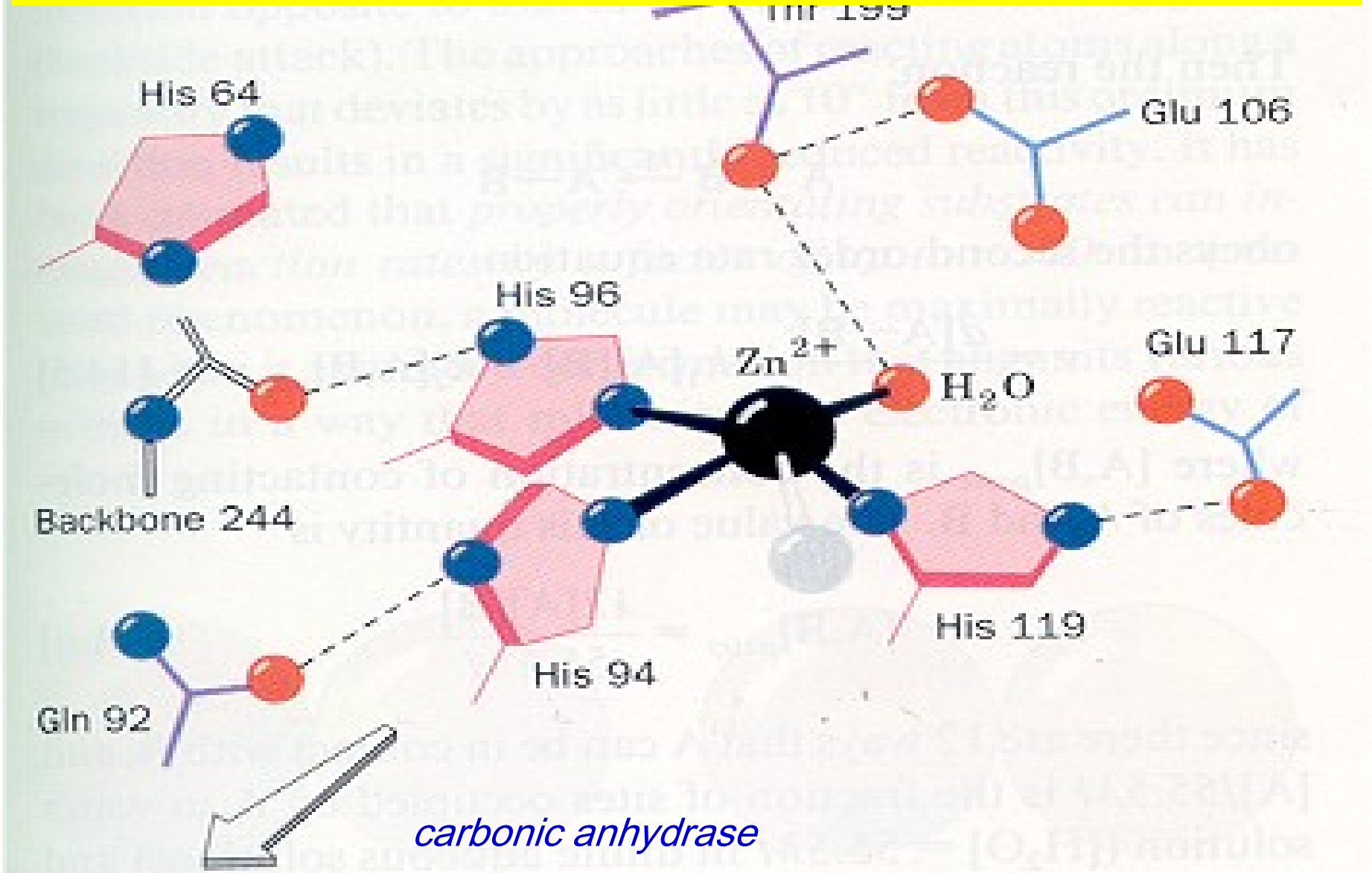
2.The **coenzyme** is required for the activation of an enzyme.

3.Metal ion catalysts

a) Metalloenzymes contain tightly bound metal ions most commonly transition metal ions such as Fe^{2+}, Fe^{3+}, Cu^{2+}, Zn^{2+}, Mn^{2+}, Se or Co^{3+}.

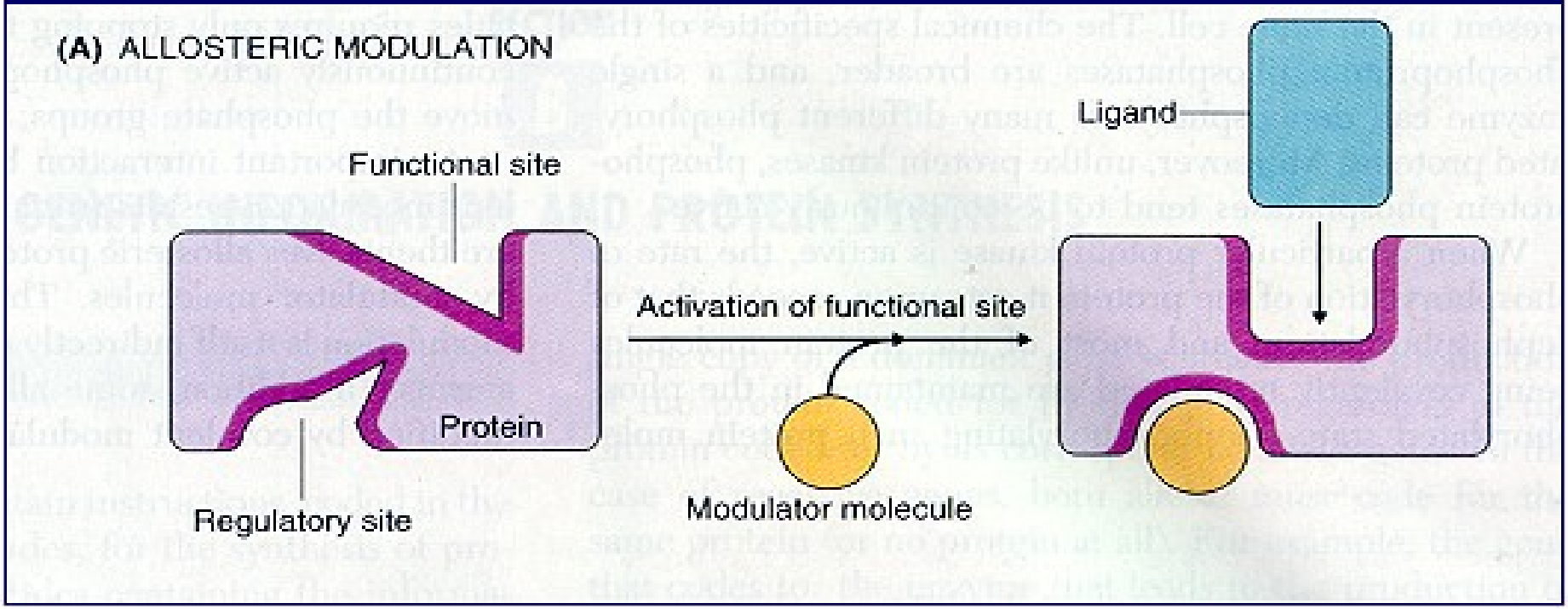
b) Metal activated enzymes loosely bind metal ions from solution, usually alkaline earth metal ions Na^{+}, K^{+}, Mg^{2+} or Ca^{2+}

$CO_2 + H_2O = H_2CO_3 = H^+ + HCO_3^-$



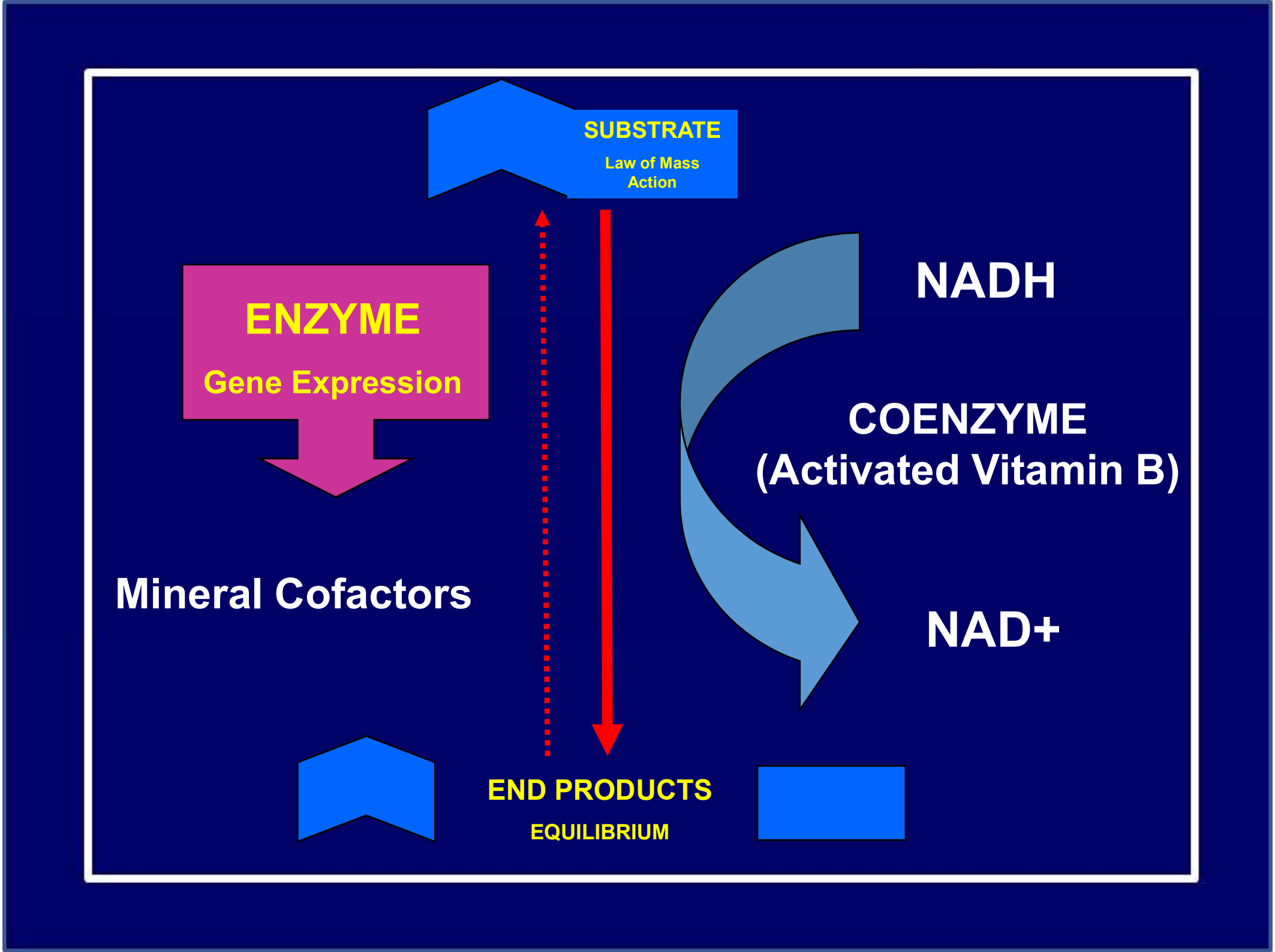
carbonic anhydrase

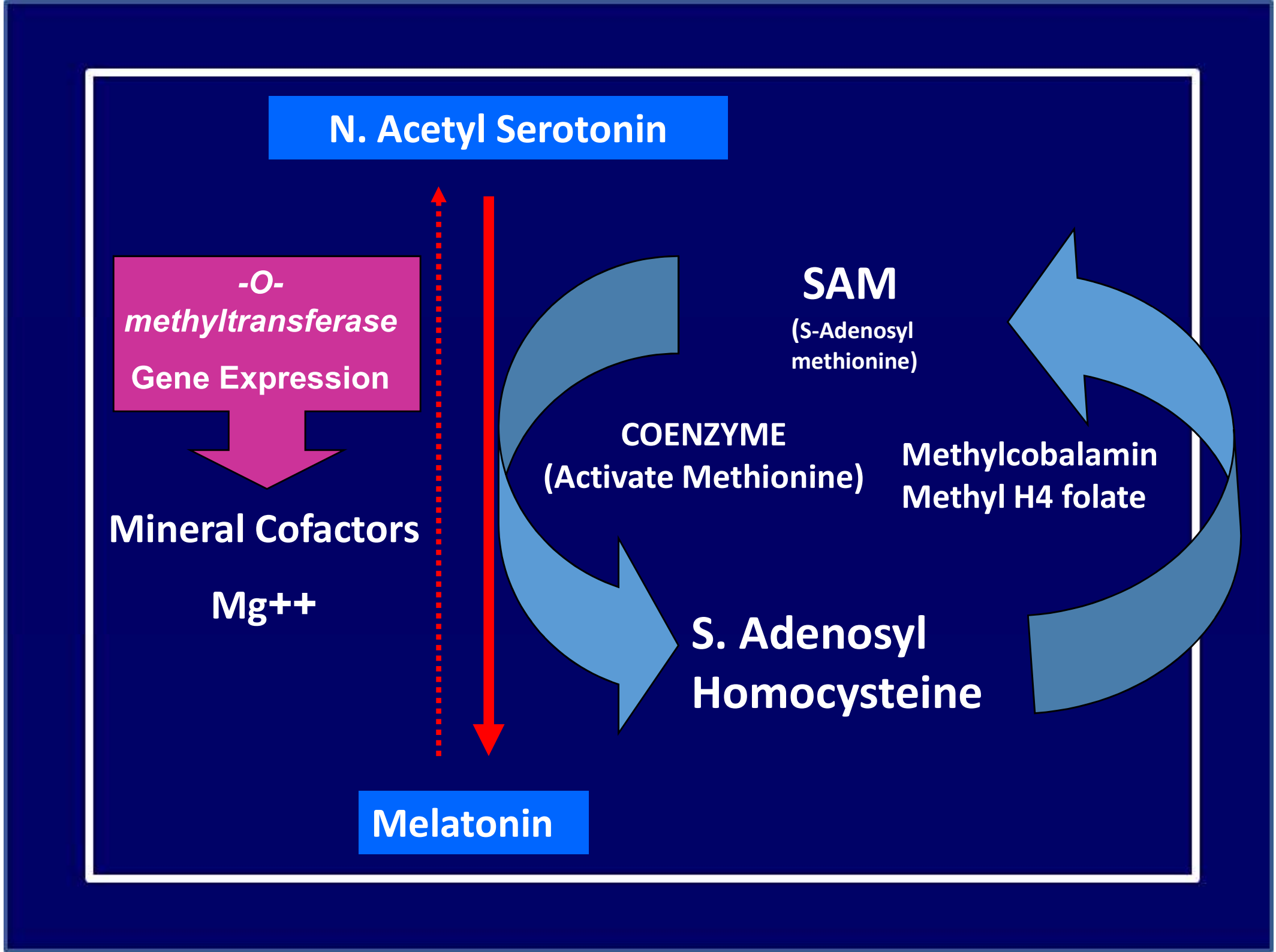
4. Low molecular weight allosteric effectors modulate the catalytic activity of certain regulatory enzymes. e.g. Silver.



Factors affecting enzyme function

1. Temperature
2. Enzyme concentrations
3. Substrate concentration
4. pH
5. Inhibitors can poison enzymes e.g. certain chemicals e.g. toiletries, cosmetics, toxic metals and mycotoxins.


SUBSTRATE
Law of Mass Action
ENZYME
Gene Expression
NADH
COENZYME
(Activated Vitamin B)
Mineral Cofactors
NAD+
END PRODUCTS
EQUILIBRIUM

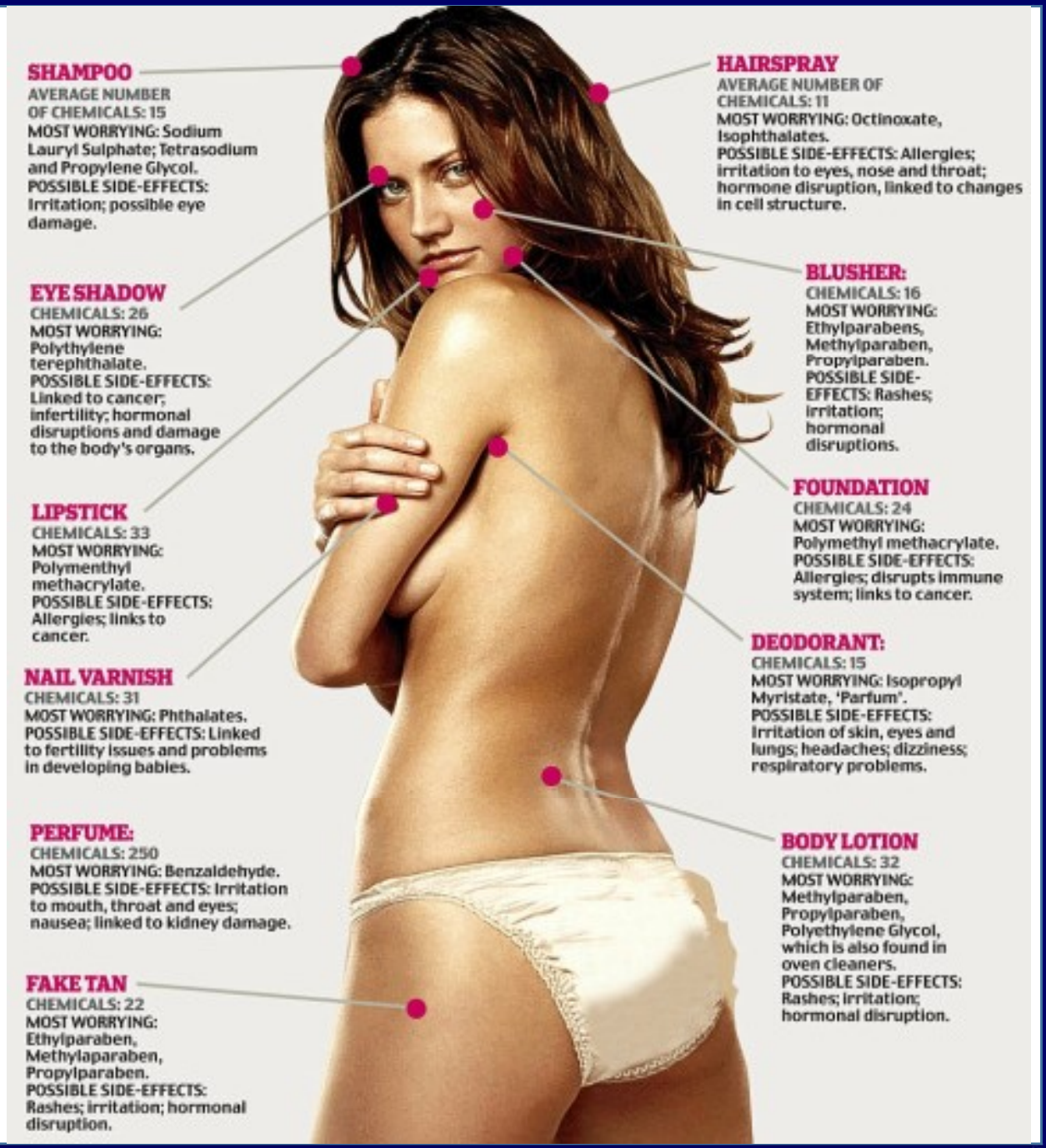

N. Acetyl Serotonin
-O-
methyltransferase
Gene Expression
Mineral Cofactors
Mg++
SAM
(S-Adenosyl
methionine)
COENZYME
(Activate Methionine)
Methylcobalamin
Methyl H4 folate
S. Adenosyl
Homocysteine
Melatonin

CHALLENGES FOR ENZYME PATHWAY INHIBITION

1. A WEAK ASSOCIATED MUSCLE WILL STRENGTHEN TO THE REQUIRED END PRODUCT.
2. A STRONG INDICATOR MUSCLE WILL WEAKEN WHEN CHALLENGED TO THE SUBSTRATE.
3. THIS WEAKNESS WILL BE NEGATED BY THE MINERAL COFACTORS AND / OR THE COENZYME (USUALLY AN ACTIVATED VITAMIN B)

Toxicity

Toxicity

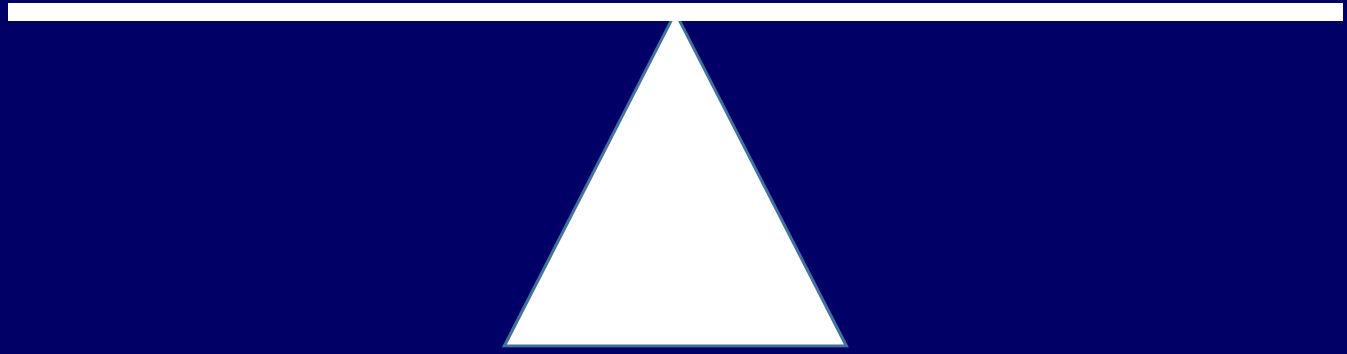

SHAMPOO
AVERAGE NUMBER OF CHEMICALS: 15
MOST WORRYING: Sodium Lauryl Sulphate; Tetrasodium and Propylene Glycol.
POSSIBLE SIDE-EFFECTS: Irritation; possible eye damage.
EYE SHADOW
CHEMICALS: 26
MOST WORRYING: Polythylene terephthalate.
POSSIBLE SIDE-EFFECTS: Linked to cancer; infertility; hormonal disruptions and damage to the body's organs.
LIPSTICK
CHEMICALS: 33
MOST WORRYING: Polymenthyl methacrylate.
POSSIBLE SIDE-EFFECTS: Allergies; links to cancer.
NAIL VARNISH
CHEMICALS: 31
MOST WORRYING: Phthalates.
POSSIBLE SIDE-EFFECTS: Linked to fertility issues and problems in developing babies.
PERFUME:
CHEMICALS: 250
MOST WORRYING: Benzaldehyde.
POSSIBLE SIDE-EFFECTS: Irritation to mouth, throat and eyes; nausea; linked to kidney damage.
FAKE TAN
CHEMICALS: 22
MOST WORRYING: Ethylparaben, Methylaparaben, Propylparaben.
POSSIBLE SIDE-EFFECTS: Rashes; irritation; hormonal disruption.
HAIRSPRAY
AVERAGE NUMBER OF CHEMICALS: 11
MOST WORRYING: Octinoxate, Isophthalates.
POSSIBLE SIDE-EFFECTS: Allergies; irritation to eyes, nose and throat; hormone disruption, linked to changes in cell structure.
BLUSHER:
CHEMICALS: 16
MOST WORRYING: Ethylparabens, Methylparaben, Propylparaben.
POSSIBLE SIDE-EFFECTS: Rashes; irritation; hormonal disruptions.
FOUNDATION
CHEMICALS: 24
MOST WORRYING: Polymethyl methacrylate.
POSSIBLE SIDE-EFFECTS: Allergies; disrupts immune system; links to cancer.
DEODORANT:
CHEMICALS: 15
MOST WORRYING: Isopropyl Myristate, 'Parfum'.
POSSIBLE SIDE-EFFECTS: Irritation of skin, eyes and lungs; headaches; dizziness; respiratory problems.
BODY LOTION
CHEMICALS: 32
MOST WORRYING: Methylparaben, Propylparaben, Polyethylene Glycol, which is also found in oven cleaners.
POSSIBLE SIDE-EFFECTS: Rashes; irritation; hormonal disruption.

