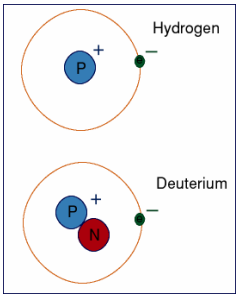
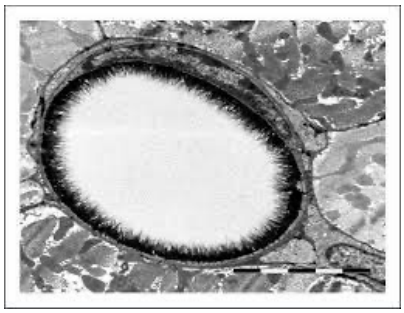
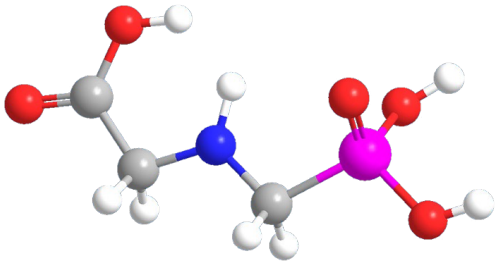
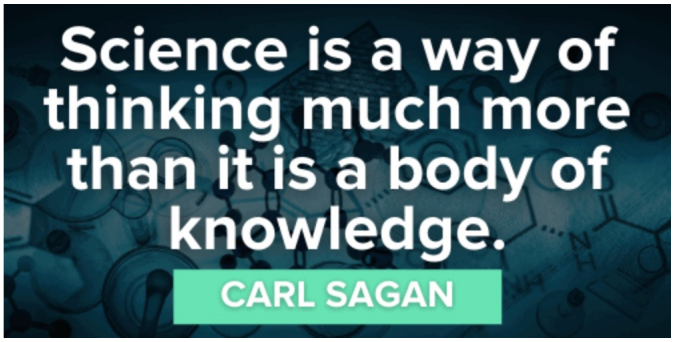


Deuterium, Glyphosate, and the Glycocalyx

Stephanie Seneff
CSAIL, MIT
Sunday, March 23, 2025







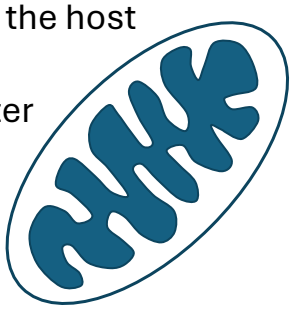
Outline

- Introduction to Deuterium
- Sulfate and the Glycocalyx
- Glyphosate: a Pervasive Toxic Herbicide
- Glyphosate Substitution for Glycine during Protein Synthesis
- Colitis and Colon Cancer
- Histamine Intolerance
- Impaired Fatty Acid Metabolism
- Summary

Introduction to Deuterium

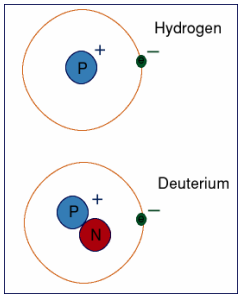
The Big Picture

- Deuterium is a natural heavy isotope of hydrogen
  - It is present in the blood at 5x the concentration of calcium
- Deuterium breaks the ATPase pumps in the mitochondria, causing energy loss and generating reactive oxygen species (ROS)
- Nicotinamide Adenine Dinucleotide (NAD) is a major carrier of deuterium-depleted hydrogen (as NADH)
- Gut microbes synthesize deuterium-depleted nutrients for the host
- Sulfation of mucins in the gut and the glycocalyx lining blood vessels supports trapping of deuterium in gelled water
- *Glyphosate suppresses many proteins involved in deuterium homeostasis*



Deuterium = "Heavy" Hydrogen

- Hydrogen has one proton and one electron
- Deuterium has one proton, one electron and one neutron
  - ~ Twice as heavy as hydrogen
  - Present in ocean water at 155.8 ppm
  - Has distinct physical and chemical properties compared to hydrogen
  - Fats are low in deuterium compared to other foods



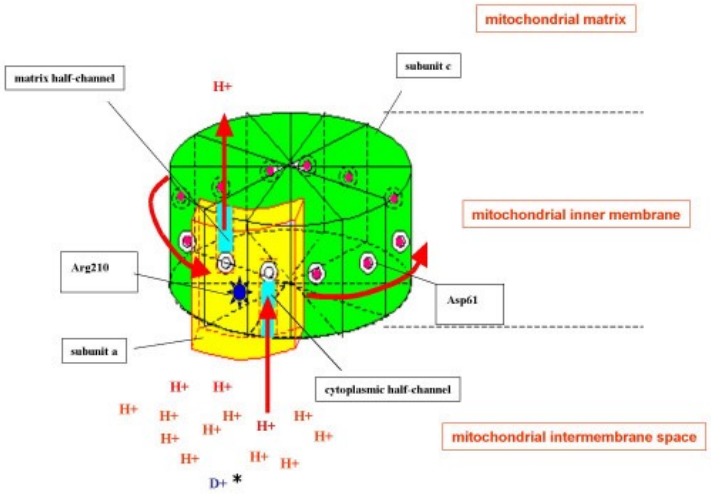
Deuterium management in the body involves trapping deuterium in gelled water outside the cell and invoking specialized enzymes that choose hydrogen over deuterium for their reaction in order to fuel the mitochondria with hydrogen rather than deuterium

"The Pathologic Anatomy of Deuterium Intoxication"*

- Mice received 5% dextrose solution in D_2O water
- "Their appetites were voracious, and constant savage attacks upon each other were continually. in progress."
- "Eventually, at varying intervals, the animals became hypoactive, lethargic, and dramatically weak."
- "Death occurred in all cases within 6-10 days."