Toxicity
at the root of many
disorders

Endogenous Toxicity

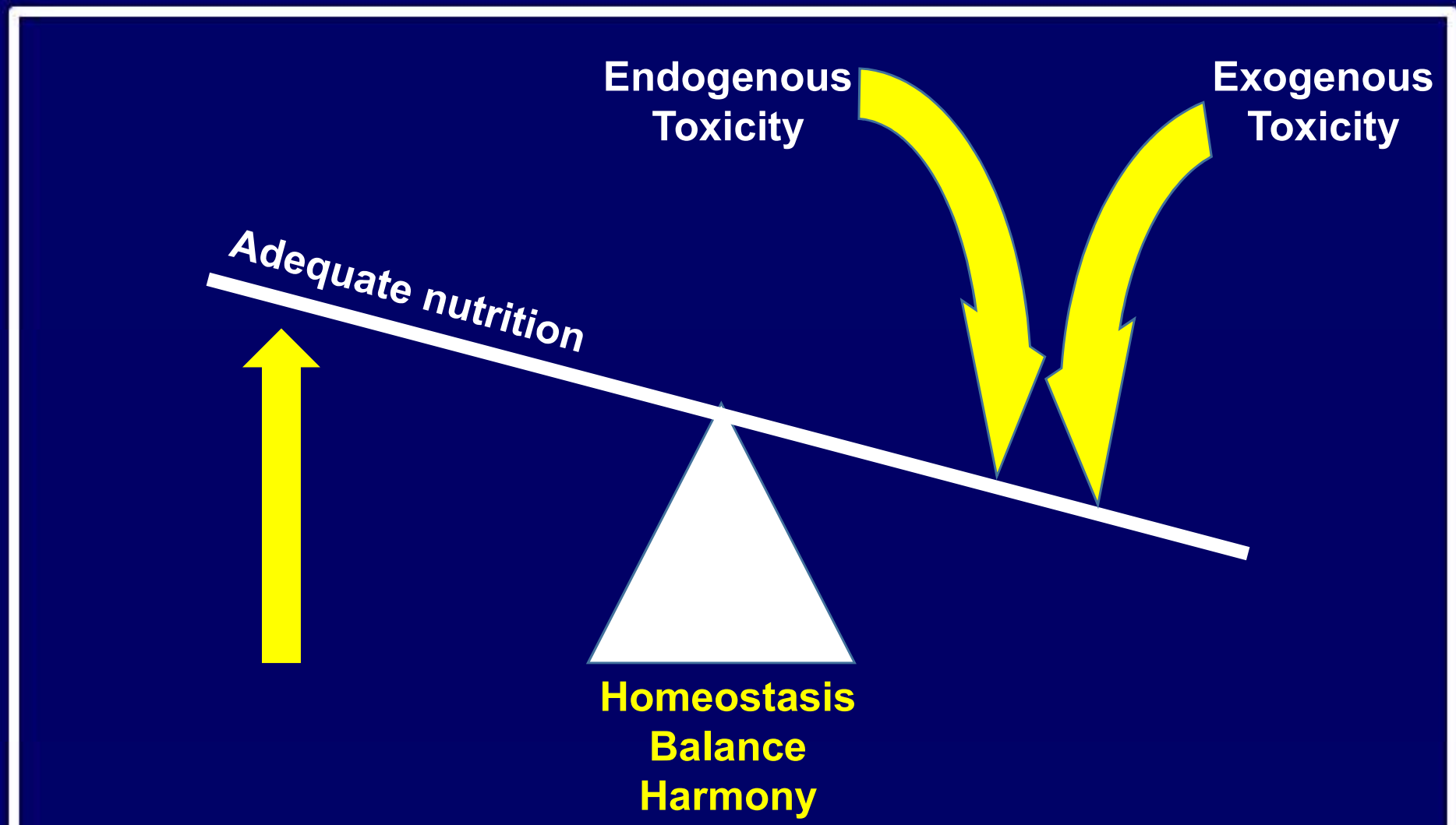
Exogenous Toxicity

Adequate nutrition



Homeostasis
Balance
Harmony

"Supply the things the patient is deficient in and remove the things that are bad for the patient." Sidney Baker M.D.



"Supply the things the patient is deficient in and remove the things that are bad for the patient." Sidney Baker M.D.

Toxicity

1. Internal Chemicals e.g. neurotransmitters, hormones generated by the mind
   External Chemicals - xenobiotics

2. Toxic metals

3. Radiation e.g. radioactive isotopes, electromagnetic stress

Endogenogous toxins can be generated from the mind are mediated by the hypothalamus hormones –

Thyrotrophic releasing hormone

Corticotrophic releasing hormone

Gonadotrophic releasing hormones

Growth hormone releasing hormone

Somatostatin

Prolactin inhibiting hormone

300 Neuropeptides

External toxins (Xenobiotics) come from

What we ingest
What we drink
What we breath
What we put on our skin
Electromagnetic pollution
Harmful solar wavelengths

Detoxification

Detoxification is a generic term for the metabolism (catabolism) of both **endogenous** and **exogenous** chemicals.

The main endogenous chemicals to be metabolised are

- Neurotransmitters
- Hormones
- Eicosonoids
- Certain Fatty acids e.g. rancid fats
- Retinoids, Uric acid

The main exogenous chemicals (xenobiotics) to be metabolised are either

- Water soluble
- Lipid soluble

Lipid soluble chemicals are generally metabolised by

1. Hydroxylation to make them more water soluble

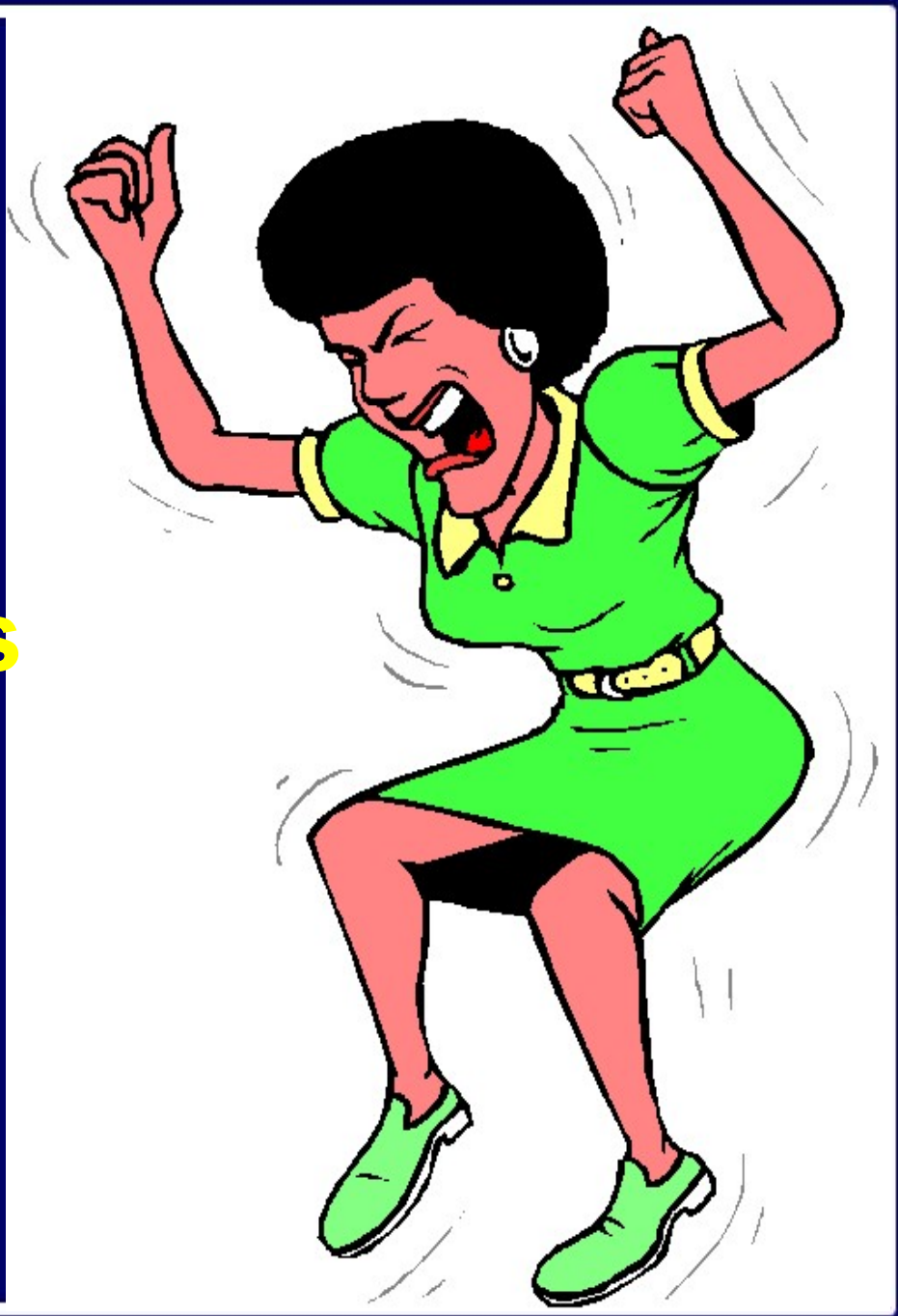
Lipid soluble chemicals are generally metabolised by

1. **Hydroxylation to make them more water soluble**

2. **Conjugation to aid their elimination through the kidneys or biliary system.**

Many hormones are methylated after hydroxylation before they are conjugated.

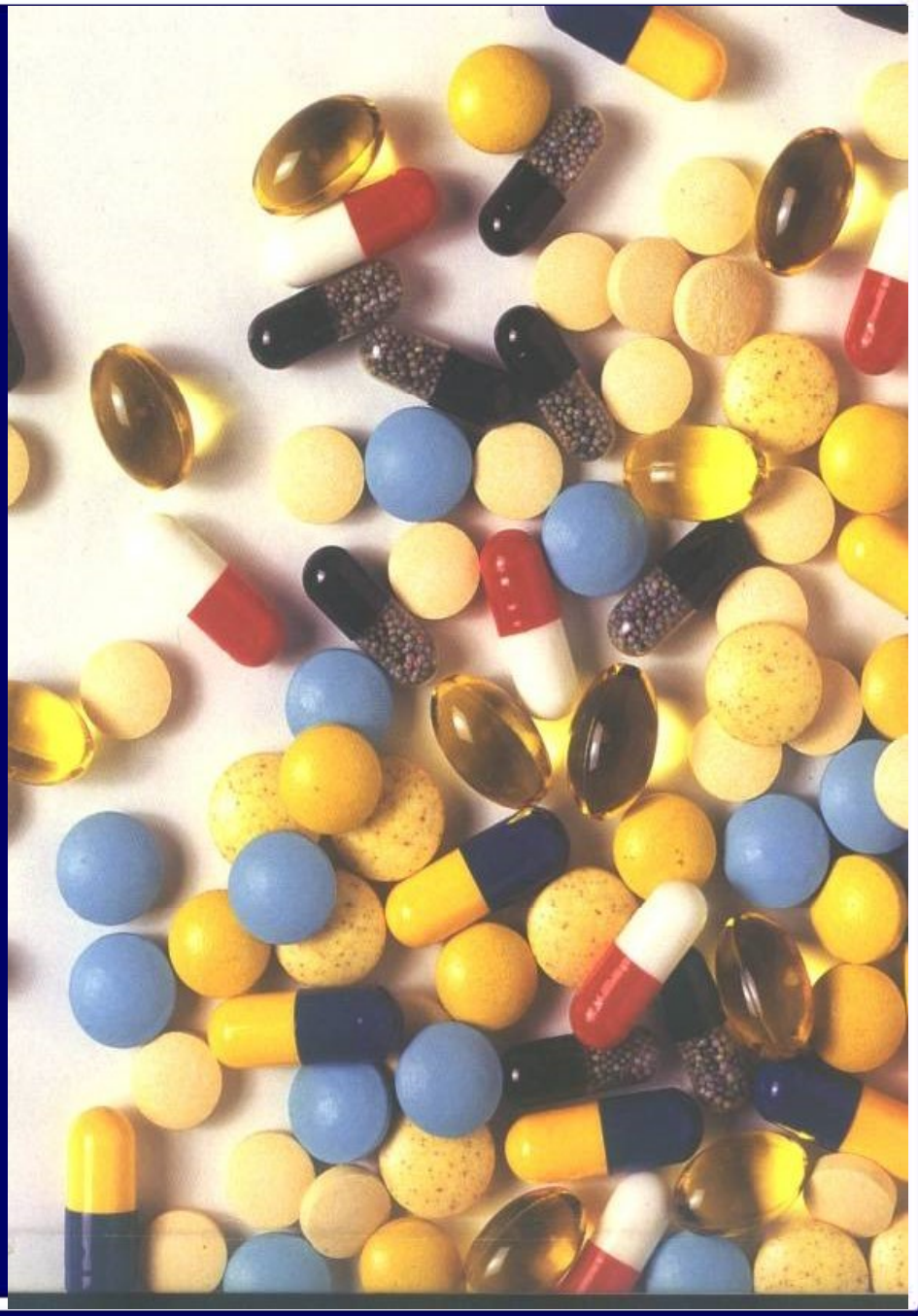
Like
Neurotransmitters
and Hormones



However to fully understand endogenous detoxification its easier to start by learning about **exogenous** detoxification.

Those of medical relevance are

1. Drugs
2. Chemical carcinogens
3. Pesticides and other various compounds.



More than 75,000 synthetic chemicals now exist. 19000+ are xeno-estrogens.

Most will require detoxification, with the liver being the main organ involved.

Occasionally a xenobiotic maybe excreted unchanged.

It is convenient to consider the metabolism of xenobiotics in two phases.

1. Phase 1 hydroxylation catalyzed by the mono-oxygenases cytochrome P450's.

2. Phase 2 Methylation or Conjugation.

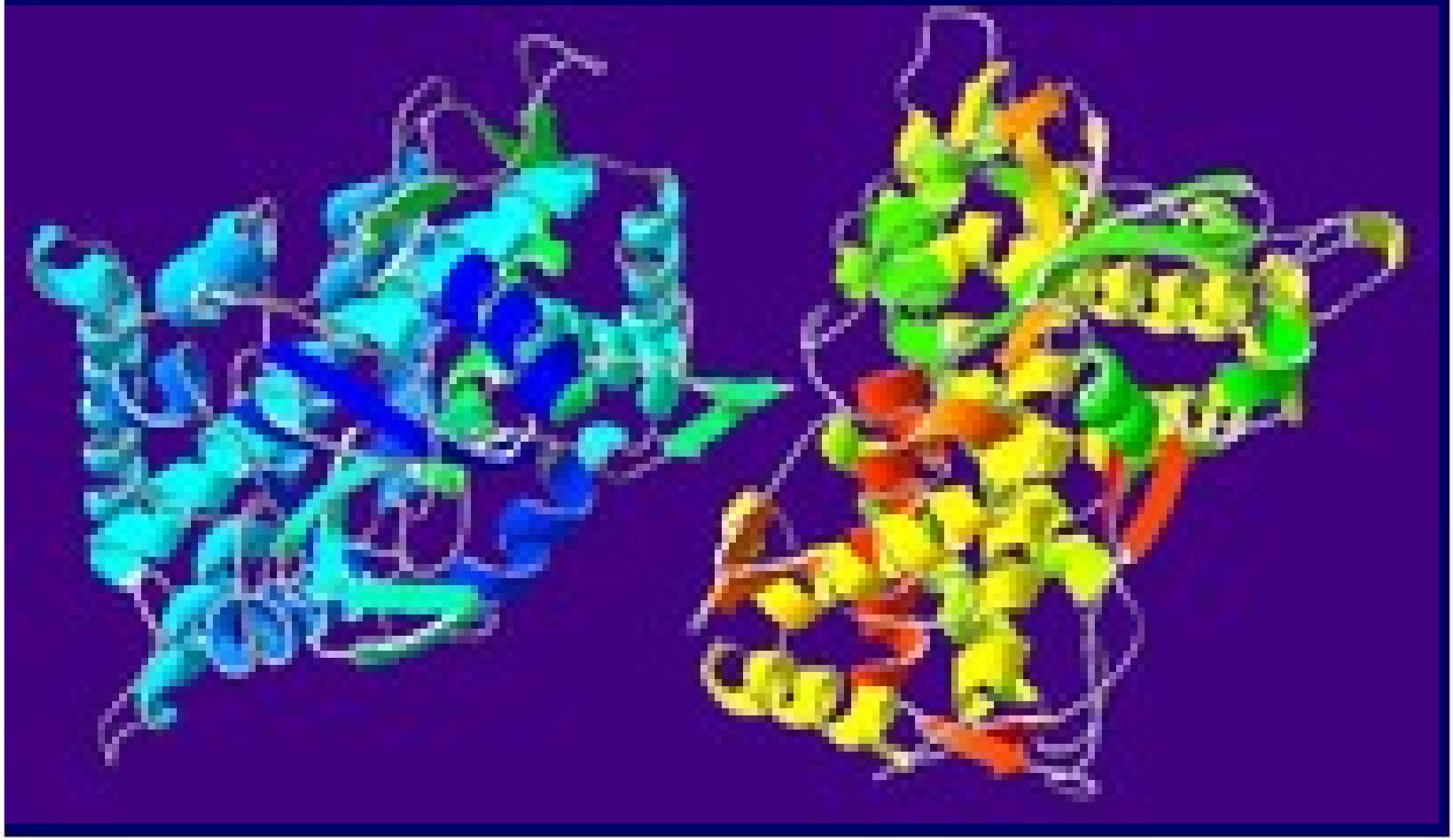
The overall purpose of the two phases is to increase their **water solubility (polarity)** and thus facilitate their excretion from the body.

Very hydrophobic xenobiotics would persist in adipose tissue indefinitely if they were not converted to more polar forms.

In certain cases, Phase 1 metabolic reactions convert xenobiotics from inactive to biologically active compounds.

In some instances the original xenobiotics are pro-carcinogens which then become converted to carcinogens by the phase 1 hydroxylation.

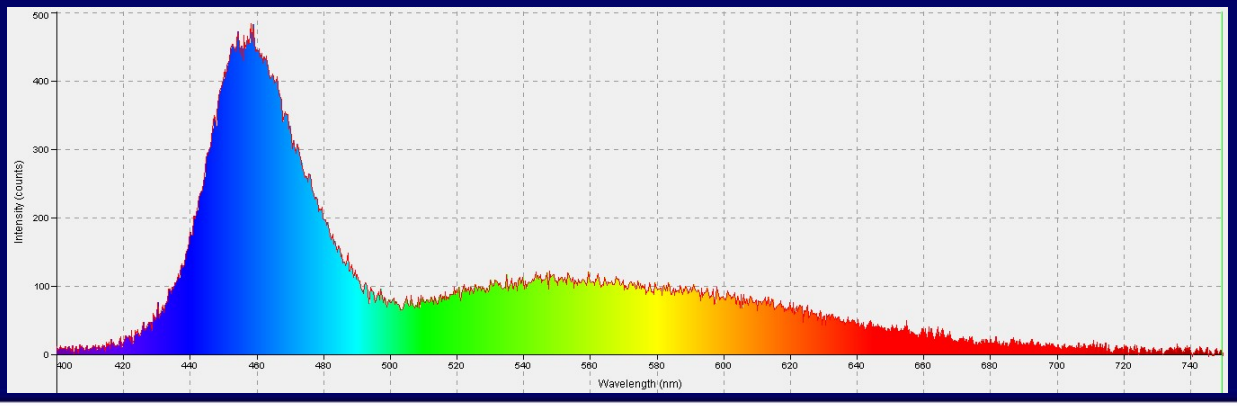
Phase 1 Hydroxylation



There are 14 families of the Cytochrome P450 enzyme encoding for between 35-60+ distinct P450 enzymes.

They all use the abbreviated root symbol CYP.

Cytochrome p450 was so named because the enzyme was discovered when it was noted that preparations of microsomes that had been chemically reduced and then exposed to carbon monoxide exhibited a distinct peak at 450nm



This is followed by a number designating the family having similar sequence identity.

This is followed by a capital letter indicating the subfamily.

Lastly this is followed by another number indicating the individual P450's in the family.

Examples:-

CYP1A1 metabolises PAH's
2-estrogens

CYPIA2 metabolises 16-estrogens

CYPIB1 metabolises 4-estrogens
and synthetic estrogens

CYP2A6 metabolises nicotine

CYP2B4 metabolises
phenobarbitol

CYP2C9 metabolises warfarin

CYP2C19 and CYP2D6 most antidepressants and antipsychotics

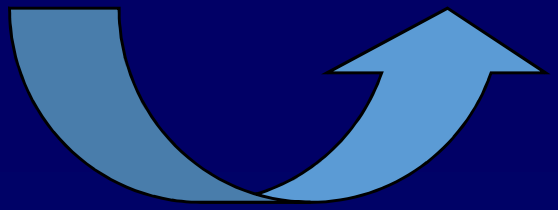
CYP2E1 metabolises ethanol, solvents and components in tobacco smoke.

CYP3A4 50% pharmaceutical drugs. Induced by St John's Wort (Hypericum). Inhibited by grapefruit.

PHASE 1 (HYDROXYLATION)
(Cytochrome P450)

$NADPH + H^+$ $\qquad$ $NADP^+$

Fe^{+++} $\qquad$ Fe^{++}



$$XH + 2O_2 \longrightarrow XOH + H_2O + O_2^{-}\cdot$$

Cytochrome P450 enzymes are

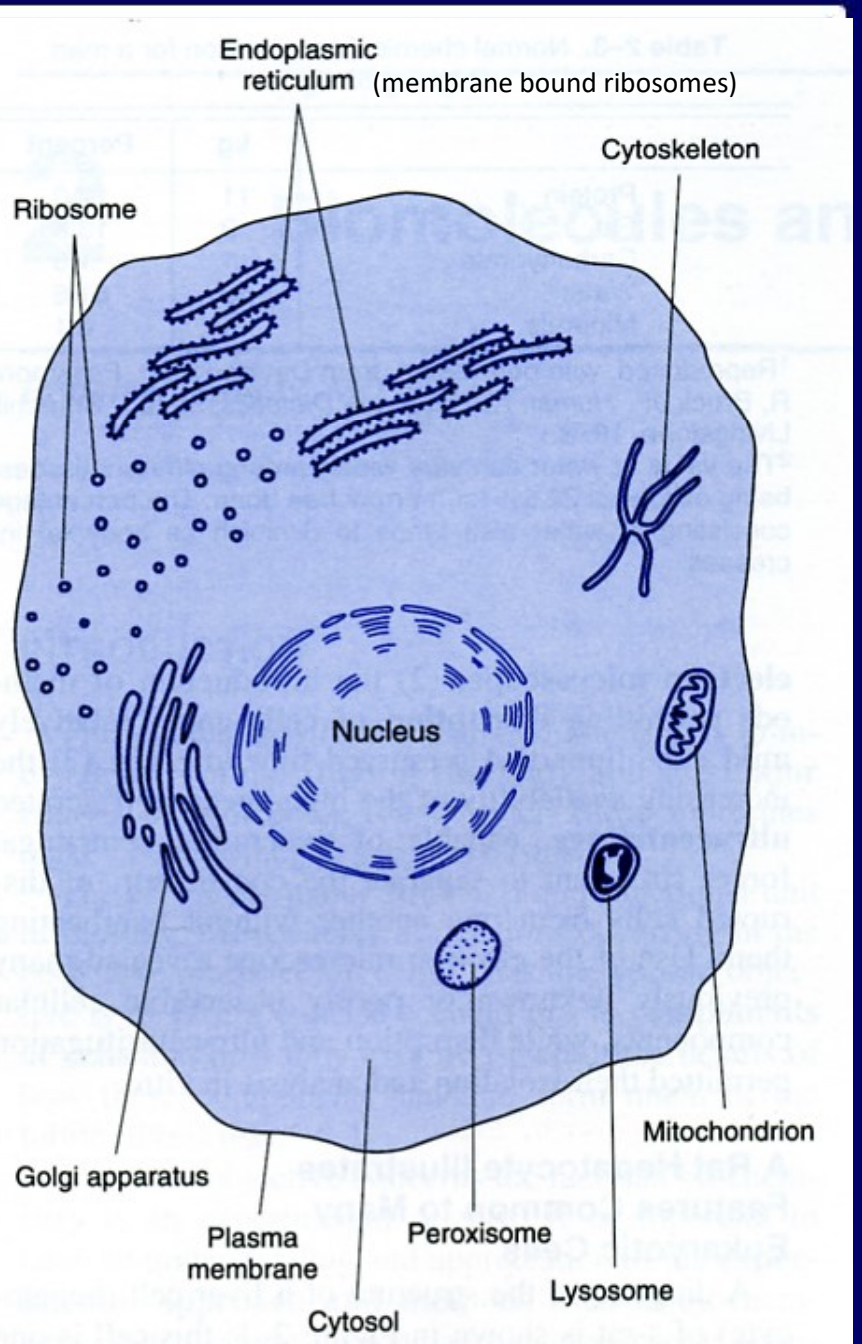
1. Hemoproteins (like hemoglobin).
2. Widely distributed across species especially in bacteria.
3. Present in the **endoplasmic reticulum of all cells** but greatest in the liver, small intestine, lung and glial cells.

Endoplasmic reticulum.

Major site of protein synthesis.

Synthesis of various lipids.

Oxidation of many xenobiotics.



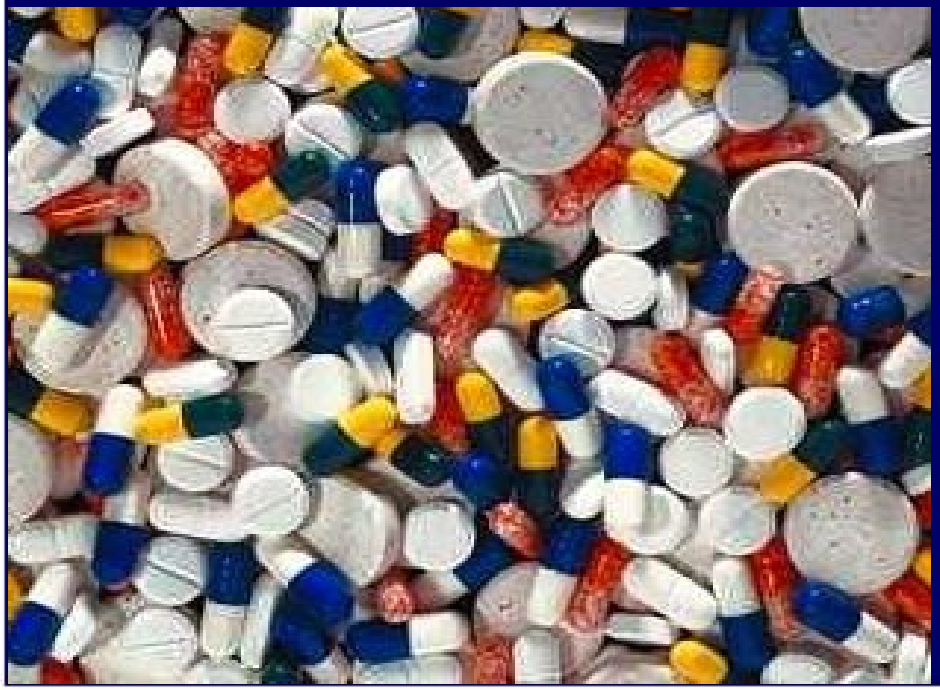
Cytochrome P450 enzymes

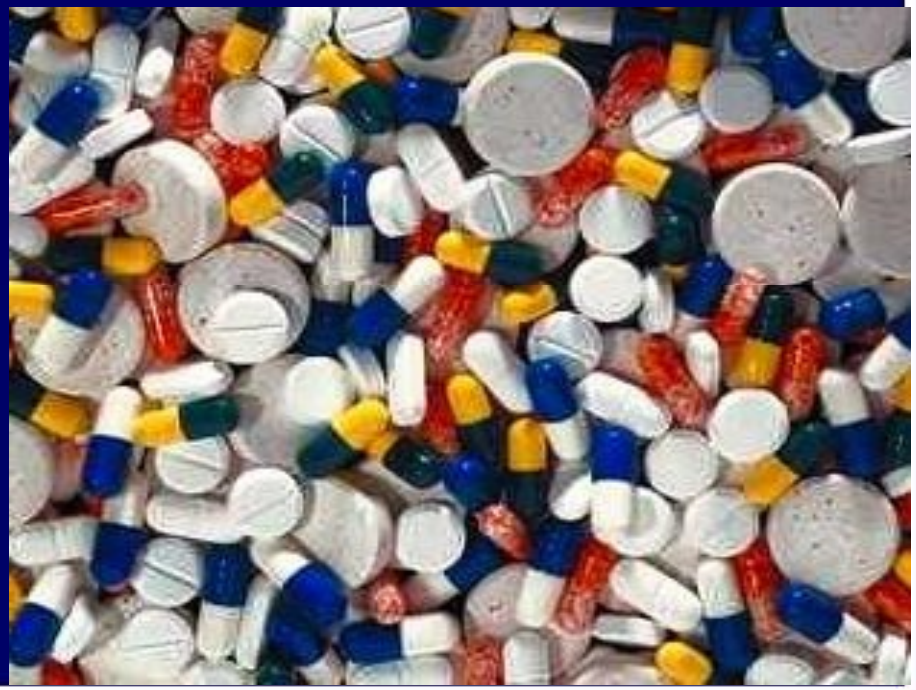
4. Require NADPH not NADH in their activation.

5. Require adequate levels of phosphatidyl choline rich in the membranes of the endoplasmic reticulum for optimal function.

Cytochrome P450 enzymes

6. Are **inducible** and is therefore the mechanism of drug interaction.





Cytochrome P450 enzymes

6. Are inducible and is therefore the mechanism of drug interaction.

7. Can have **polymorphisms** (individual genetic isoforms) which can exhibit low catalytic activity.

50% of all drugs prescribed to humans are metabolised by the various P450 enzymes.

However many P450 enzymes are inhibited by various drugs or their metabolic products, producing another cause of drug interaction.

Inability to Phase 1 detoxify

1. Leads to either the absorption and displacement in phospholipid cell membranes,
2. Inactivation of specific enzymes
3. The toxin binding with serum albumin, which is antigenic leading to the production of antibodies against it.

P450 INDUCTION NUTRIENTS

Phosphatidylcholine, NADPH, (thus Mg), Fe, FMN, FAD, Thiolate (α-lipoic for Sulfur),

Broccoli (IA2), Brussel sprouts (1A2), St John's Wort (3A4,5,7), Licorice, Black Walnut

High protein, Low carbohydrate, Ethanol (2E1),

Zn, Cu, Cr, Ca, Mol, Se, Vit E, Vit C, Bioflavonoids, Beta Carotene, NAC,

SUPPLEMENT ACCORDINGLY

COMMENTARY

Our Toxic World; Is Roundup Slowly Killing Us?

George D. Lundberg, MD

DISCLOSURES | August 02, 2016

Remember the gut microbiome? We are learning a great deal about how it influences so much of human health. There is a project called Qmulus, at the Computer Science and Artificial Intelligence Laboratory at the Massachusetts Institute of Technology and funded in part by Quanta Computers of Taiwan. Under its auspices, authors Anthony Samsel and Stephanie Seneff, in a 40-plus-page review[6] with 286 references, paint a very troubling picture of glyphosate's inhibition of cytochrome P450 enzymes. For example, one role of this enzyme is to detoxify xenobiotics. The authors propose that the consequences of this inhibition, when coupled with other synergistic disruptions, may insidiously induce many diseases associated with a Western diet, including diabetes, obesity, cancer, autism, Alzheimer's, and others.

A 2015 paper[7] by the same authors takes these and new findings and deductions even further to manganese deficiency in cows fed genetically modified Roundup Ready feed. This update is 55 pages long with 328 supporting references. Both are in open access; peruse them if you choose.

COMMENTARY

Demonizing Processed Foods: It's the Additives, Stupid

George D. Lundberg, MD

DISCLOSURES | August 30, 2017

The gut microbiome is very complicated, [and] probably very important in obesity, diabetes, and metabolic syndrome. We have previously written about the probable adverse effects of ubiquitous antibiotics on the microbiome.[3]

Oil and water don't mix. They naturally separate, unless an emulsifier is present. Many emulsifiers are natural, such as gelatin, lanolin, and lecithin in milk and eggs. But antifat zealotry drove the food industry away from milk and egg products. So, synthetic and semisynthetic emulsifiers came into widespread use in the food processing industry in the latter 20th century. They are in many foods, such as ice cream, biscuits, cakes, bread, cookies, caramel, mayonnaise, jam, and breakfast cereals.

> Seven common emulsifiers are carboxymethycellulose (CMC), polysorbate 80 (P80), lecithin, mono-and diglycerides (MDGs), stearoyl lactylates, sucrose esters, and polyglycerol polyricinoleate.[4]

Seven common emulsifiers are carboxymethycellulose (CMC), polysorbate 80 (P80), lecithin, mono-and diglycerides (MDGs), stearoyl lactylates, sucrose esters, and polyglycerol polyricinoleate.[4]

Of course they, like all food products, have passed through US Food and Drug Administration testing for adverse effects. But those tests may not detect more subtle pathobiological effects.

Mouse studies demonstrate that the diminished gut mucus associated with two emulsifiers (CMC and P80) may permit penetration of gut microbes through the epithelium.[5] Relatively low concentrations of those same two commonly used emulsifiers, CMC and P80, induced low-grade inflammation and obesity/metabolic syndrome in wild-type hosts and promoted robust colitis in mice predisposed to this disorder.[5] Of course, that is mice.

Recent studies using microscopy in human colon specimens have demonstrated that the distance between colonic microbes and the epithelial surfaces is narrowed.[6] This colonic microbiota encroachment correlates with dysglycemia, but not with obesity. Obviously, much more research is indicated to connect (or not) these dots. As for me, to the extent possible, no more emulsifiers.

Phase 2

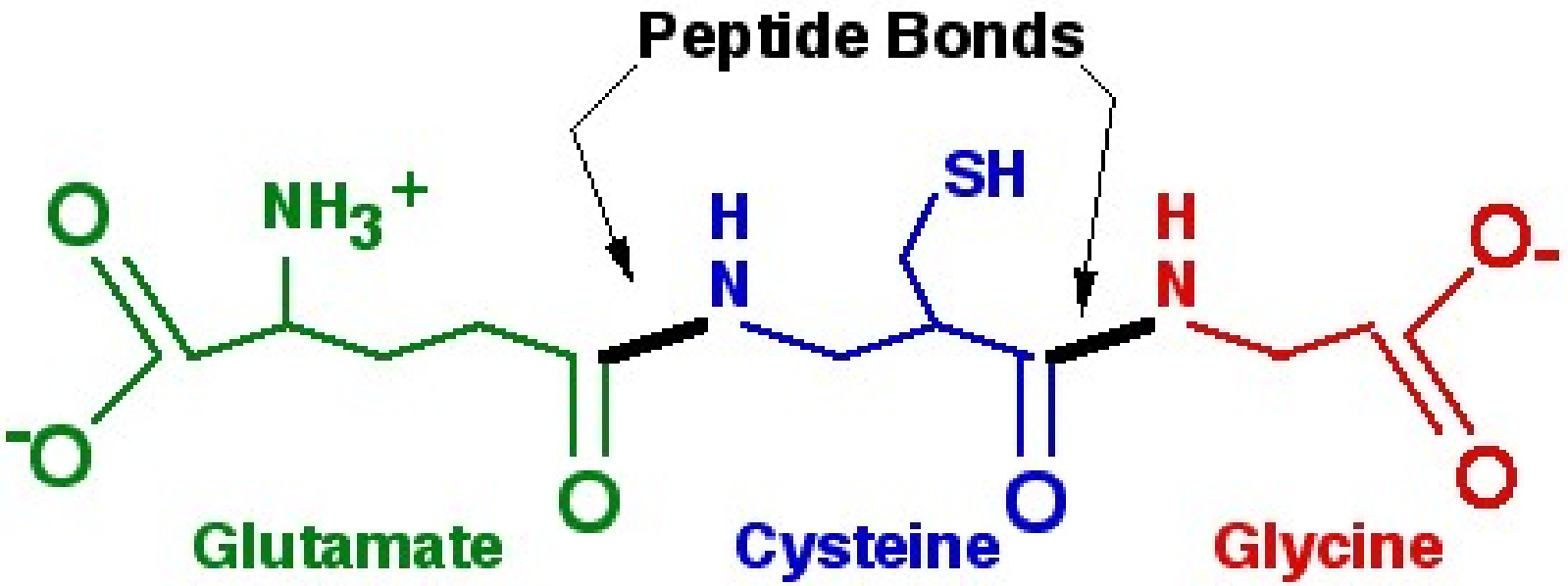
Conjugation

Phase 2 reactions conjugate the derivatives from Phase 1, where applicable, with molecules such as
Glutathione,
Glucuronic acid,
Sulfate,
Acetyl CoA,
SAM,
Taurine, Cysteine, Glycine and Threonine.

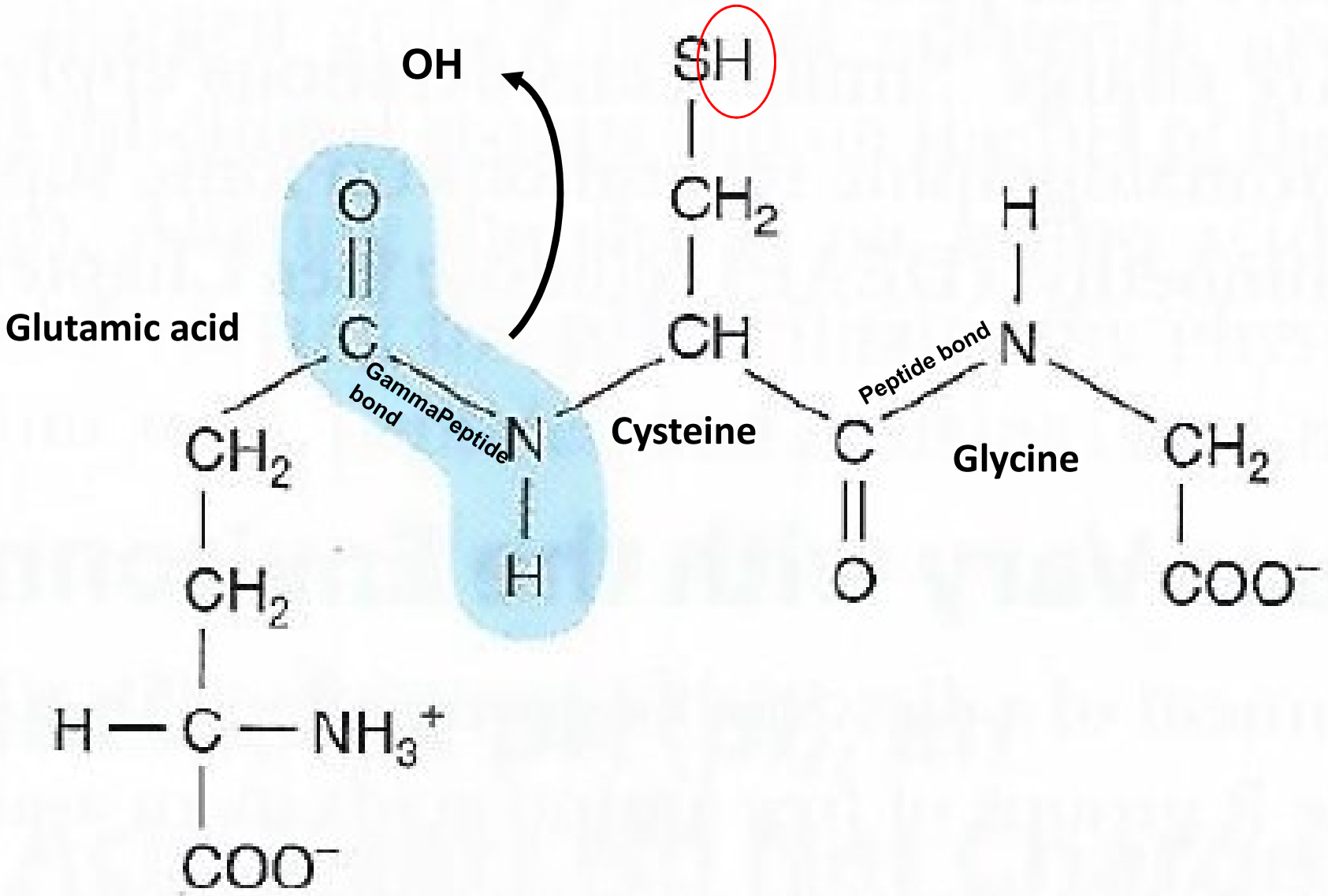
This makes the derivatives even more **water soluble** for excretion through the urine or bile.

Glutathione

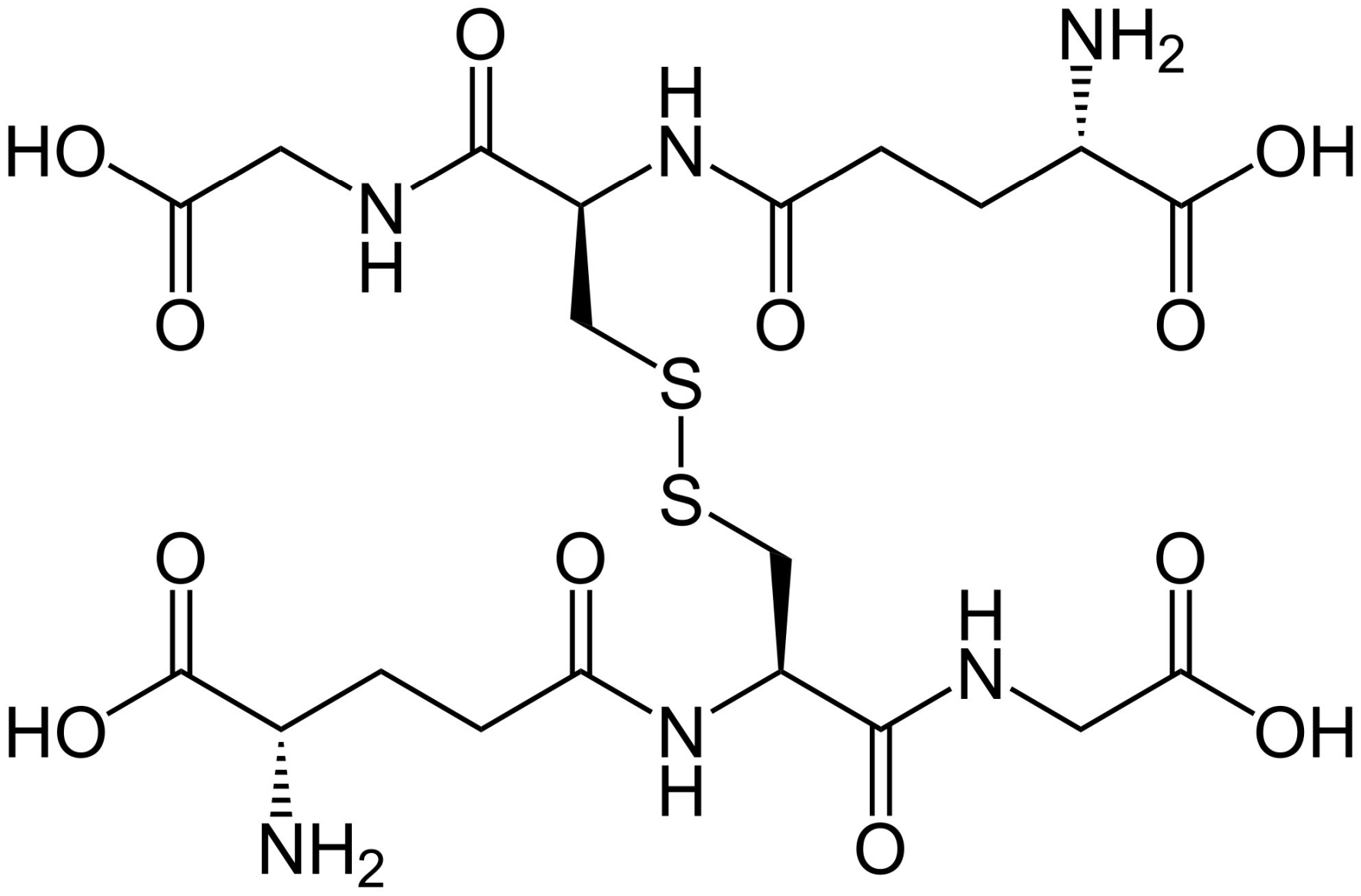
Glutathione

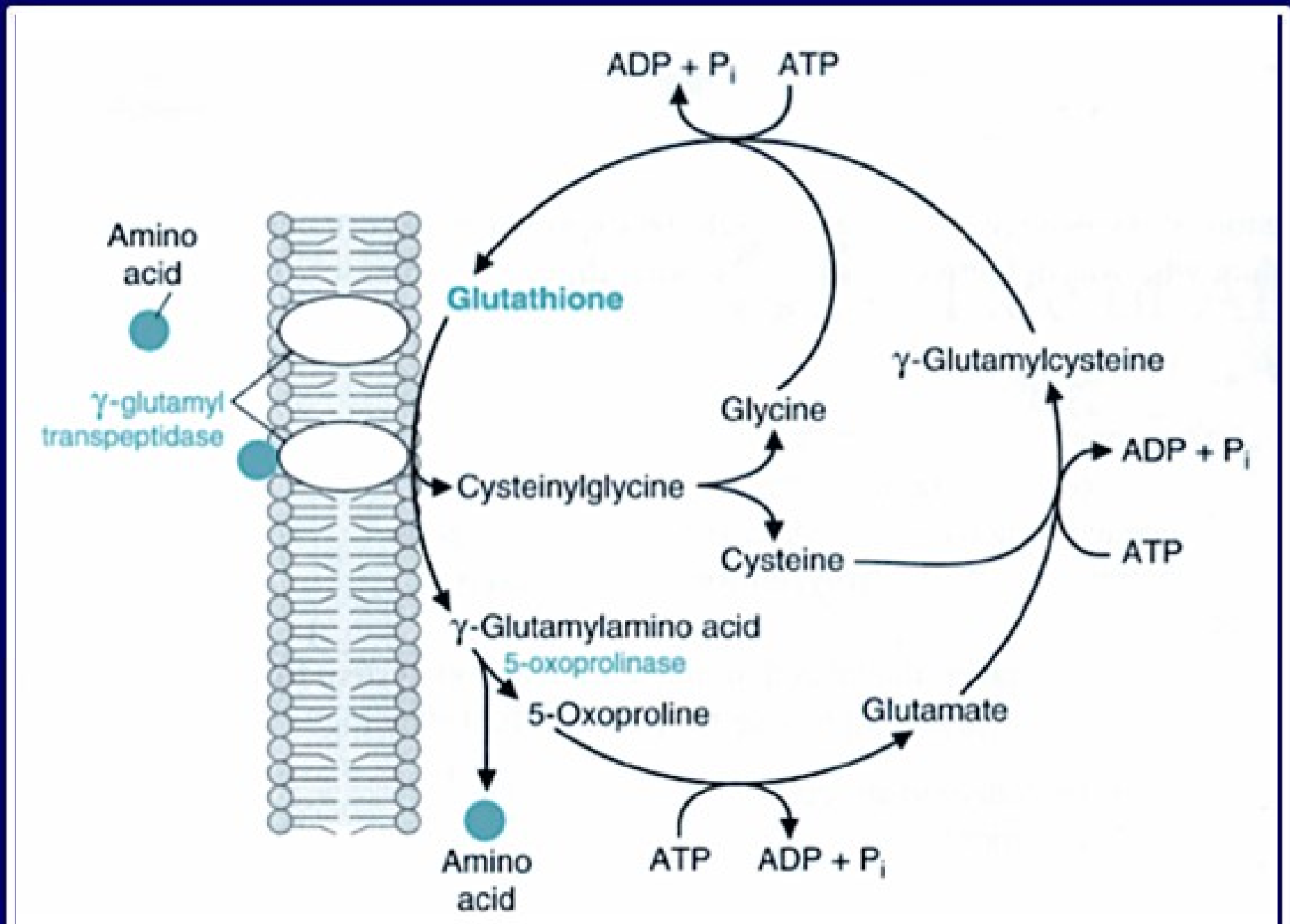


Reduced Glutathione (GSH)



Oxidised Glutathione (GSSG)




ADP + Pi
ATP
Amino acid
Glutathione
γ-glutamyl transpeptidase
Glycine
γ-Glutamylcysteine
ADP + Pi
Cysteinylglycine
ATP
Cysteine
γ-Glutamylamino acid
5-oxoprolinase
5-Oxoproline
Glutamate
Amino acid
ATP
ADP + Pi

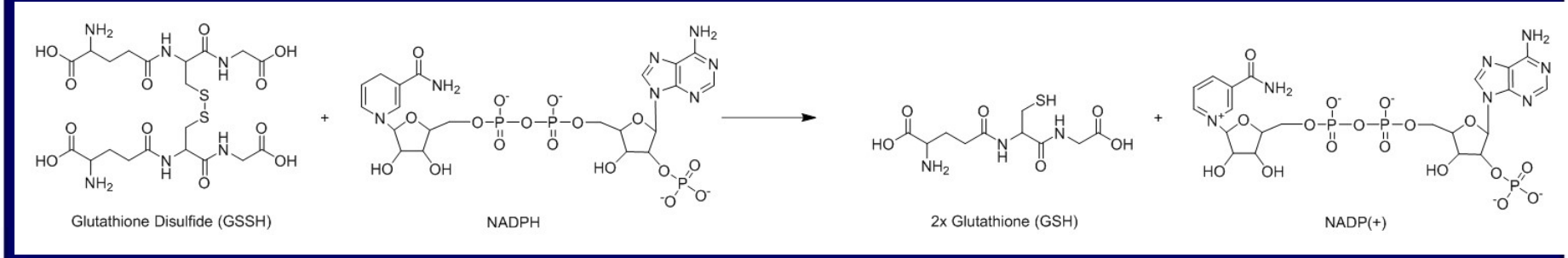
Glutathione is the main intracellular antioxidant and detoxifier. It is capable of preventing damage to important cellular components caused by reactive oxygen species such as free radicals, peroxides, lipid peroxides, and heavy metals.*

**Pompella A, Visvikis A, Paolicchi A, De Tata V, Casini AF (October 2003). "The changing faces of glutathione, a cellular protagonist". Biochemical Pharmacology. 66 (8): 1499–503*

It is a tripeptide with a gamma peptide linkage between the carboxyl group of the glutamate side chain and the amine group of cysteine, and the carboxyl group of cysteine is attached by normal peptide linkage to a glycine.

Source: MeSH
Record Name: Glutathione
URL: https://www.ncbi.nlm.nih.gov/mesh/68005978

Once oxidized, glutathione can be reduced back by glutathione reductase, using NADPH and FAD as an electron donor.*



*Lu SC (May 2013). "Glutathione synthesis". *Biochimica et Biophysica Acta*. 1830 (5): 3143–53.

The ratio of reduced glutathione to oxidized glutathione within cells is often used as a measure of cellular oxidative stress.*

*Lu SC (May 2013). "Glutathione synthesis". *Biochimica et Biophysica Acta*. 1830 (5): 3143–53.

In healthy cells and tissue, more than 90% of the total glutathione pool is in the reduced form (GSH) and less than 10% exists in the disulfide form (GSSG). An increased **GSSG-to-GSH ratio** is considered indicative of oxidative stress.*

*Halprin KM, Ohkawara A (1967). "The measurement of glutathione in human epidermis using glutathione reductase". *The Journal of Investigative Dermatology*. 48 (2): 149–52.

Functions of Glutathione

1. Maintains levels of glutathione peroxidase.*
2. Major endogenous antioxidant and maintains Vitamin C and E in their reduced active forms.**

•Grant CM (2001). "Role of the glutathione/glutaredoxin and thioredoxin systems in yeast growth and response to stress conditions". *Molecular Microbiology*. 39 (3): 533–41.

•** *Dringen R (December 2000). "Metabolism and functions of glutathione in brain". Progress in Neurobiology. 62 (6): 649–71.*

3. Regulates **Nitric Oxide cycle** by enhancing the function of citrulline.*

4. It is used in metabolic an biochemical reactions such as **DNA synthesis** and repair, protein synthesis, prostaglandin synthesis, amino acid transport, and enzyme activation.

• *Ha SB, Smith AP, Howden R, Dietrich WM, Bugg S, O'Connell MJ, Goldsbrough PB, Cobbett CS (June 1999)..*

Thus, every system in the body can be affected by the state of the glutathione system, especially the immune system, the nervous system, the gastrointestinal system, and the lungs.

• *Ha SB, Smith AP, Howden R, Dietrich WM, Bugg S, O'Connell MJ, Goldsbrough PB, Cobbett CS (June 1999)..*

5. It has roles in progression of the cell cycle, including cell death. *

GSH levels regulate redox changes to nuclear proteins necessary for the initiation of cell differentiation.

•8 Lu SC (May 2013). "Glutathione synthesis". Biochimica et Biophysica Acta. 1830 (5): 3143–53.

6. GSH is known as a substrate in conjugation reactions, which is catalyzed by **glutathione S-transferase** enzymes in cytosol, microsomes, and mitochondria. However, GSH is also capable of participating in non-enzymatic conjugation with some chemicals.

7. Glutathione (GSH) inhibits leukotriene synthesis from arachidonic acid and transforming inflammatory molecules (leukotriene C4 to leukotriene D4)*.

*Gamma-glutamyl transferase and cardiovascular disease
Gjin Ndrepepa and Adnan Kastrati

8. It is also important as a hydrophilic molecule that is added to lipophilic toxins and waste in the liver during biotransformation before they can become part of the bile.*

*Source: Human Metabolome Database (HMDB)
Record Name: Glutathione
URL: http://www.hmdb.ca/metabolites/HMDB0000125

9. **Glutathione**, along with oxidized glutathione (GSSG) and S-nitrosoglutathione (GSNO), have been found to bind to the glutamate recognition site of the NMDA and AMPA receptors (via their γ-glutamyl moieties), and may be endogenous neuromodulators.*

*Steullet P, Neijt HC, Cuénod M, Do KQ (February 2006). "Synaptic plasticity impairment and hypofunction of NMDA receptors induced by glutathione deficit: relevance to schizophrenia". *Neuroscience*. 137 (3): 807–19.

10. Other antioxidants such as **Vitamin C** and compounds such as **N-acetylcysteine** (NAC)* and **alpha Lipoic acid** may also work synergistically with glutathione, preventing depletion of either.

*"Acetylcysteine Monograph for Professionals - Drugs..com

The glutathione-ascorbate cycle, which works to detoxify hydrogen peroxide (H_2O_2), is one very specific example of this phenomenon.*

*Steullet P, Neijt HC, Cuénod M, Do KQ (February 2006). "Synaptic plasticity impairment and hypofunction of NMDA receptors induced by glutathione deficit: relevance to schizophrenia". *Neuroscience*. 137 (3): 807–19.

11. **Calcitriol (1,25-dihydroxyvitamin D_3),** an active metabolite of vitamin D_3, after being synthesized from calcifediol in the kidney, increases glutathione levels in the brain and appears to be a catalyst for glutathione production. * takes 10 days.

*Garcion E, Wion-Barbot N, Montero-Menei CN, Berger F, Wion D (April 2002). "New clues about vitamin D functions in the nervous system". *Trends in Endocrinology and Metabolism*. 13 (3): 100–5.

12. **S-adenosylmethionine (SAMe),** a co-substrate involved in methyl group transfer, has also been shown to increase cellular glutathione content in persons suffering from a disease-related glutathione deficiency.*

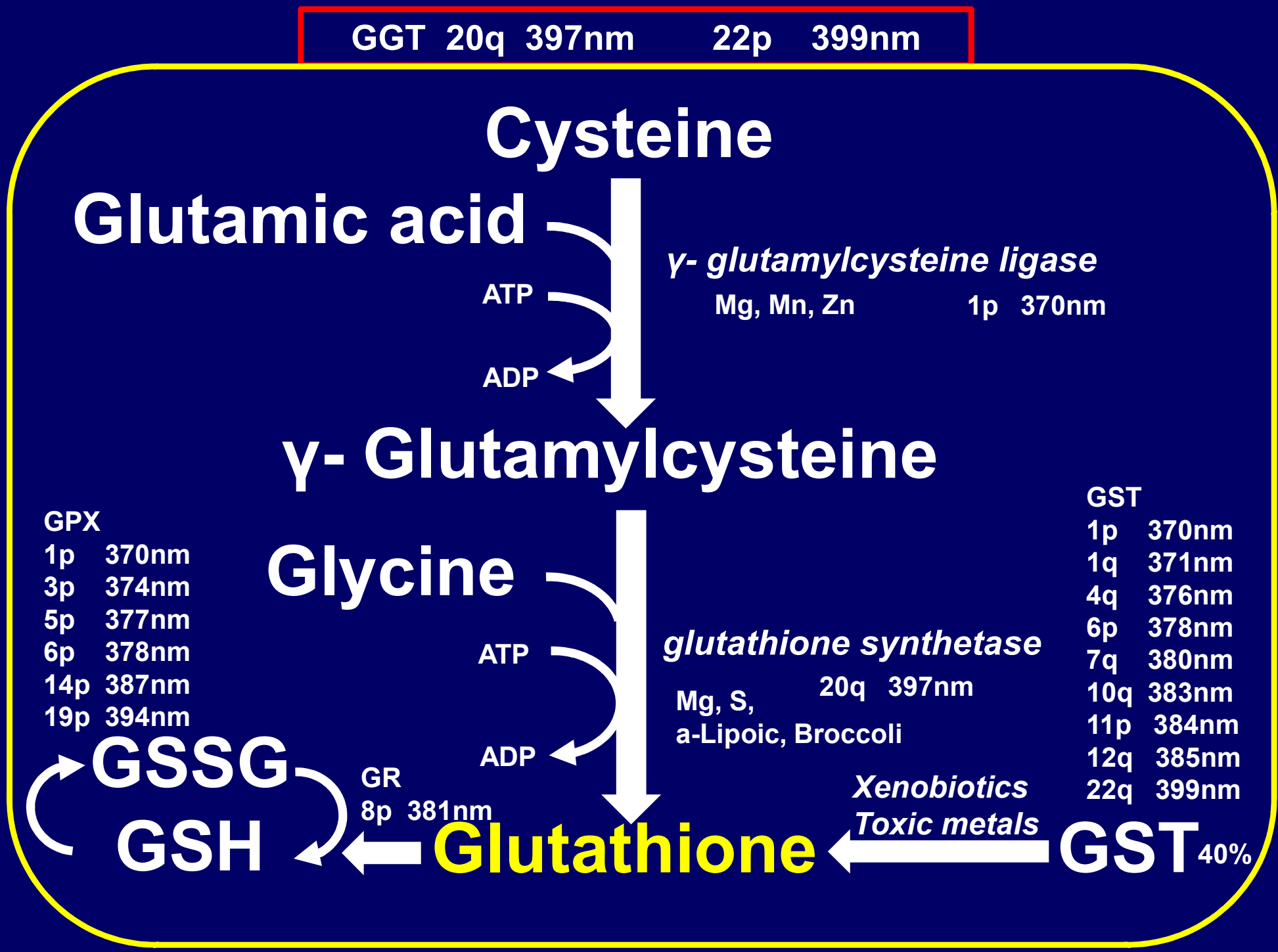
*Lieber CS (November 2002). "S-adenosyl-L-methionine: its role in the treatment of liver disorders". *The American Journal of Clinical Nutrition*. 76 (5):

Glutathione

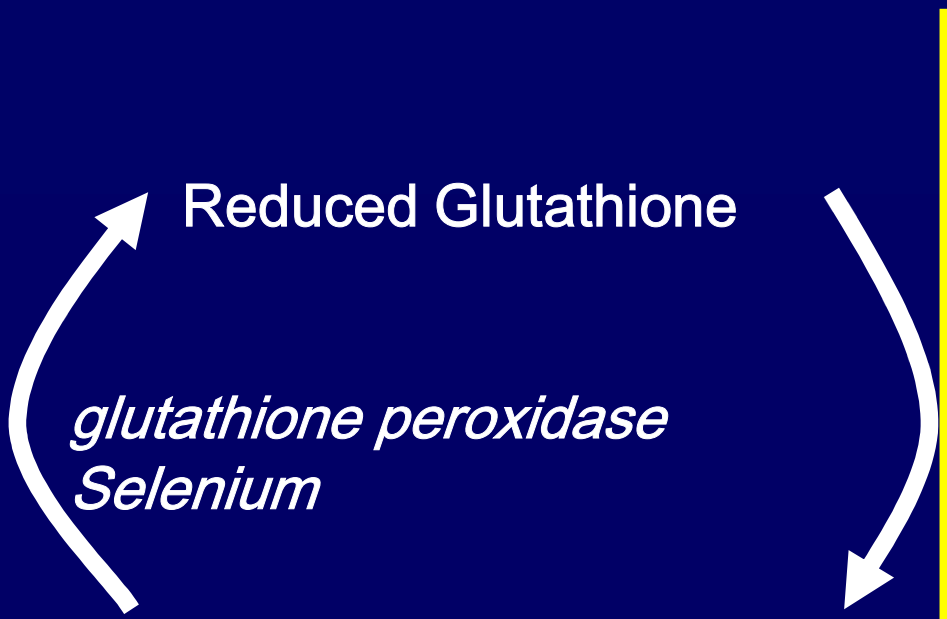
Detoxifies xenobiotics such as aromatic disulfides, napthalene, anthracene, phenanthacin compounds, aliphatic disulfides and the regeneration of endogenous thiols from disulfides.

Harper's Illustrated Biochemistry 29th Edition Pub Lange. Page 679

Hayes JD, Flanagan JU, Jowsey IR (2005). "Glutathione transferases". *Annu. Rev. Pharmacol. Toxicol.* 45: 51–88. doi:10.1146/annurev.pharmtox.45.120403.095857. PMID 15822171


GGT 20q 397nm 22p 399nm
Cysteine
Glutamic acid
ATP
ADP
γ- glutamylcysteine ligase
Mg, Mn, Zn 1p 370nm
γ- Glutamylcysteine
GPX
1p 370nm
3p 374nm
5p 377nm
6p 378nm
14p 387nm
19p 394nm
Glycine
ATP
ADP
glutathione synthetase
Mg, S,
a-Lipoic, Broccoli
20q 397nm
GST
1p 370nm
1q 371nm
4q 376nm
6p 378nm
7q 380nm
10q 383nm
11p 384nm
12q 385nm
22q 399nm
GSSG
GSH
GR
8p 381nm
Glutathione
Xenobiotics
Toxic metals
GST 40%

Phase 1 toxic intermediate



Reduced Glutathione

glutathione peroxidase
Selenium

Oxidised Glutathione

glutathione-s-transferase
Zn ++
Spinach
Onion
Garlic *
Broccoli *
Lemongrass
Celery *
Watercress

Glutathione (P-5-P) conjugate

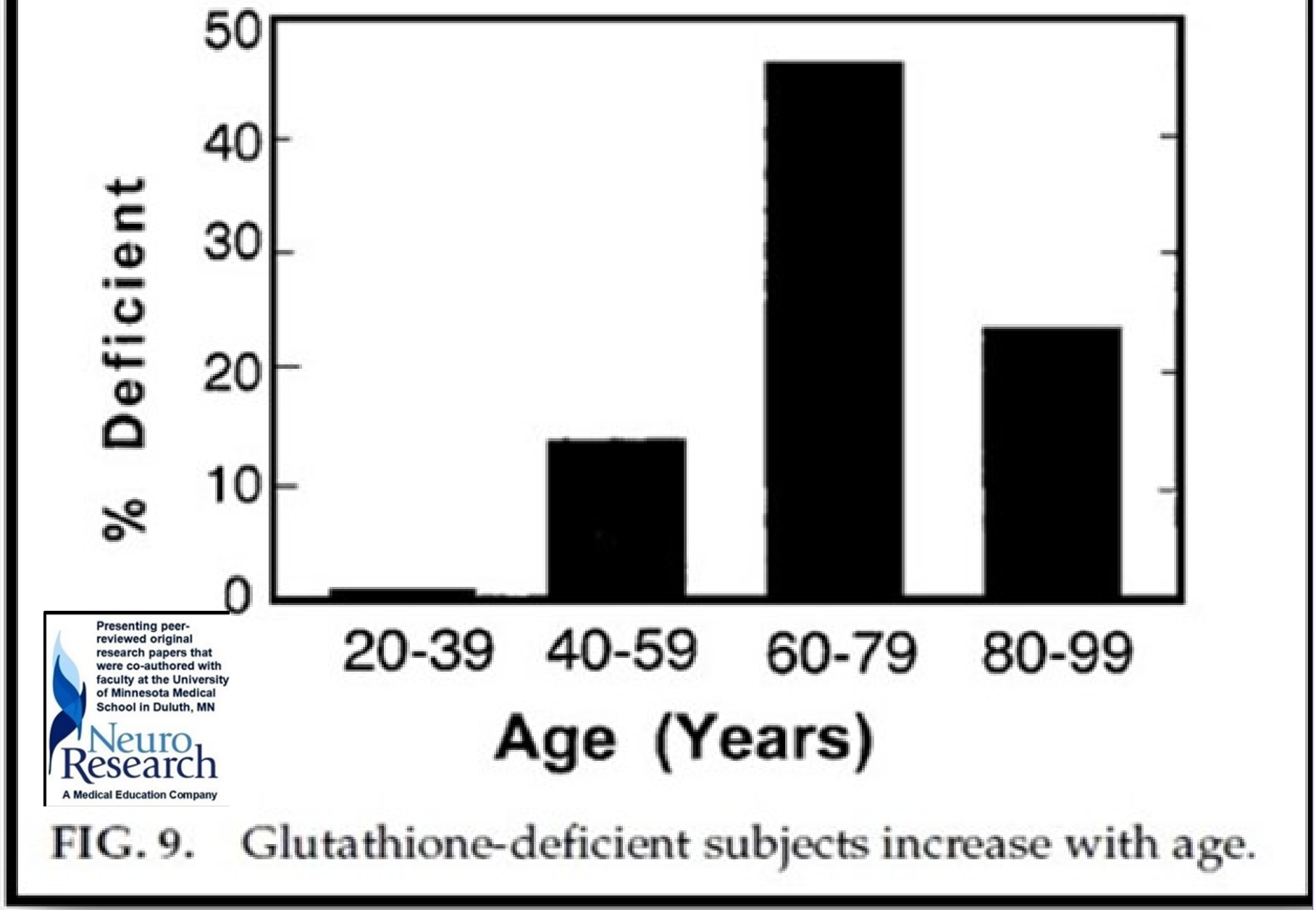


FIG. 9. Glutathione-deficient subjects increase with age.

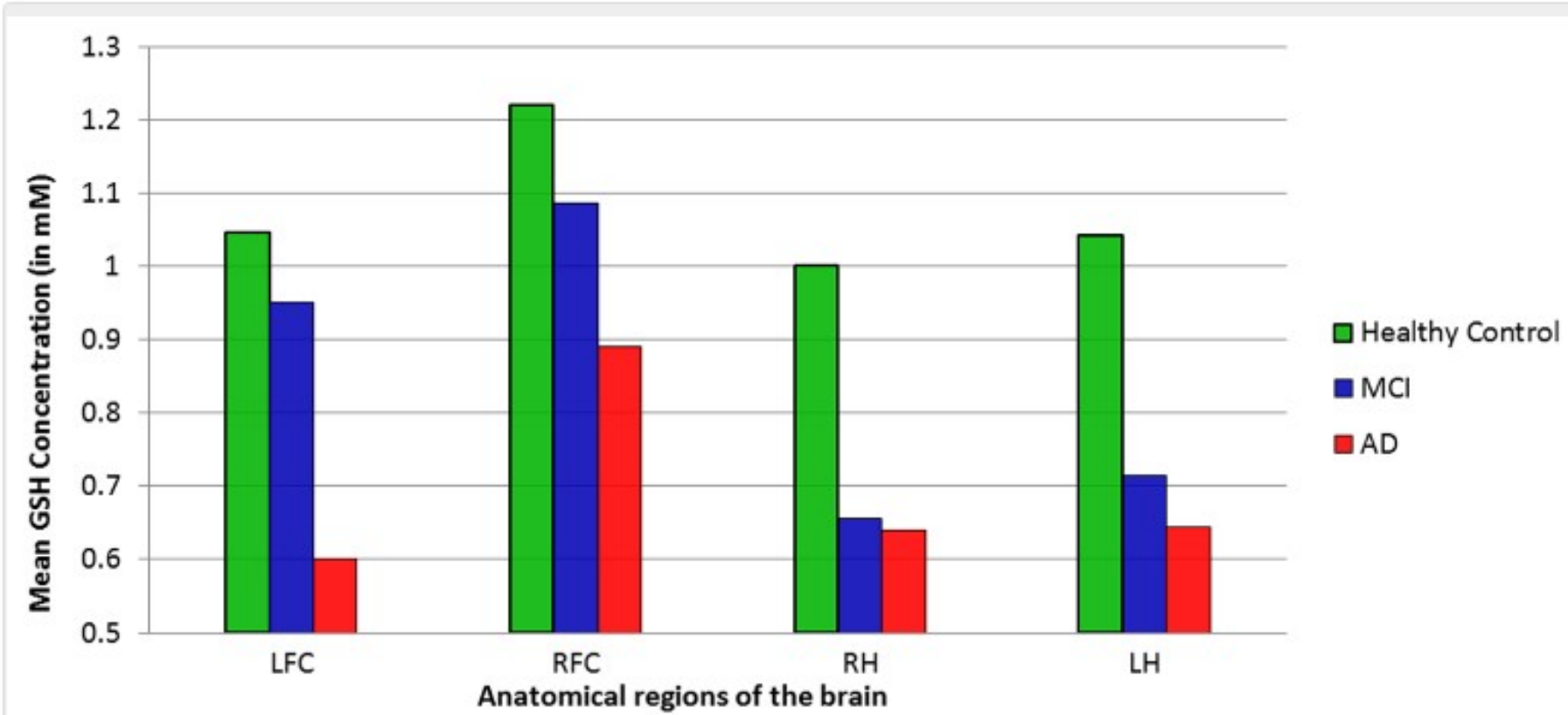


Fig.1. Glutathione levels plummet with Alzheimer's progression

LFC: Left frontal cortex; RFC: Right frontal cortex; RH: Right hippocampus; LH: Left hippocampus

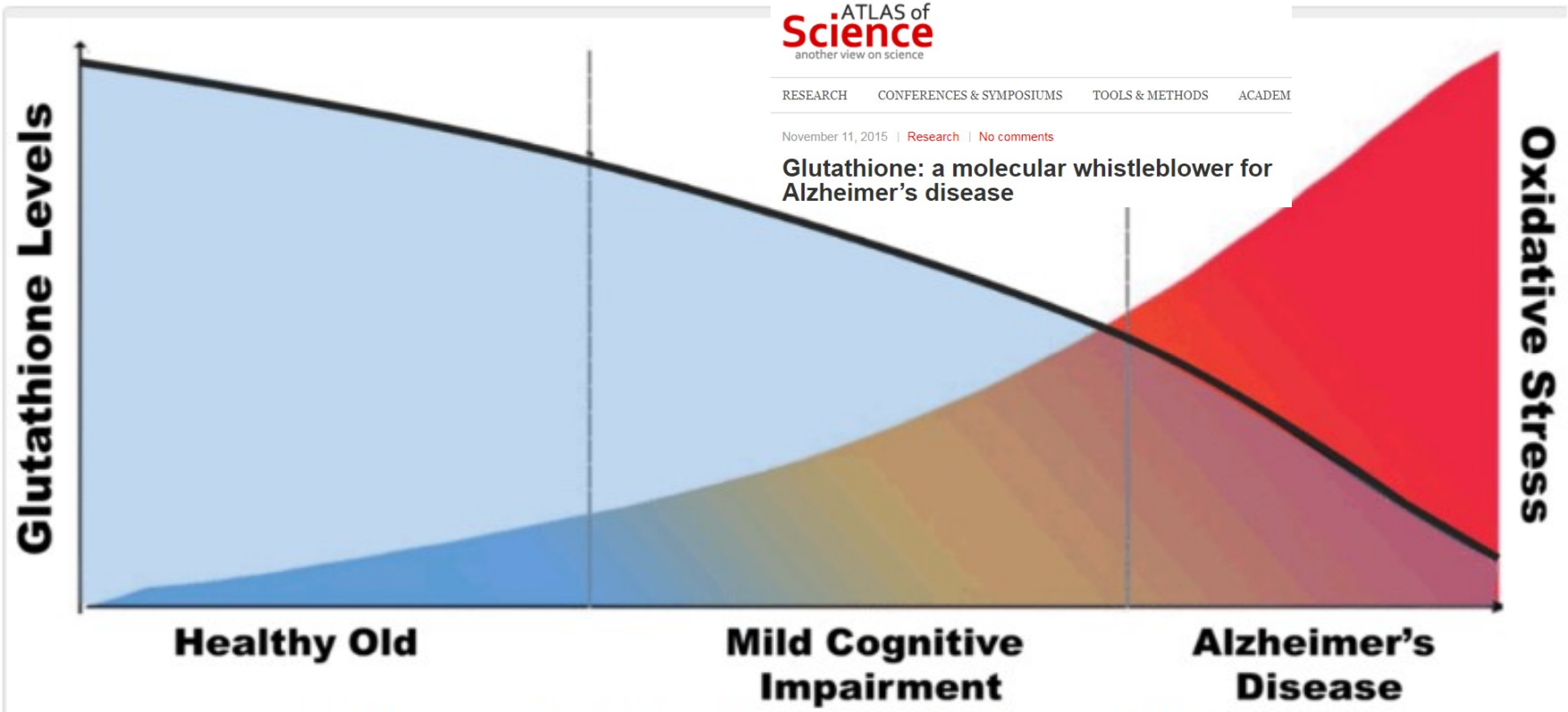


Fig.2. The Relationship between Glutathione, Oxidative Stress, and Alzheimer's

Our findings reveal GSH levels to be tightly associated with and diagnostically reflective of Alzheimer's progression (Fig. 2). They make a loud and strong case for GSH as a potential diagnostic marker for Alzheimer's – a possible whistleblower that uncovers the disease. Given that GSH appears to be a key character in the molecular script that incubates and propagates Alzheimer's, we are presently working towards conducting a clinical trial aimed at assessing GSH as therapeutic target. GSH may well turn out to be the therapeutic 'anti(oxi)dote' to this deadly disease.

Dr. Sumiti Saharan

Note the decrease in deficiency after age 80. The article formulated the hypothesis that those with severe glutathione deficiency do not live past 80 years and only those not suffering from severe glutathione deficiency reach the age of those living longer than 80 years.*

*Neuro Research article Nov 2018

Identification of about 1,200 fat-soluble neurotoxins has occurred. Glutathione protects the brain against fat-soluble neurotoxins.

Glutathione does not cross the blood-brain barrier.

Consider the fact that ALL patients with chronic disease suffer from glutathione depletion.

*Neuro Research article Nov 2018

Glutathione/Ribose stimulates glutathione

NAC stimulates glutathione.

Vitamin C helps recycle Glutathione

Yarrow (Achilles milifolium) stimulates the Glutathione pathway.

L-α-Lipoic acid stimulates Glutathione synthesis

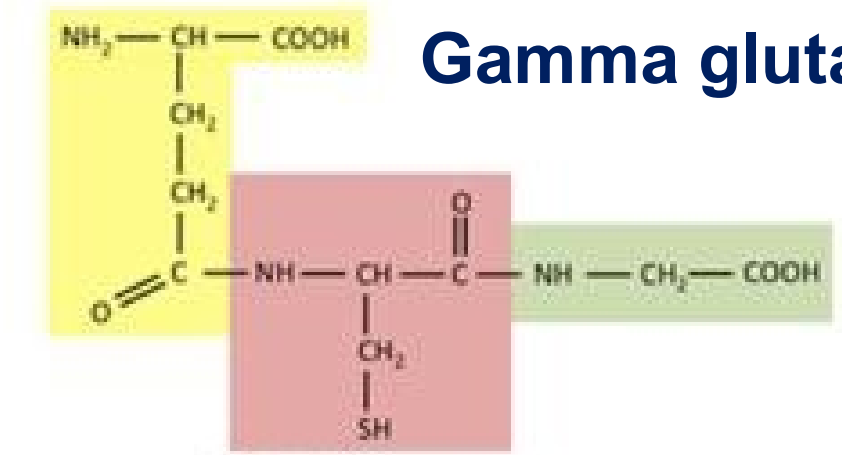
Glutathione-s-transferase catalyzes the conjugation of the reduced form of glutathione (GSH) to xenobiotic substrates and lipid peroxides for the purpose of detoxification. The conjugation products are converted into mercapturic acids and excreted via the urine or bile.*

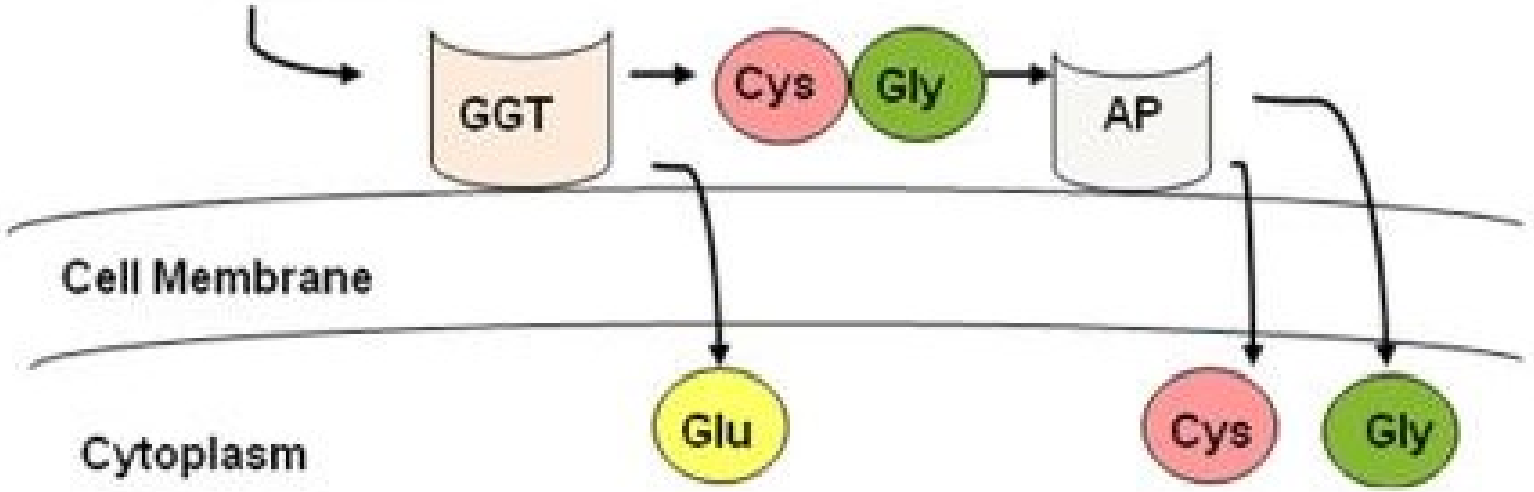
**Josephy PD (June 2010). "Genetic variations in human glutathione transferase enzymes: significance for pharmacology and toxicology". Human Genomics and Proteomics. 2010:*

Gamma glutamyltransferase (GGT)

Gamma glutamyltransferase (GGT)

20q 397nm
22p 399nm





Hydrolysis of extracellular glutathione by GGT. GGT releases glutamate and cysteinyl-glycine. Cysteinyl-glycine hydrolysed by aminopeptidase (AP) releasing cysteine and glycine. All three amino acids can then be taken up into the cell to synthesise glutathione but process not very efficient. Glutathione cannot be taken up intact in most cells.

Gammaglutamyltransferase (GGT) is a transferase enzyme that catalyzes the transfer of gamma-glutamyl functional groups from molecules such as glutathione to an acceptor that may be an amino acid, a peptide or water (forming glutamate).*

**Tate SS, Meister A (1985). "gamma-Glutamyl transpeptidase from kidney". Methods in Enzymology. 113: 400–19*

Research indicates that GGT can also exert a pro-oxidant role, with regulatory effects at various levels in cellular signal transduction and cellular pathophysiology.*

** Dominici S, Paolicchi A, Corti A, Maellaro E, Pompella A (2005). "Prooxidant reactions promoted by soluble and cell-bound gamma-glutamyltransferase activity". Methods in Enzymology. 401: 484–501.*

GGT is present in the cell membranes of many tissues, including the kidneys, bile duct, pancreas, gallbladder, spleen, heart, brain, prostate and seminal vesicles. Smaller amounts are found in the lungs, testis, and thyroid gland.*

* Raulf M, Stüning M, König W (May 1985). "Metabolism of leukotrienes by L-gamma-glutamyl-transpeptidase and dipeptidase from human polymorphonuclear granulocytes". *Immunology*. 55(1): 135–47.

It is involved in the transfer of amino acids across the cellular membrane and leukotriene metabolism*.

* Raulf M, Stüning M, König W (May 1985). "Metabolism of leukotrienes by L-gamma-glutamyl-transpeptidase and dipeptidase from human polymorphonuclear granulocytes". *Immunology*. 55(1): 135–47.

GGT alone does not directly cause a particular disease or disorder. High levels of GGT may contribute to disease by acting a **pro-oxidant.** GGT may increase oxidative stress, starting with the breakdown of glutathione (and production of cysteinylglycine). Other toxic molecules are then formed, leading to tissue, cellular, and DNA damage .*

*Human Atherosclerotic Plaques Contain Gamma-Glutamyl Transpeptidase Enzyme Activity Aldo Paolicchi, Michele Emdin

GGT is present in plaques because it attaches itself to circulating fats (LDL). Once in the plaque, GGT can become pro-oxidant, injuring blood vessels (via **oxidative stress**), and contribute to heart disease.*

*Human Atherosclerotic Plaques Contain Gamma-Glutamyl Transpeptidase Enzyme Activity Aldo Paolicchi, Michele Emdin

Gamma-glutamyltransferase (GGT)

High in

Alcohol abuse, Barbituates, NSAIs, Aspirin, St John's Wort (Hypericum).

Biliary, Liver and Pancreas diseases

CVD and Atherosclerosis

Metabolic syndrome. High body mass index is associated with type 2 diabetes only in persons with high serum GGT.

Lim JS, Lee DH, Park JY, Jin SH, Jacobs DR (June 2007). "A strong interaction between serum gamma-glutamyltransferase and obesity on the risk of prevalent type 2 diabetes: results from the Third National Health and Nutrition Examination Survey". Clinical Chemistry. 53 (6): 1092–8. doi:10.1373/clinchem.2006.079814. PMID 17478563.

Serum elevated gamma glutamyltransferase levels may be a marker for oxidative stress in Alzheimer's disease

Burcu Balam Yavuz,[1] Bunyamin Yavuz,[2] Meltem Halil,[1] Mustafa Cankurtaran,[1] Zekeriya Ulger,[1] Eylem Sahin Cankurtaran,[3] Kudret Aytemir[4] and Servet Ariogul[1]

[1] *Hacettepe University Faculty of Medicine, Department of Internal Medicine, Division of Geriatric Medicine, Ankara, Turkey*
[2] *Kecioren Research Hospital, Department of Cardiology, Ankara, Turkey*
[3] *Ankara Oncology Hospital, Department of Psychiatry, Ankara, Turkey.*
[4] *Hacettepe University Faculty of Medicine, Department of Cardiology, Ankara, Turkey*

ABSTRACT

Background: Gamma glutamyltransferase (GGT) plays a role in cellular glutathione uptake, which is an important element of antioxidant mechanisms. An increase in serum GGT is thought to be an early and sensitive marker of oxidative stress. Oxidative stress has a role in the pathogenesis of Alzheimer's disease (AD). The aim of this study was to investigate the GGT levels in AD

High GGT can cause

- Liver disease
- Biliary tract disease
- CHD
- CVA
- Arteriosclerosis
- Heart failure
- High BP
- Cardiac arrhythmias
- Diabetes
- Metabolic-syndrome
- Cancer
- Kidney disease
- Alzheimer's
- Thyroid
- Bone density loss

To lower GGT levels

Decrease alcohol
Avoid pollutants
More fruit and veg
High protein
More coffee
Less red meat
Moderate exercise
Cloves
Curcumin
Vitamin C
Vitamin D
Vitamin E
Fish/Flax/DHA
Milk thistle
Magnesium
Zinc
Glutathione

What are ORAC Units?

The ORAC (Oxygen Radical Absorbance Capacity) unit, ORAC value, or "ORAC score" is a method of measuring the *in vitro* antioxidant capacity of different foods and supplements.

ORAC Values*

Cloves	290283
Oregano	175295
Rosemary	165280
Peppermint	160820
Thyme	157380
Cinnamon	131420
Turmeric	127068
Sage	119929
Allspice	100400

^National Institute on Aging (NIA) at the National Institutes of Health (NIH).

Persistent Organic Pollutants (POPs)

Hormone disruptors

Xeno-estrogens –

PCBs (electric and coolant fluids)

Bisphenol A (solvent)

Bisphenol S (adhesives)

Nonylphenols (lubricants)

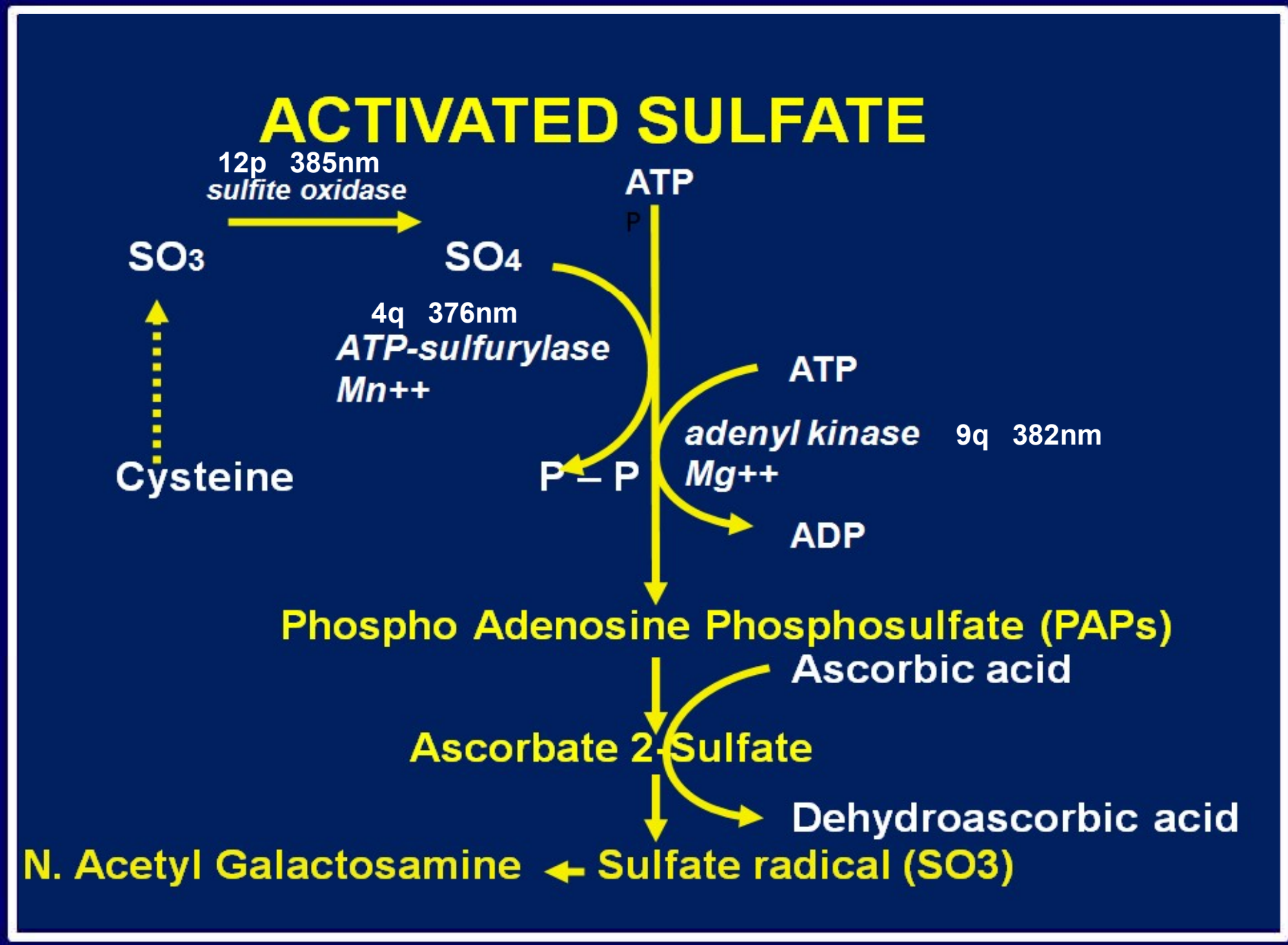
DDT (insecticide)

Polybrominated diphenyl ethers (flame retardant)

Perfluorooctanoic acid (flame retardant)
Endosulfan (insecticide)
Kepone (insecticide)
Vinclozolin (fungicide)
17-alpha ethinylestradiol (birth pill)
Genistein (isoflavone)
Zearalenone (fungal toxin)
Oxybenzone (sunscreen)
Tributyltin (biocide)

Sulfite oxidase

Sulfite oxidase produces free radicals which, when under a strict physiological control, act as a natural antifungal.


ACTIVATED SULFATE
12p 385nm
sulfite oxidase
SO3
SO4
4q 376nm
ATP-sulfurylase
Mn++
Cysteine
ATP
P
ATP
adenyl kinase 9q 382nm
Mg++
P – P
ADP
Phospho Adenosine Phosphosulfate (PAPs)
Ascorbic acid
Ascorbate 2-Sulfate
Dehydroascorbic acid
N. Acetyl Galactosamine
Sulfate radical (SO3)

Sulfites can inhibit the production of positive GUT flora bacteria. They have been shown to deplete glutathione levels which aid in the metabolism of alcohol.
EU labelling laws require winemakers to label “contains sulfites” on any wines that contain more than 10mg per litre.

*What is natural wine? By Katy Severson, Huffpost

The WHO recommends an intake of no more than 70mcg per kilo of body weight meaning that an average sized man can safely drink less than a third of a bottle of conventional white wine per day. One third of Americans are allergic to sulfites – some fatally – leading to asthma, gastrointestinal and skin irritations.*

*What is natural wine? By Katy Severson, Huffpost

PLOS ONE A Peer-Reviewed, Open Access Journal

PLoS One. 2017; 12(10): e0186629.
Published online 2017 Oct 18. doi: [10.1371/journal.pone.0186629]
PMCID: PMC5646858
PMID: 29045472

Sulfites inhibit the growth of four species of beneficial gut bacteria at concentrations regarded as safe for food

Sally V. Irwin, Conceptualization, Data curation, Formal analysis, Funding acquisition, Investigation, Methodology, Project administration, Resources, Software, Supervision, Writing – original draft, Writing – review & editing,[#*] Peter Fisher, Formal analysis, Methodology, Software, Supervision, Writing – review & editing,[#] Emily Graham, Data curation, Formal analysis, Investigation, Validation, Writing – review & editing,[#] Ashley Malek, Data curation, Formal analysis, Investigation, Software, Validation, Writing – review & editing,[#] and Adriel Robidoux, Data curation, Formal analysis, Investigation, Validation, Writing – review & editing[#]

damage beneficial bacteria in the human gut and this damage has been associated with several diseases. In the present study, bactericidal and bacteriostatic effects of two common food preservatives, sodium bisulfite and sodium sulfite, were tested on four known beneficial bacterial species common as probiotics and members of the human gut microbiota. *Lactobacillus* species *casei*, *plantarum* and *rhamnosus*, and *Streptococcus thermophilus* were grown under optimal environmental conditions to achieve early log phase at start of experiments. Bacterial cultures were challenged with sulfite concentrations ranging between 10

Wine

Sulfites occur naturally in all wines to some extent.* Sulfites are commonly introduced to arrest fermentation at a desired time, and may also be added to wine as preservatives to prevent spoilage and oxidation at several stages of the winemaking.

**Zacharkiw B (July 15, 2008). "Can't hold the sulphites". Montreal Gazette.*

https://www.bonappetit.com/drinks/wine/article/sulfite-free-wine.

https://www.thekitchn.com/the-truth-about-sulfites-in-wine-myths-of-red-wine-headaches-100878.


Erbaluce
skietto

Sulfur dioxide (SO_2) protects wine from not only oxidation, but also from bacteria. Without sulfites, grape juice would quickly turn to vinegar. *

* Spencer B. "Sulfur in Wine Demystified"

Organic wines are not necessarily sulfite-free, but generally have lower amounts and regulations stipulate lower maximum sulfite contents for these wines. In general, white wines contain more sulfites than red wines and sweeter wines contain more sulfites than drier ones.*

*McCarthy E, Ewing-Mulligan M (2012). *Wine for dummies* (5th ed.). Hoboken, N.J.: Wiley. ISBN 978-1-118-28872-6

In the United States, wines bottled after mid-1987 must have a label stating that they contain sulfites if they contain more than 10 parts per million.*

*Breton F. "Many organic wines contain sulfites". *French Scout*.

In the European Union an equivalent regulation came into force in November 2005.* In 2012, a new regulation for organic wines came into force. **In the United Kingdom, similar laws apply.

** "Food Labeling - Community Legislation". European Commission. Retrieved 2007-09-10.*

*** "Commission Implementing Regulation (EU) No 203/2012". Official Journal of the European Union. 8 March 2012.*

Bottles of wine that contain over 10 mg/l sulfites are required to bear "contains sulphites" on the label. This does not differ whether sulfites are naturally occurring or added in the winemaking process.*

*Safonov D. "7 Myths of Natural Wines with no sulphites added". Organic Wine Club.

Gastroenterology and Hepatology from Bed to Bench
Journal | Aim & Scope | Author Guideline | Submit a Manuscript

Gastroenterol Hepatol Bed Bench. 2012 Winter; 5(1): 3–6.

PMCID: PMC4017445
PMID: 24834191

Considerations for the diagnosis and management of sulphite sensitivity

Justine Bold

Author information

The review article by Vally and Misso (1) published in the current edition of this journal outlines the broad range of signs and symptoms associated with sulphite sensitivity. These include bronchoconstriction, wheezing, dyspnea, nausea, stomach cramps, diarrhoea, urticaria/angiodema, diaphoresis, hives, laryngeal oedema, generalised itching and swelling, tingling sensations, flushing, hypotension, cyanosis, shock and loss of consciousness (2). Many of the symptoms mirror those of anaphylaxis. Indeed reactions to sulphites can be life threatening, as a number of fatal cases have been reported (3, 4). In many areas of the world, sulphites are now one of the potential allergens (along with the likes of peanuts, fish, crustaceans, gluten and milk) that have to be labelled on food and drink products. In the European Union (EU), levels in foods and drinks above 10 mg/kg or 10 mg per litre have to be labelled. Warning labels are now commonplace,

A SO2 metabolite (glutathione S-sulfonate) has been demonstrated in studies on rat liver, lung and human lung cells to be a competitive inhibitor of the liver enzyme glutathione S-transferase (GST) (15). Researchers suggested that SO2 may have a detrimental effect on the general detoxification of xenobiotic compounds generally detoxified in the glutathione conjugation pathway, involving GST (15). They suggest it may deplete glutathione supply and it could be a contributory factor in sulphite sensitivity. Obviously, further studies would be required to validate this.

A failure in the glutathione conjugation would lead to covalent combination to DNA and RNA and other cell proteins creating serious cell damage. Natural inducers of glutathione-s-transferase are *Spinach, Onion, Garlic, Broccoli, Lemon grass, Celery, Rosemary and Watercress*.

Glutathione conjugates are further metabolised before excretion.

The glutamic and glycine groups are removed and an acetyl group donated by Acetyl CoA is added to the cysteine moiety.

The resulting compound is a mercapturic acid, a conjugate of N. Acetyl Cysteine (NAC), which is then excreted in the urine.

N.Acetyl Cysteine (NAC) is thus an excellent supplement to use to activate this pathway.

N. Acetyl Cysteine may activate detoxification via -

1. Glutathione
2. Acetylation
3. Sulfation
4. Cysteine

Glucuronidation conjugation is catalyzed by a variety of *glucuronosyl-transferases* with UDP-glucuronic acid as the glucuronyl donor.

Glucuronidation conjugation is the favoured pathway for the metabolism of many neurotransmitters, hormones, phenol and benzoic acid.

Natural Glucuronates

Jerusalem Artichokes
Cashew
Soy
Liquorice
Flax
Alfalfa

Sulfation conjugation uses 3-phosphoadenosine-5-phosphosulfate (PAPs), or sulfates or most commonly elemental sulfur or MSM or cysteine or α-lipoic acid as the sulfur donor.

Many neurotransmitters and hormones are conjugated via this pathway.

Natural Sulfate donors

Broccoli
Asparagus
Garlic , Onion
Mustard
Dill
Parsnip
Horseradish
Cabbage
Stinging nettle

Chemicals conjugated by Sulfation

1. Acetone
2. DDT / DDE
3. Ethylene glycol
4. Fluorine
5. Toluene
6. TRIC

Acetylation conjugation uses Acetyl CoA as the acetyl donor. The reactions are catalyzed by *acetyltransferases.* Natural acetylaters - Endive, Pea, Cucumber, Watercress, Tomato

The drug **isoniazid** used in the treatment of tuberculosis is conjugated by acetylation.

Chemicals conjugated by Acetylation

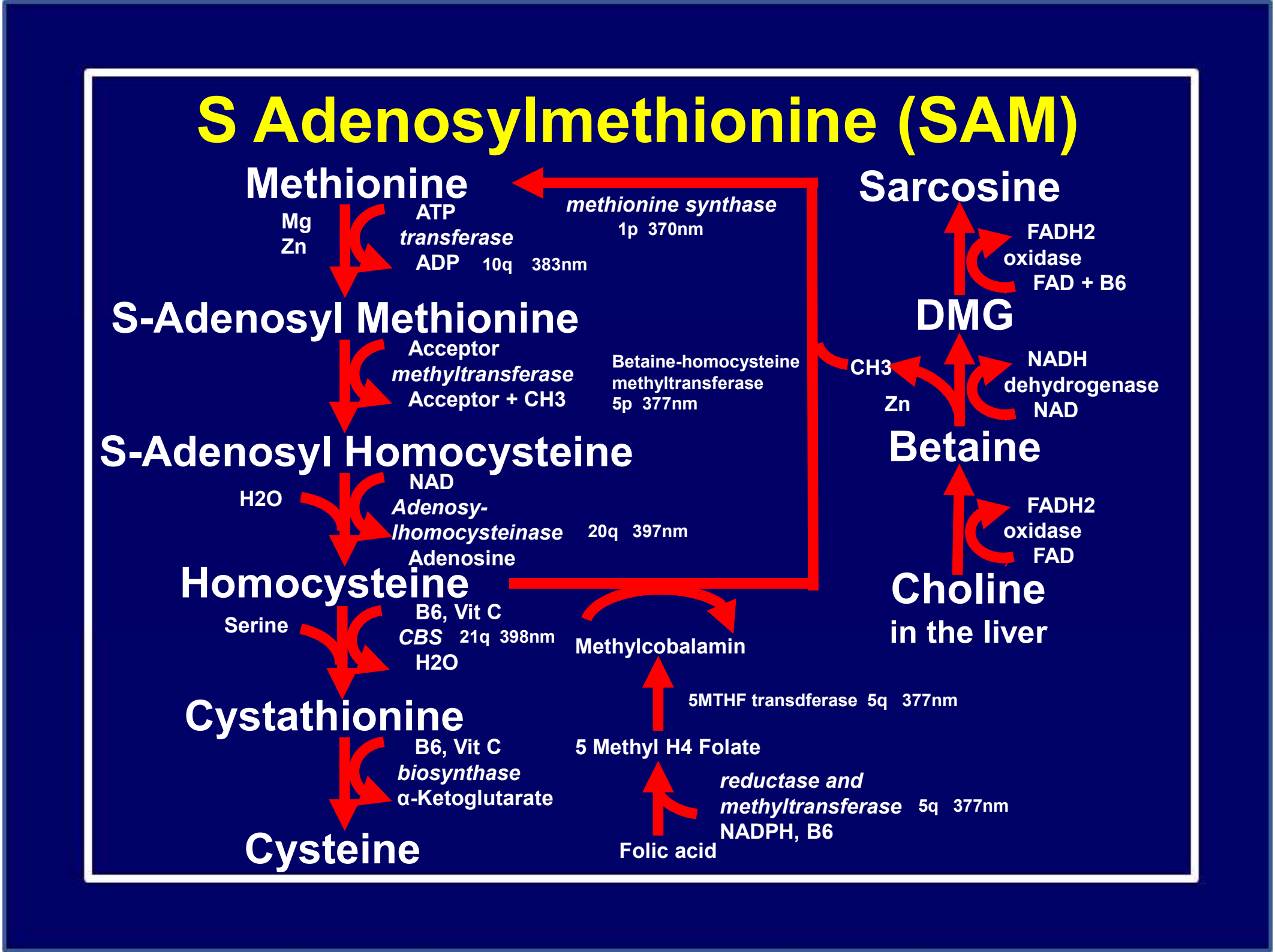
1. Petroleum
2. Newsprint
3. Hypochlorite

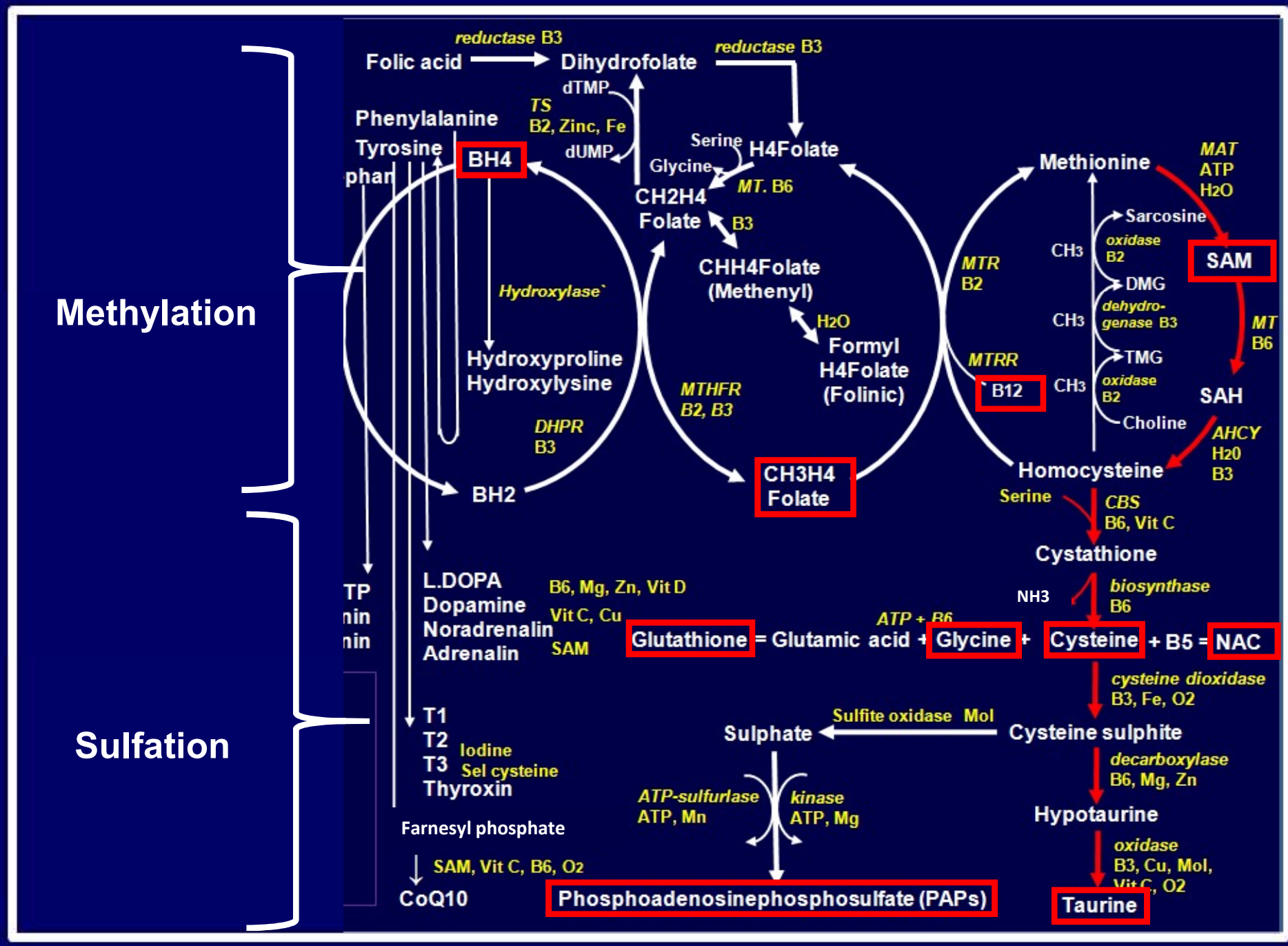
Methylation conjugation
is catalyzed by the various *methyltransferases* employing S-Adenosyl methionine as the methyl donor (SAM).

Many hormones are initially
hydroxylated,
then methylated
and lastly conjugated
usually by glucuronidation or
sulfation.

Test with caffeine
Sellotape glue*

Chris Astill-Smith ICAK-USA meeting San Diego 2018


S Adenosylmethionine (SAM)
Methionine
Mg
Zn
ATP
transferase
ADP
10q
383nm
methionine synthase
1p
370nm
S-Adenosyl Methionine
Acceptor
methyltransferase
Acceptor + CH3
Betaine-homocysteine
methyltransferase
5p
377nm
S-Adenosyl Homocysteine
H2O
NAD
Adenosy-
lhomocysteinase
20q
397nm
Adenosine
Homocysteine
Serine
B6, Vit C
CBS
21q
398nm
H2O
Cystathionine
B6, Vit C
biosynthase
α-Ketoglutarate
Cysteine
Methylcobalamin
5MTHF transdferase
5q
377nm
5 Methyl H4 Folate
reductase and
methyltransferase
5q
377nm
NADPH, B6
Folic acid
Sarcosine
FADH2
oxidase
FAD + B6
DMG
CH3
Zn
NADH
dehydrogenase
NAD
Betaine
FADH2
oxidase
FAD
Choline
in the liver


Methylation
Sulfation
reductase B3
Folic acid
Dihydrofolate
reductase B3
dTMP
TS
B2, Zinc, Fe
dUMP
Phenylalanine
Tyrosine
BH4
Serine
H4Folate
Glycine
MT. B6
CH2H4
Folate
B3
CHH4Folate
(Methenyl)
H2O
Formyl
H4Folate
(Folinic)
Hydroxylase`
Hydroxyproline
Hydroxylysine
DHPR
B3
BH2
MTHFR
B2, B3
CH3H4
Folate
MTR
B2
MTRR
B12
Methionine
MAT
ATP
H2O
SAM
MT
B6
SAH
AHCY
H20
B3
Homocysteine
Serine
CBS
B6, Vit C
Cystathione
CH3
Sarcosine
oxidase
B2
DMG
dehydro-
genase B3
TMG
oxidase
B2
Choline
L.DOPA
Dopamine
Noradrenalin
Adrenalin
B6, Mg, Zn, Vit D
Vit C, Cu
SAM
NH3
biosynthase
B6
ATP + B6
Glutathione = Glutamic acid + Glycine + Cysteine + B5 = NAC
cysteine dioxidase
B3, Fe, O2
T1
T2
T3
Thyroxin
Iodine
Sel cysteine
Sulfite oxidase Mol
Sulphate
Cysteine sulphite
decarboxylase
B6, Mg, Zn
Hypotaurine
oxidase
B3, Cu, Mol,
Vit C, O2
Taurine
ATP-sulfurlase
ATP, Mn
kinase
ATP, Mg
Farnesyl phosphate
SAM, Vit C, B6, O2
CoQ10
Phosphoadenosinephosphosulfate (PAPs)

Amino acid conjugation can use either
Taurine,
Glycine,
Cysteine or
Threonine as conjugating donors.

Sodium benzoate is conjugated with glycine.

CONJUGATE	BIOMARKER	NUTRIENTS
XOH + GLUTATHIONE	GLUTATHIONE-S-TRANSFERASE	GLUTATHIONE (NAC, Glutamate, Glycine) B6, Zn
XOH + GLUCURONIDATION	GLUCURONIC ACID	GLUCURONIC ACID
1. XOH + SULFATION 2. SULFITE OXIDASE	1. PAPs 2. SULFITE OXIDASE	S, MSM Mol, Fe.
XOH + ACETYLATION	ACETYL CoA	Acetyl CoA (B5, Mg,)
XOH + METHYLATION	SAM	Methionine, B12, Folic, Betaine,
XOH + TAURINE	TAURINE	Taurine, NAD, Vit C, Vit A
XOH + THREONINE	THREONINE	Threonine
XOH + GLYCINE	GLYCINE	Glycine, B6, B2, Mg, Folic.
XOH + CYSTEINE	CYSTEINE	Cysteine, NAC, Methionine, B6

Naturally occurring endogenous chemicals as intermediates in metabolism f

Common naturally endogenously occurring reactive intermediates

Acetaldehyde
Acetic acid
Acetone
Ammonia*
Butyric acid
Cyanide
Ethane
Formaldehyde
Formic acid*
Glutamate
Hydrogen sulfite*
H2O2*
4-Hydroxynonenol*
Indole
L. Lactic acid
D. Lactic acid
D/L Lactic acid
Malondialdehyde*
Methane
Methanol, Oxalate*
Phenol*
Propionic acid*
Pyruvate
Toluene
Tyramine*
Uric acid*

* Most common

Naturally occurring ingested chemicals in foods and drinks f

Common naturally occurring food and drink chemicals

Alpha Solanene
Betaine
Caffeine
Cysteine
Glutamate
Histamine
Isothiocyanate
Malondialdehyde
Oxalates
Salicylates
Sulfites
Thiobromine
Atropine
Tyramine
Uric acid

Many changes in gene expression are due to faulty signals caused by toxins or are inherited.

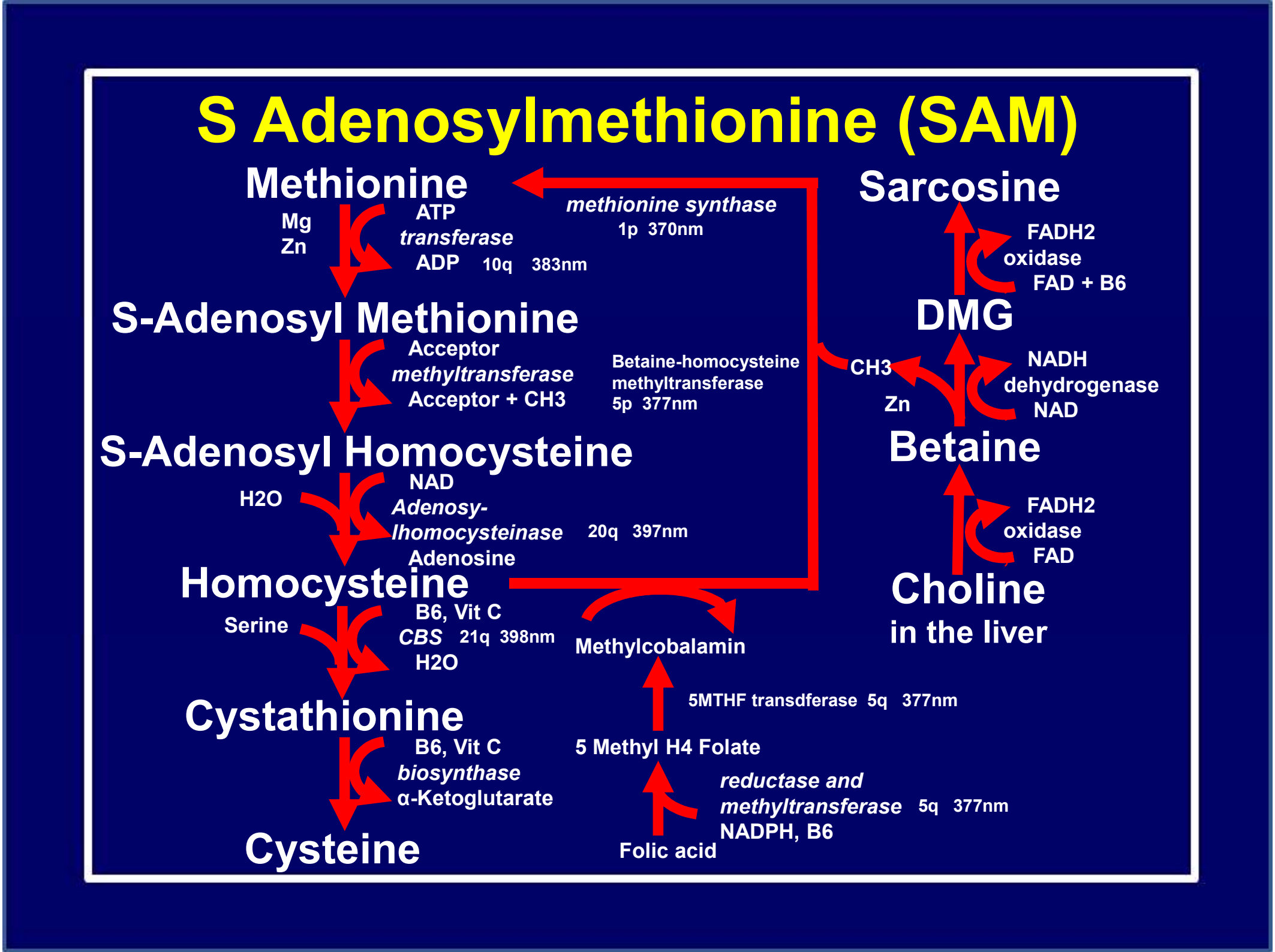
The most common toxins are naturally occurring chemicals within the foods we eat or drink or natural endogenously produced reactive intermediates which fail to be metabolised completely.

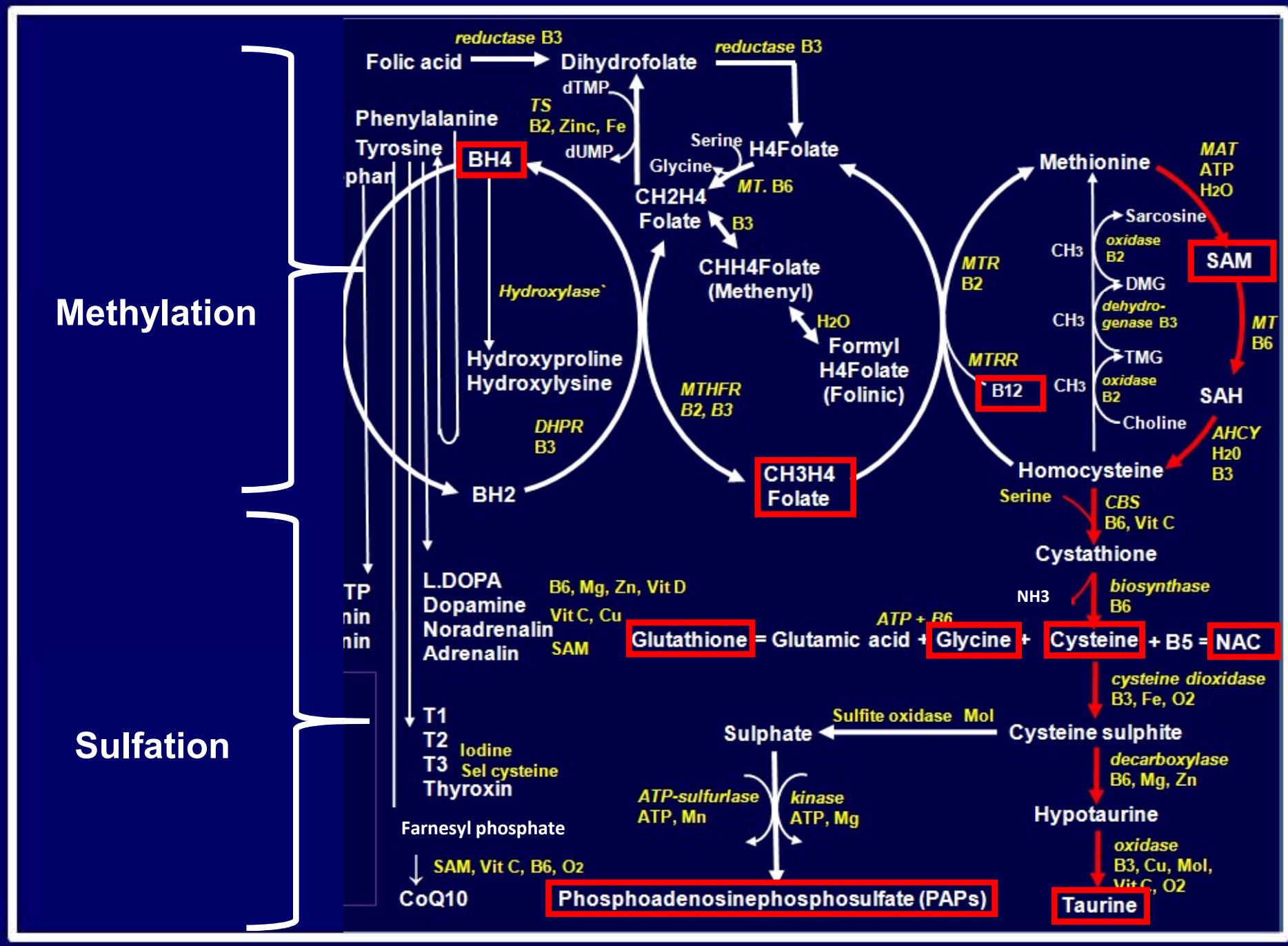
Isothiocyanates

Isothiocyanate foods 20%

Brussels sprouts, Broccoli, Cabbage, Cauliflower
Kale, Spinach, Pak choi
Watercress, Garden cress, Mustard, Turnip, Kohlrabi, Horseradish, Radishes, Capers
Globe artichoke, Celery

Possibly Egg, Oats, Bulgur wheat in some cases.


S Adenosylmethionine (SAM)
Methionine
Mg
Zn
ATP
transferase
ADP
10q
383nm
methionine synthase
1p
370nm
S-Adenosyl Methionine
Acceptor
methyltransferase
Acceptor + CH3
Betaine-homocysteine
methyltransferase
5p
377nm
S-Adenosyl Homocysteine
H2O
NAD
Adenosy-
lhomocysteinase
20q
397nm
Adenosine
Homocysteine
Serine
B6, Vit C
CBS
21q
398nm
H2O
Cystathionine
B6, Vit C
biosynthase
α-Ketoglutarate
Cysteine
Methylcobalamin
5MTHF transdferase
5q
377nm
5 Methyl H4 Folate
reductase and
methyltransferase
5q
377nm
NADPH, B6
Folic acid
Sarcosine
FADH2
oxidase
FAD + B6
DMG
CH3
Zn
NADH
dehydrogenase
NAD
Betaine
FADH2
oxidase
FAD
Choline
in the liver


Methylation
Sulfation
reductase B3
Folic acid
Dihydrofolate
reductase B3
dTMP
TS
B2, Zinc, Fe
dUMP
Phenylalanine
Tyrosine
BH4
Serine
H4Folate
Glycine
MT. B6
CH2H4
Folate
B3
CHH4Folate
(Methenyl)
H2O
Formyl
H4Folate
(Folinic)
Hydroxylase`
Hydroxyproline
Hydroxylysine
DHPR
B3
BH2
MTHFR
B2, B3
CH3H4
Folate
MTR
B2
MTRR
B12
Methionine
MAT
ATP
H2O
SAM
MT
B6
SAH
AHCY
H20
B3
Homocysteine
Serine
CBS
B6, Vit C
Cystathione
CH3
Sarcosine
oxidase
B2
DMG
dehydro-
genase B3
TMG
oxidase
B2
Choline
L.DOPA
Dopamine
Noradrenalin
Adrenalin
B6, Mg, Zn, Vit D
Vit C, Cu
SAM
NH3
biosynthase
B6
ATP + B6
Glutathione = Glutamic acid + Glycine + Cysteine + B5 = NAC
cysteine dioxidase
B3, Fe, O2
T1
T2
T3
Thyroxin
Iodine
Sel cysteine
Sulfite oxidase Mol
Sulphate
Cysteine sulphite
decarboxylase
B6, Mg, Zn
Hypotaurine
oxidase
B3, Cu, Mol,
Vit C, O2
Taurine
ATP-sulfurlase
ATP, Mn
kinase
ATP, Mg
Farnesyl phosphate
SAM, Vit C, B6, O2
CoQ10
Phosphoadenosinephosphosulfate (PAPs)

Their mechanism of action is proposed to involve inhibition of cytochrome b in Complex 3 of the mitochondria and inhibition of P450 enzymes, which oxidize a wide range of xenobiotics.

Common diseases - Parkinson's disease, High Leukotrien B4.
Detoxification - Methylation
SAM, 5-MTHFolate, Methylcobalamin

α-Solanine

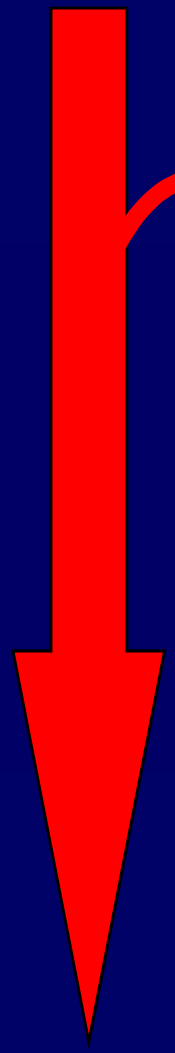
α-Solanine foods15%

Potatoes especially if green (also chaconine)
Tomatoes
Green peppers (also capsaicin)
Aubergines (egg plants)
Tobacco
Paprika
Goji berries
Ashwagandha

The following foods contain solanine, but are not a part of the nightshade family, including:
Blueberries / Bilberries
Apples
Cherries
Sugar beets
Okra
Artichokes
Ascorbyl Palmitate (it's potatoes)
Yeast (Most yeast contains potato)

ACETYLCHOLINE

Inhibited by
Chemicals – α-Solanene



H_2O

acetylcholinesterase

7q 380nm

B2

B3

Mn++

Zn++ Cysteine

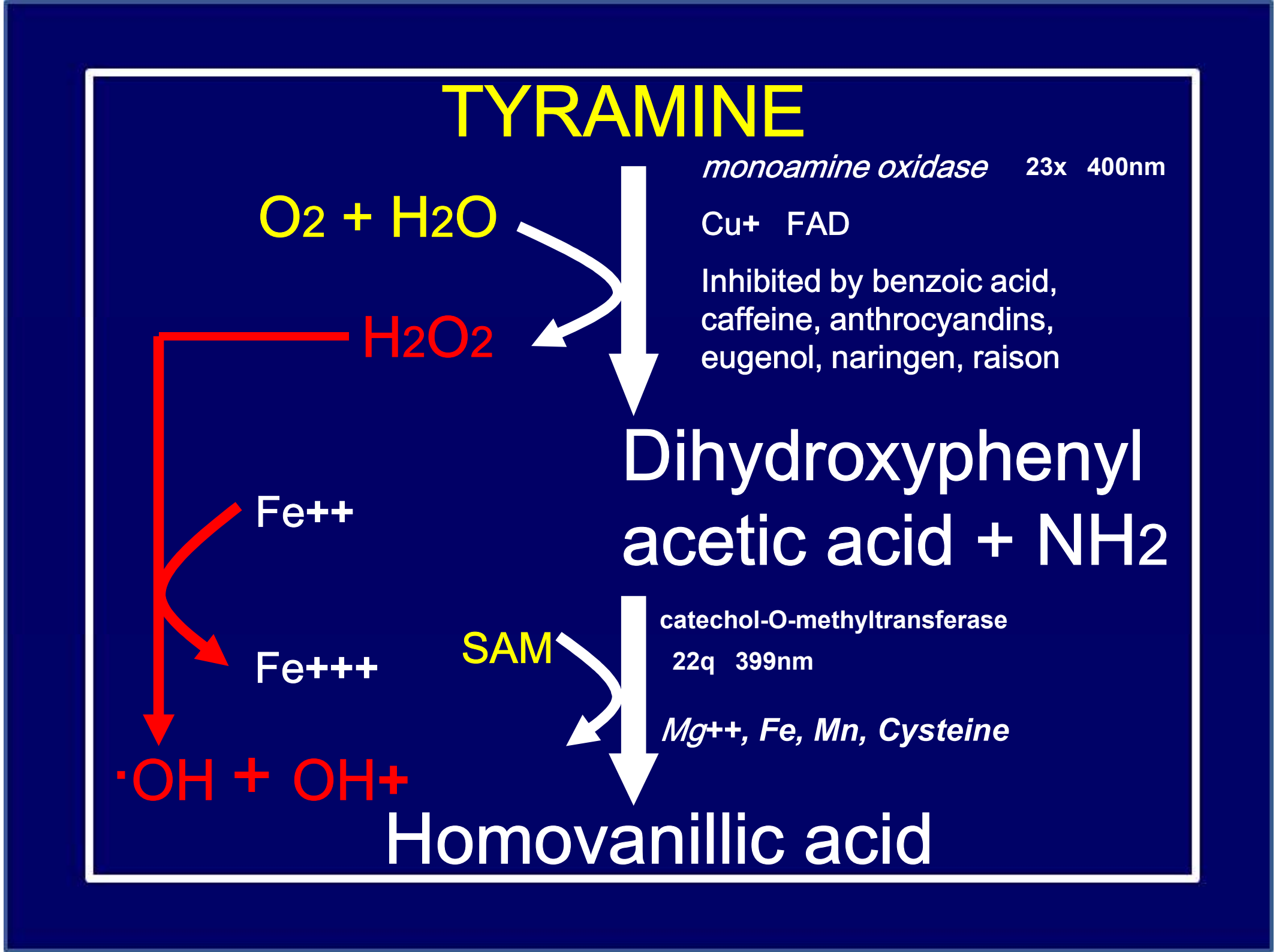
Recycled

Acetate + Choline

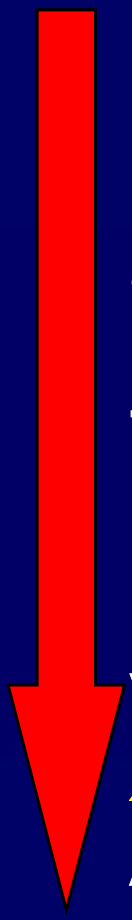
Solanum glycoalkaloids inhibit acetylcholinesterase. Intestinal bacteria aids in the detoxification by hydrolyzing the glycoside into solanidine (aglycone), which is less toxic than solanine and also poorly absorbed.

Liver meridian
Detoxified by Methylation
SAM, B12, Folate, Betaine

Tyramine


TYRAMINE
monoamine oxidase
23x 400nm
O2 + H2O
Cu+ FAD
Inhibited by benzoic acid, caffeine, anthrocyandins, eugenol, naringen, raison
H2O2
Dihydroxyphenyl acetic acid + NH2
Fe++
Fe+++
SAM
catechol-O-methyltransferase
22q 399nm
Mg++, Fe, Mn, Cysteine
·OH + OH+
Homovanillic acid

Homovanillic acid



Glutathione (Cysteine, Glycine, Glutamic acid) NAC, Zn++, P5P, Sel

a-Lipoic or

Sulfation S, MSM

Taurine or

Glucuronidation (UDP Gucuronic acid) Glucuronate, Vit C, or

Acetylation (Acetyl CoA) B5, Acetyl CoA

Conjugates excreted through the bile or urine

Tyramine foods10%

Cheese – aged cheese: blue, brick, brie, cheddar, swiss, roquefort, mozzarella, provolone, emmental, colby, american, parmesan

Fruits – Over ripe bananas and avocados, figs, grapes, oranges, pineapples, raspberries, plums, prunes, raisins, overripe fruit and dried fruit

Meat & Fish – aged, dried, fermented, salted, smoked or pickled – pepperoni, salami, liverwurst, bologna, bacon, frankfurters, ham.

Vegetables – snow peas, fava or broad beans, sauerkraut, pickles, olives, avocados, eggplant, tomatoes

Soy – fermented: miso, soy sauce, teriyaki sauce, tofu, tempeh

Nuts and Seeds – all nuts

Beverages – all alcoholic beverages, all non-alcoholic fermented beverages

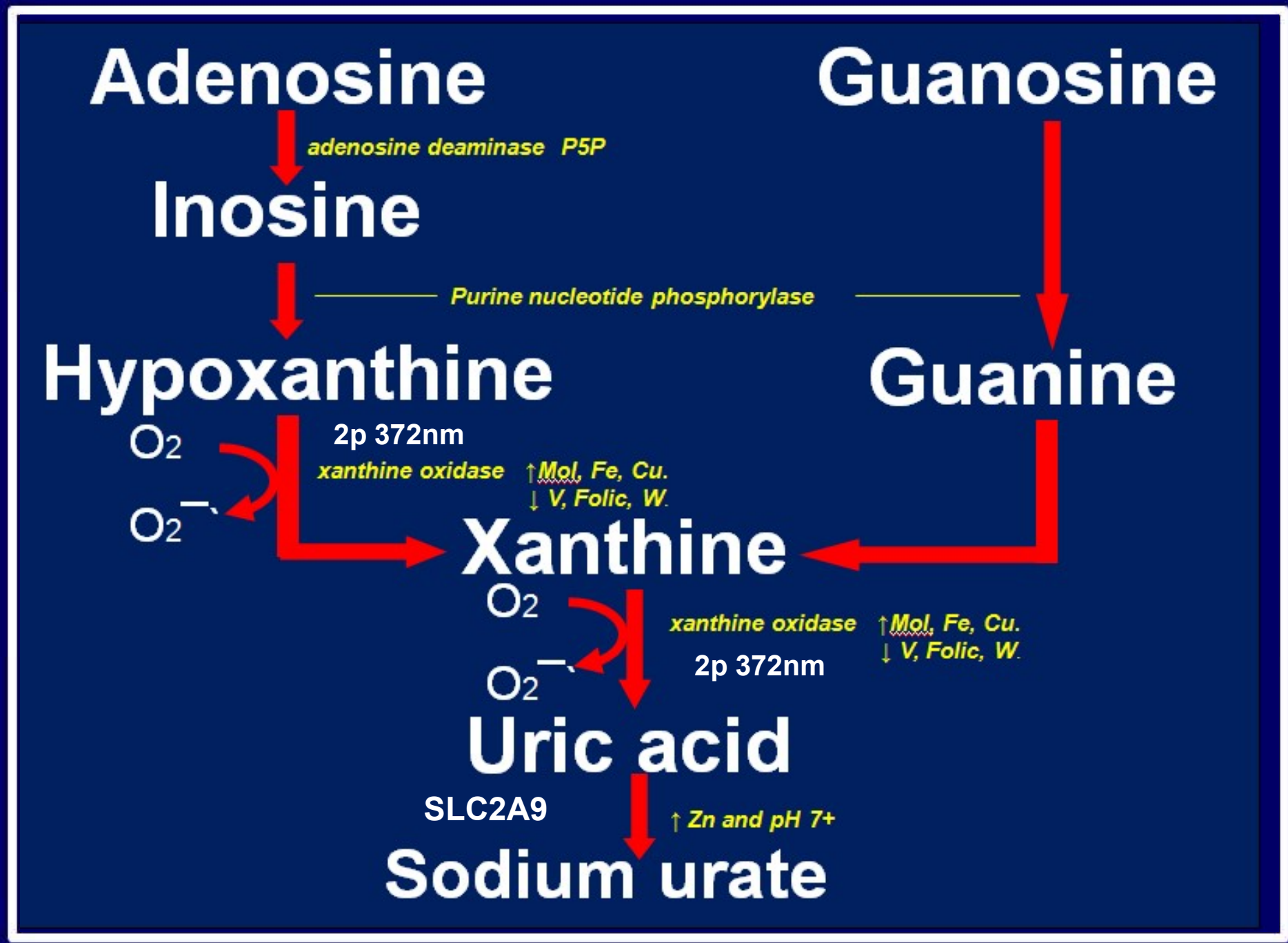
Other – yeast, brewers extracts, chocolate, caffeine, coke

:

Tyramine foods10%

Detoxified by MAO
B2, Cu, Vitamin C
:

Purines forming Uric acid


Adenosine
Guanosine
adenosine deaminase P5P
Inosine
Purine nucleotide phosphorylase
Hypoxanthine
Guanine
O2
O2 —·
2p 372nm
xanthine oxidase
↑Mol, Fe, Cu.
↓ V, Folic, W.
Xanthine
O2
O2 —·
xanthine oxidase
2p 372nm
↑Mol, Fe, Cu.
↓ V, Folic, W.
Uric acid
SLC2A9
↑ Zn and pH 7+
Sodium urate

Purine high foods > High Uric acid

Red meats which come from cows or sheep and include steak, chops, corned beef and larger pieces of meat usually roasted in the oven. Game. Meat extracts (e.g Oxo, Bovril). Gravy.

Brains, kidneys, liver & heart (offal), sweetbreads (thymus and panceas).

Shellfish such as , mussels, oysters and sea eggs.

Anchovies, herrings, mackerel, sardines.

Peas and beans, carrot.

Alcohol. especially beer and wine.

Phenolic foods

Phenols Foods

Phenols are present naturally in certain foods and are also found in food additives or preservatives in processed foods and food packaging.

Phenylalanine

The types of phenols known to cause symptoms are:

Salicylates

Amines (e.g. Histamine)

Glutamates

Salicylates

Salicylate foods

Cold & flu remedies
Medicines used for pain for headache, periods, sinus
Some antacids
Drugs used for inflammatory bowel disease
Many complementary and alternative medicines, especially those used for Pain and joint problems
Teething gels.
Foods containing high levels of salicylate include tea (except fruit and camomile tea), coffee, almonds, dried herbs and spices, cloves, black pepper, paprika, sharp green apples, apricots, bananas, cherries, strawberries, dried fruit, peaches, plums, prunes, tomatoes (fresh, puree and ketchup), cucumber, pickles, fruit juices, grapes, nectarines, oranges, cider, cider vinegar, wine, wine vinegar, peppermints and liquorice. Oil of wintergreen, rosehips, acerola, food colourings and preservers, broccoli

Fruits

Apricot
Blackberries
Blueberries
Boysenberries
Cantaloupe Rockmelon
Cherries (canned sweet)
Cranberry (sauce and canned)
Currants
Dates
Grapes (fresh)
Guava
Loganberries
Orange
Pineapple
Plum (canned)
Prunes
Raisons
Raspberry
Redcurrants
Strawberries
Sultanas
Youngberry

Vegetables

Capsicum (green)
Champignon (canned)
Chili (red)
Chicory
Courgette
Endive
Gherkin
Mushroom (canned)
Olives (green)
Pepper (sweet)
Radish
Tomato (paste and sauce)
Zucchini

Sweets

Licorice
Mints and Peppermints
Chewing gum
Fruit flavorings

Nuts

Almonds
Peanuts
Chips and crackers (savory flavored)

Beverages

Tea (all varieties)
Liqueur
Peppermint tea
Port
Rum
Champagne
Wines
Cordials

Herbs

All spice
Anise seed
Cayenne
Celery
Cinnamon
Cumin
Curry powder
Dill
Fenugreek
Five spice
Garam masala
Ginger
Honey
Jam
Mace
Mint
Mixed herbs
Mustard
Oregano
Paprika (hot)
Paprika (sweet)
Pepper
Rosemary
Sage
Tarragon
Turmeric
Thyme
Worcestershire sauce

Salicylate foods

Common diseases – Epilepsy, eczema, Wheezing.
Detoxified by Glutathione, Sulfation (Taurine)

Histamine

HISTAMINE

methyltransferase 2q 373nm

SAM (Mg++, Zn++, P5P)
Methylcobalamin
Methyltetrahydrofolate

diamine oxidase

O2 10q 383nm?
(adenosylcobalamin)

Vit C
Fe++

P5P

2q 373nm
aldehyde oxidase

O2
(adenosylcobalamin)

NAD, FAD

Mol, Fe++

K, Thiols

Methylhistamine

Imidazole acetic acid

monoamine oxidase

O2 23x 400nm
(Fe++,
Adenosylcobalamin)

FMN / FAD
Cu

(systemic histamine)
Natural anti histamines -
Vit E, Zn, Mg,
Bioflavonoids

Methyl imidazole acetic acid

Histamine foods

Bananas, Prickly pear, Stinging nettle, Cabbage, Milk thistle, Shepherds purse, Celendine, Melon, Sunflower, Strawberries, Sauerkraut, Salami, Bacon, Bass, Beer, Chicken, Cocoa, Chocolate, Cod, Crab, Haddock, Ham, Lobster, Mackerel, Milk (cow and goat), Mutton, Oyster, Salmon, Scallop, Shrimp, Trout, Tuna, Turkey, Yeast, Yoghurt, Avocados.

Histamine foods

Common diseases – Allergy, Chronic infections

Detoxified by *Diamine oxidase*

Adenosylcobalamin, Vit C, P-5-P

Aldehyde dehydrogenase

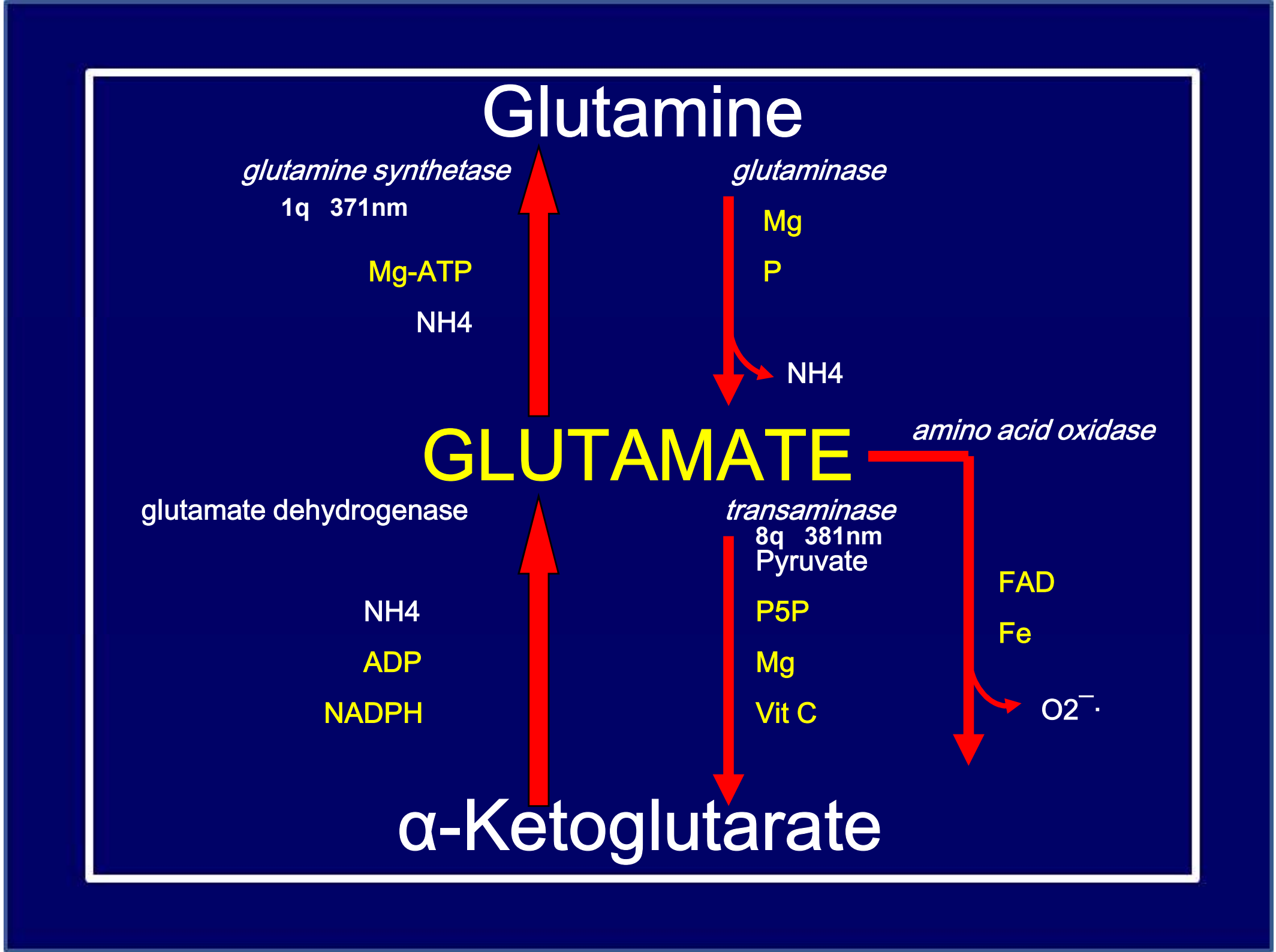
Adenosylcobalamin, FAD, NAD, Mol

Antihistamine- Hesperidin, Quercitin Vit E, Mg, Zinc

Glutamate

Glutamate Foods

Celery, Foods matured, cured or preserved – eg mature cheeses, Parmesan, cured meats
Fish sauce
Soy sauce and soy protein
Mushrooms
Ripe tomatoes
Broccoli
Peas
Walnuts
Grape juice
Bone broths
Meats cooked for a long time – eg braising, stews
Malted barley in breads and beer
Wheat gluten, Dairy casein

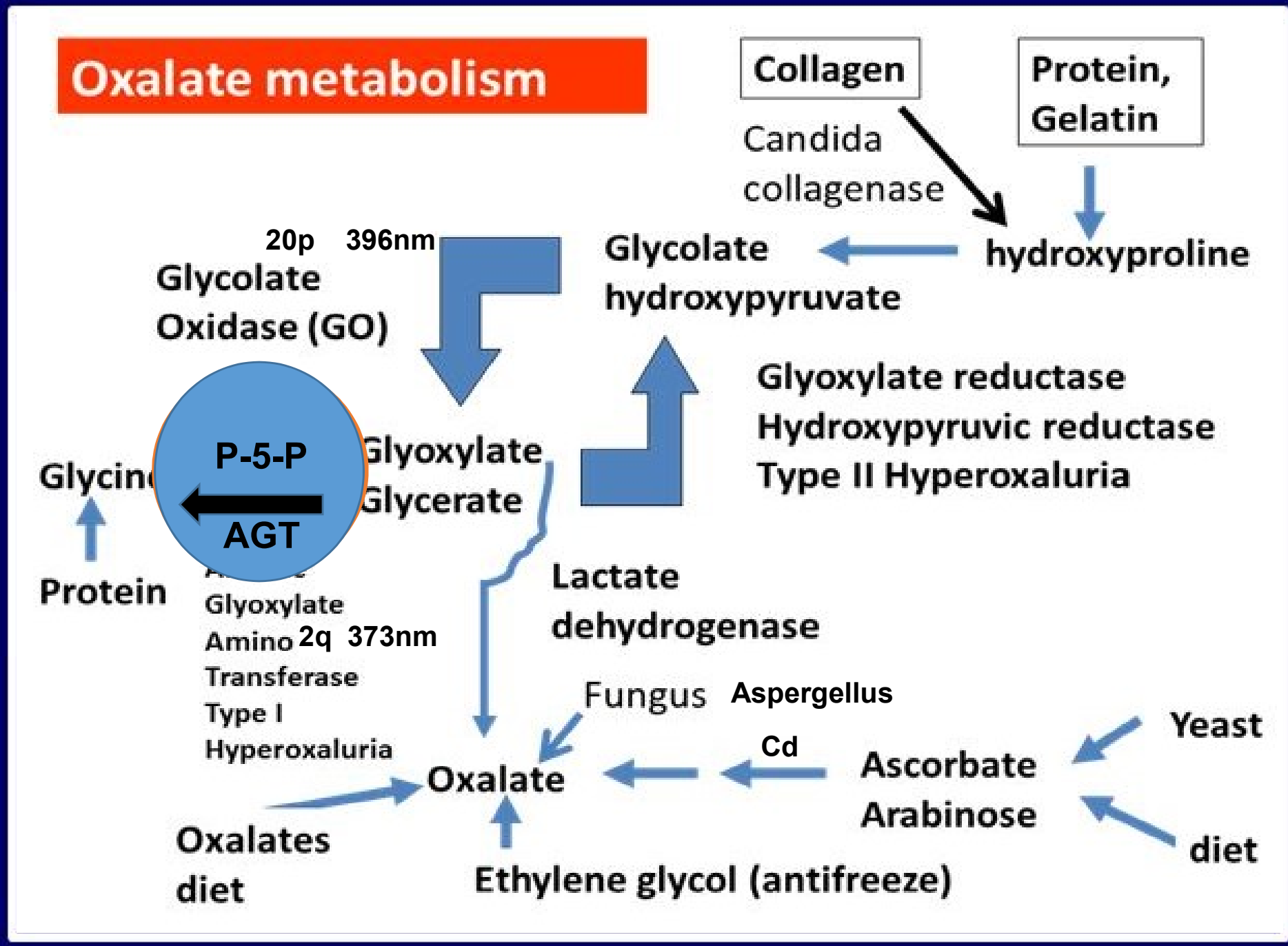

Glutamine
glutamine synthetase
1q 371nm
Mg-ATP
NH4
glutaminase
Mg
P
NH4
GLUTAMATE
amino acid oxidase
glutamate dehydrogenase
NH4
ADP
NADPH
transaminase
8q 381nm
Pyruvate
P5P
Mg
Vit C
FAD
Fe
O2¯·
α-Ketoglutarate

Glutamate Foods

Common diseases – Hyperactivity, Hypertonicity in muscles

Antidote- NAC, Yarrow (for Glutathione)

Oxalates


Oxalate metabolism
Collagen
Protein, Gelatin
Candida collagenase
hydroxyproline
Glycolate hydroxypyruvate
20p 396nm
Glycolate Oxidase (GO)
Glyoxylate reductase
Hydroxypyruvic reductase
Type II Hyperoxaluria
P-5-P
AGT
Glyoxylate
Glycerate
Glycin
Protein
Glyoxylate Amino Transferase Type I Hyperoxaluria
2q 373nm
Lactate dehydrogenase
Fungus
Aspergellus
Cd
Yeast
Ascorbate
Arabinose
diet
Oxalate
Oxalates diet
Ethylene glycol (antifreeze)

Glycolate oxidase oxidizes glycolic acid to glyoxylate, and can also oxidize glyoxylate into oxalate. These reactions are central to the toxicity of ethylene glycol poisoning. *

*Woolf, Alan D.; Wynshaw-Boris, Anthony; Rinaldo, Piero; Levy, Harvey L. (March 1992). "Intentional infantile ethylene glycol poisoning presenting as an inherited metabolic disorder". *The Journal of Pediatrics*. 120 (3): 421–424.

Oxalates

Very high -

Avocados, Dates, Grapefruit, Kiwi, Oranges, Raspberries, Canned and dried pineapple, Dried figs, Bamboo shoots, Beets, Fava beans, Okra, Olives, Parsnip, Kidney beans, Rhubarb, Spinach, Tomato sauce, Raw carrots, Soy beans, Brussel sprouts, Potatoes, Brown rice,

Couscous, Tahini, Pasta, Veggie burgers, All nuts, Carrot juice, Hot chocolate, Lemonade, Rice milk, Soy milk, Tea, Clam chowder, Miso soup, Lentil soup. CABBAGE.

High – Tangerines, Figs, Dried prunes, Celery, Collards, Whole wheat, White rice.

Oxalates

Common diseases – Kidney stones, Interstitial cystitis

Detoxified by Sulfotransferase

Taurine, Folinic acid, P-5-P, Magnesium, EFAs

Caffeine

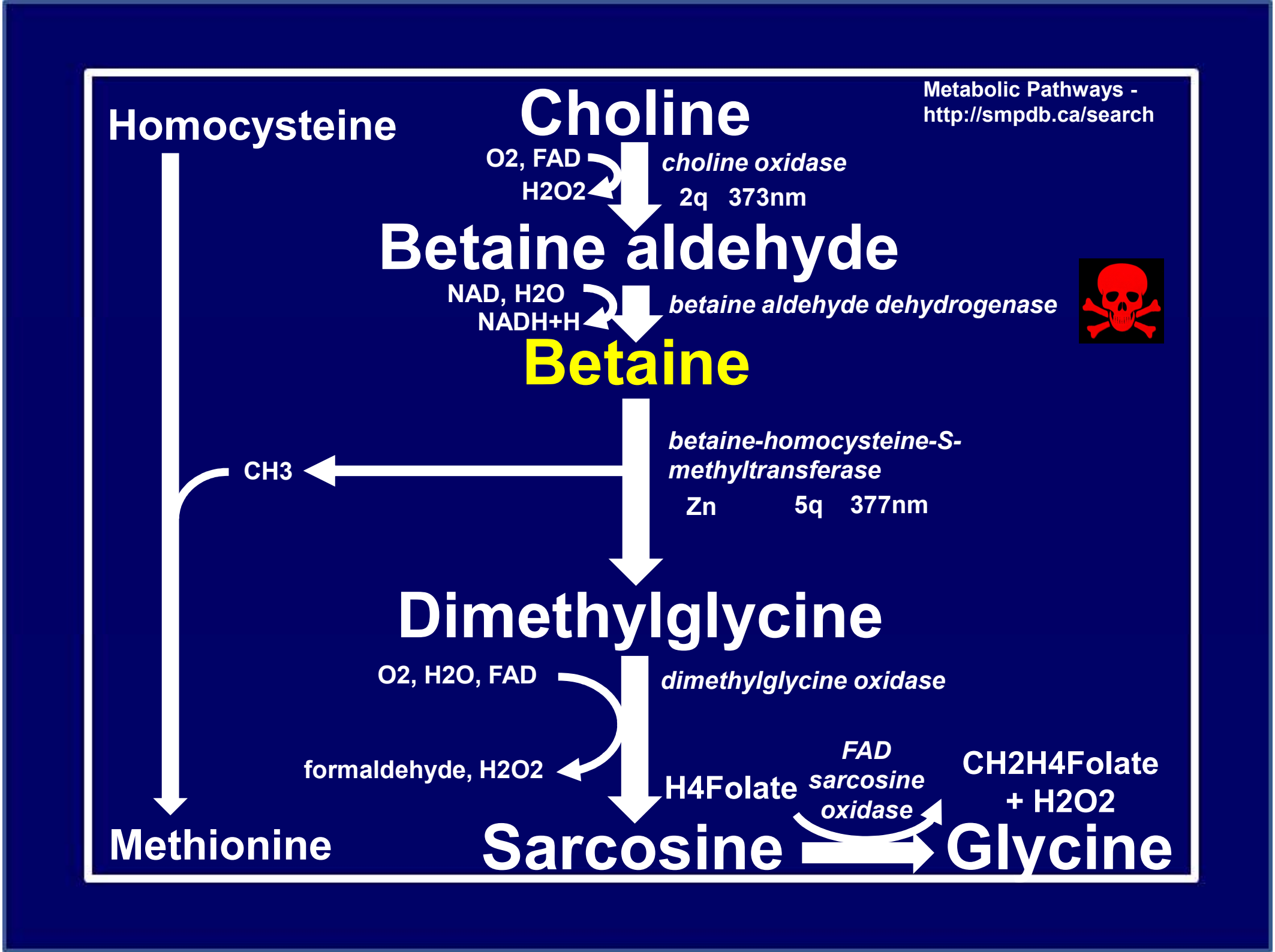
Caffeine

Coffee (also avoid decaf – is only 97% caffeine free) and Tea
Soda, energy drinks other beverages
Chocolate (also contains theobromine)
Hot Chocolate, mocha- and coffee-flavoured ice cream and frozen yogurt.
Caffeine-Fortified Foods such as sunflower seeds, nuts, frozen waffles, snack chips, beef jerky -- even marshmallows, jelly beans and gummy bears.
Protein bars and candy bars
Fancy flavoured water
Alcohol flavoured energy drinks
Weight loss pills, Pain relievers
Breath fresheners, Caffeinated mints
Some instant oatmeal
Antidote -Thyme

Caffeine

Common diseases – Hypertension
Detoxified by Methylation
SAM, Vit B12, Folate, Betaine

Betaine

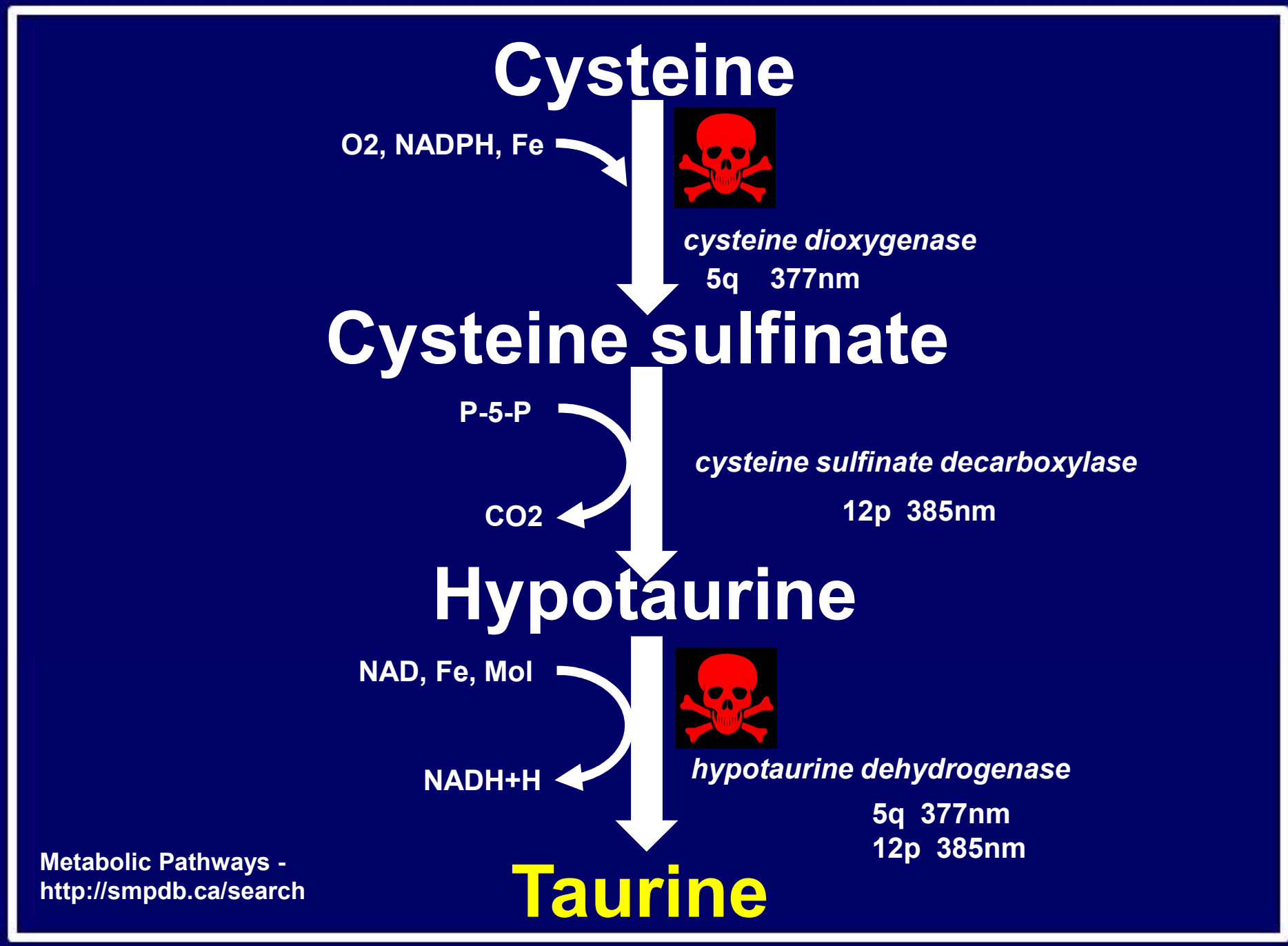

Metabolic Pathways -
http://smpdb.ca/search
Homocysteine
Choline
O2, FAD
H2O2
choline oxidase
2q 373nm
Betaine aldehyde
NAD, H2O
NADH+H
betaine aldehyde dehydrogenase
Betaine
CH3
betaine-homocysteine-S-methyltransferase
Zn 5q 377nm
Dimethylglycine
O2, H2O, FAD
dimethylglycine oxidase
formaldehyde, H2O2
H4Folate
FAD
sarcosine oxidase
CH2H4Folate + H2O2
Methionine
Sarcosine
Glycine

Betaine

in descending order

Wheat Bran
Quinoa
Beets (root and sugar)
Spinach
Amaranth Grain
Rye Grain
Kamut Wheat Grain
Bulgar Wheat Grain
Sweet Potato
Turkey Breast
Veal
Beef
Onions
Mushrooms
Shrimp
Scallops,
Broccoli
Chicken
Eggs
Pork
Soya
Pork
Oats
Brown rice
Wine
Beer
Green tea.

Cysteine


Cysteine
O2, NADPH, Fe
cysteine dioxygenase
5q 377nm
Cysteine sulfinate
P-5-P
CO2
cysteine sulfinate decarboxylase
12p 385nm
Hypotaurine
NAD, Fe, Mol
NADH+H
hypotaurine dehydrogenase
5q 377nm
12p 385nm
Taurine
Metabolic Pathways -
http://smpdb.ca/search

Cysteine foods

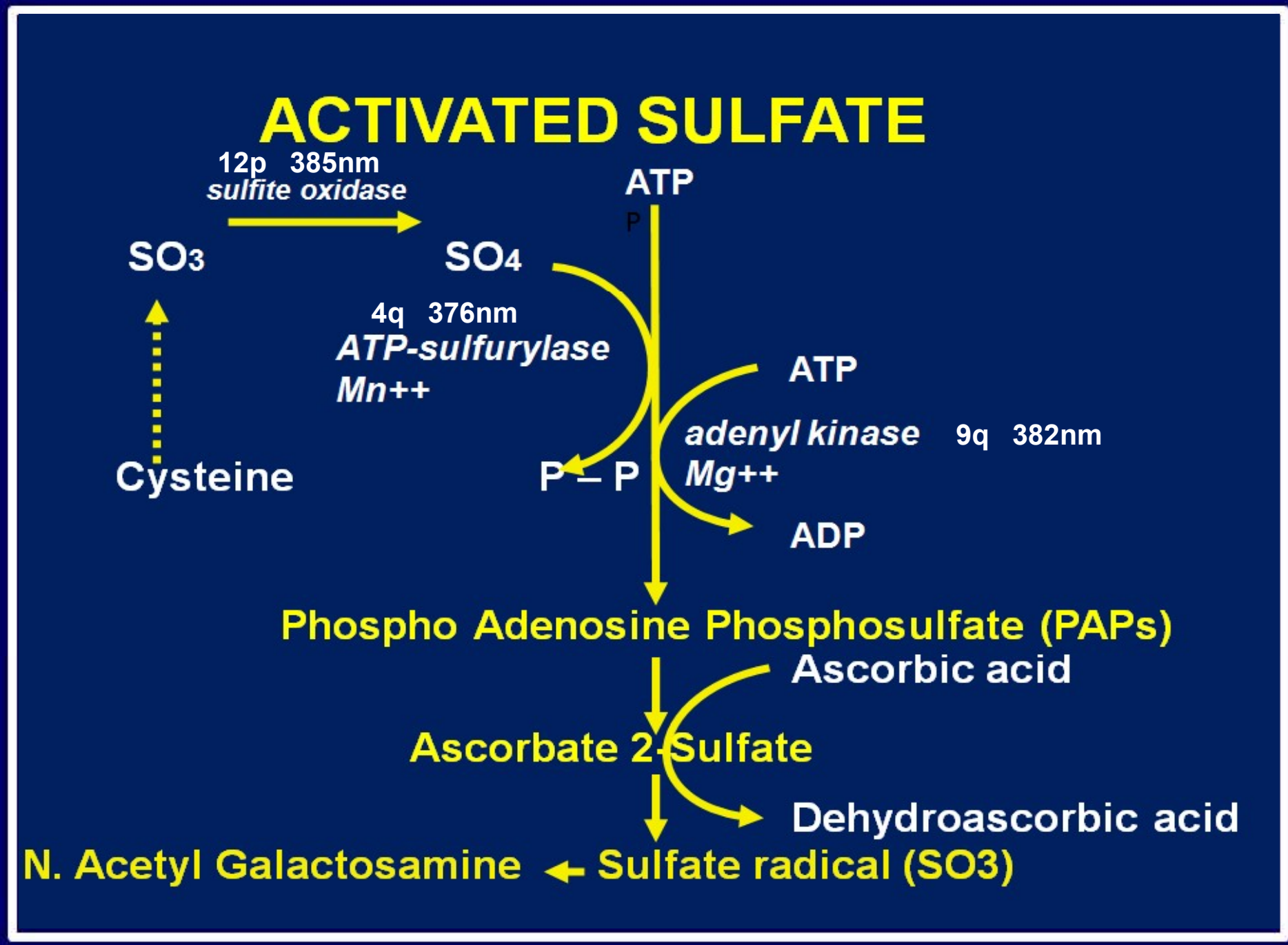
Animal: meat (including pork and poultry), eggs, dairy;
Plant: Red peppers
Garlic, Onions (Onions also produce sulfenic acids), Broccoli, Brussels sprout, Oats, Sweet potato
Wheat germ, Sprouted lentils, Spinach

Cysteine

Common diseases –

Detoxified by Cysteine dioxidase, P-5-P, Folinic acid,

Sulfites


ACTIVATED SULFATE
12p 385nm
sulfite oxidase
SO3
SO4
4q 376nm
ATP-sulfurylase
Mn++
Cysteine
ATP
P
ATP
adenyl kinase 9q 382nm
Mg++
P – P
ADP
Phospho Adenosine Phosphosulfate (PAPs)
Ascorbic acid
Ascorbate 2-Sulfate
Dehydroascorbic acid
N. Acetyl Galactosamine
Sulfate radical (SO3)

Sulphites

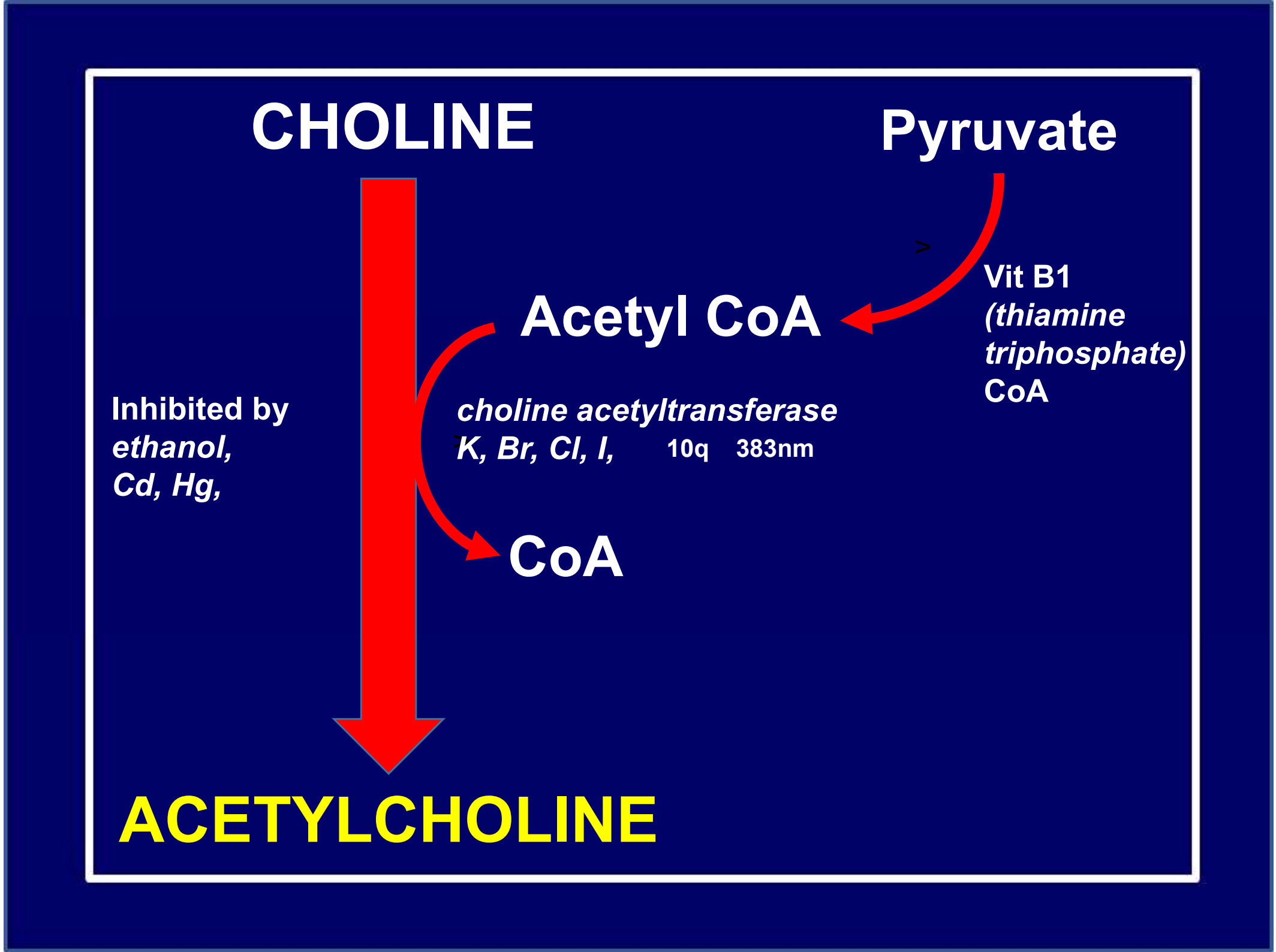
Wine, beer, cocktail mixes, soft drinks, instant tea
Cookies, crackers, dried fruit or vegetables
Dried citrus fruit beverage bases
Horseradish, pickled onions, pickles, olives, wine vinegar
White sugar from sugar beet
Antiemetics, CVS drugs, antibiotics, tranquilizers, muscle relaxants, analgesics, steroids, bronchial dilators.
Canned clams; fresh, frozen, canned or dried shrimp; frozen lobster; scallops; dried cod.
Fruit fillings, flavoured and unflavoured gelatine, pectin jelling agents.
Cornstarch, modified food starch, spinach pasta, gravies, breadings, batters, noodle/rice mixes.
Jams, jellies, shredded coconut
Canned, bottled or frozen fruit juices (including lemon, lime, grape and apple); dried fruit; canned, bottled or frozen dietetic fruit or fruit juices; maraschino cherries and glazed fruit.
Vegetable juice, canned vegetables (including potatoes), pickled vegetables (including sauerkraut), dried vegetables, instant mashed potatoes, frozen potatoes and potato salad.

Sulphites

Common diseases – Inhibits acetylcholine synthesis – snoring

Detoxified by Sulfite oxidase Fe, Mol, Yarrow, Vit C, NAC, Glutathione.

Atropine
(Tomato / Potato Toxin)


CHOLINE
Pyruvate
Vit B1
(thiamine
triphosphate)
CoA
Acetyl CoA
Inhibited by
ethanol,
Cd, Hg,
choline acetyltransferase
K, Br, Cl, I,
10q
383nm
CoA
ACETYLCHOLINE

Atropine is present in

Tomato

Potato

Aubergine

Bell peppers

Chilli

Egg Tobacco

Datura, Herbane

Mandrake root

Atropine counters the "rest and digest" activity of glands regulated by the parasympathetic nervous system.

Atropine is a competitive, reversible antagonist of the muscarinic acetylcholine receptors types M1, M2, M3, M4 and M5 in the parasympathetic nervous system.

Rang, Dale, Ritter and More: Pharmacology, p. 139. Elsevier 2003.

Gall bladder meridian

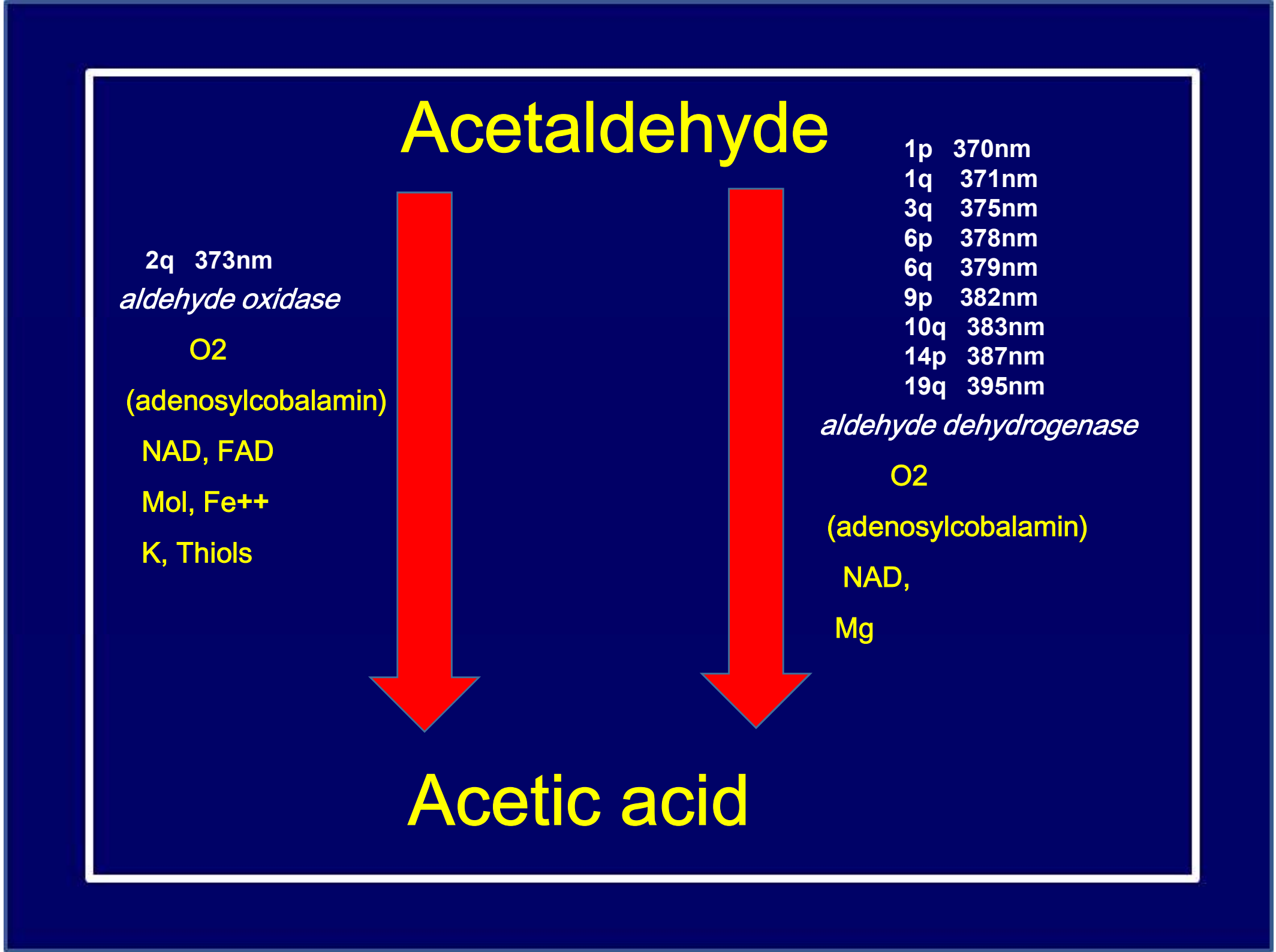
Common diseases – Detoxified by Methylation
SAM, Vit B12, 5MTHF, Betaine

Galantamine – Lemon balm, Rosemary, Fennel, Black walnut

High atropine "hot as a hare, blind as a bat, dry as a bone, red as a beet, and mad as a hatter". These associations reflect the specific changes of warm, dry skin from decreased sweating, blurry vision, decreased sweating / lacrimation, vasodilation, and central nervous system effects on muscarinic receptors, type 4 and 5.

Robert S. Holzman, MD (July 1998). "The Legacy of Atropos". *Anesthesiology*. 89 (1): 241–249.

Malondialdehyde


Acetaldehyde
2q 373nm
aldehyde oxidase
O2
(adenosylcobalamin)
NAD, FAD
Mol, Fe++
K, Thiols
1p 370nm
1q 371nm
3q 375nm
6p 378nm
6q 379nm
9p 382nm
10q 383nm
14p 387nm
19q 395nm
aldehyde dehydrogenase
O2
(adenosylcobalamin)
NAD,
Mg
Acetic acid

Malondialdehyde from rancid fats.

Beware of Flax, Olive, Rapeseed, Sunflower. Corn, Groundnut, Safflower oils.

Most packaged, bottles and processed foods e.g. Mayonnaise, Humus, Sardines, Anchovies etc

Malondialdehyde from rancid fats. 50%

Common diseases – Neurological disorders, Skin, High PgE2.

Detoxified by Sulfotransferase
Aldehyde dehydrogenase
Aldehyde oxidase
Glutathione

B2, B3, Mol, Adenosylcobalamin, Glutathione, P-5-P, Folinic acid, Non rancid oils, Vitamin E, Selenium, Yarrow,