*Paul Bachner et al. PNAS 1964; 51: 464-471.

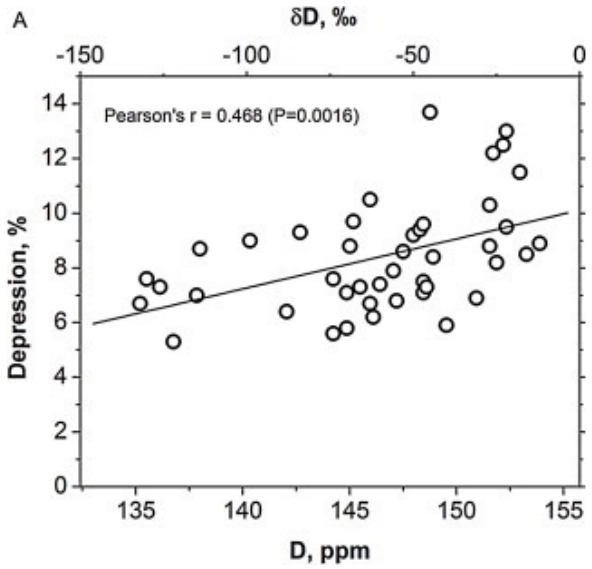
Deuterons Disrupt the ATPase Pump*



- There are around 15,000 ATPase pumps in a single mitochondrion
- Proton force rotates the ATPase pumps at a rate of 1,000 cycles per second
- Deuterons resist letting go and stall the pump, producing a stutter
- Deuterons also disrupt proton-coupled electron transport (PCET) which is based on proton tunneling
- *This causes decreased production of ATP and increased production of reactive oxygen species, damaging the pumps*

*Abdullah Olgun. Theoretical Biology and Medical Modelling 2007, 4: 9.

Deuterium in Water and Depression*



B

Prevalence of Depression

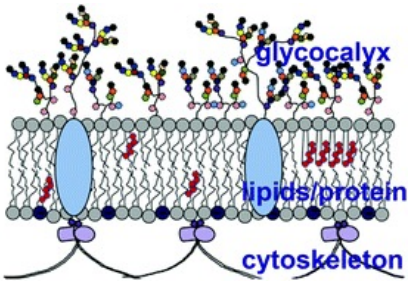
C

Deuterium levels in tap water

*Tatyana Strekalova et al. Behavioural Brain Research 277 (2015) 237–244.

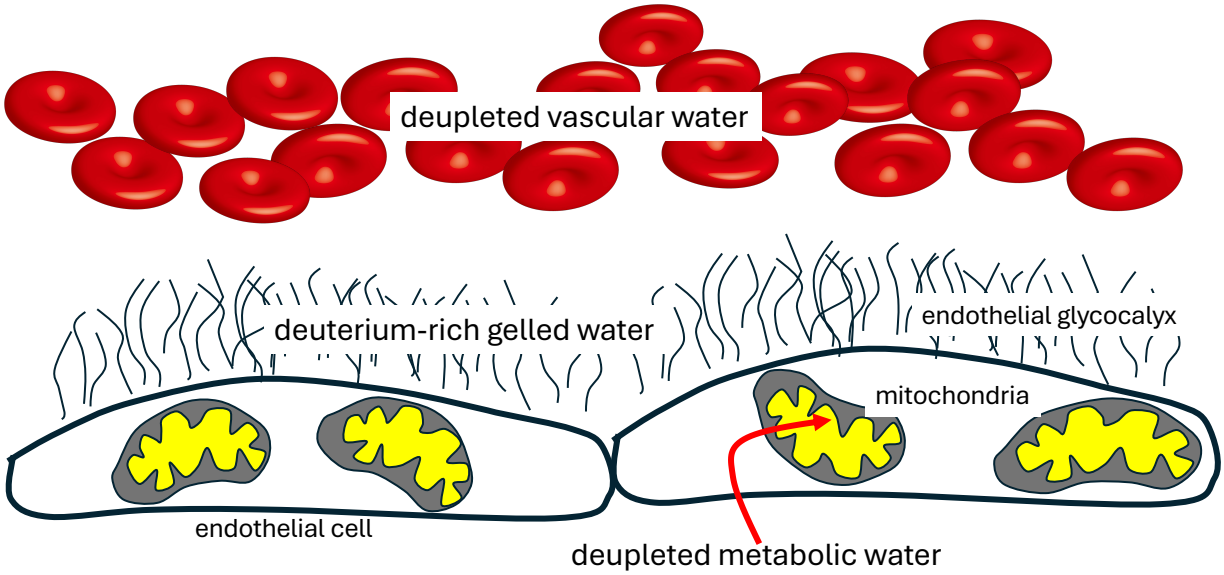
Sulfate's Critical Role for Maintaining Exclusion Zone Water*

- The glycocalyx which lines blood vessels releases protons (H+) and creates a battery
- (Hypothesis) The glycocalyx traps deuterium and extrudes D-depleted protons
  - HDO ionizes mainly into H+ and OD-
- Sulfate is crucial for maintaining gelled water in the glycocalyx
- The sulfomucins lining the epithelium in the gut serve a similar purpose
- Sulfated glycosaminoglycans (GAGs) become depleted in sulfate when chronically exposed to glyphosate



*S Seneff and G Nigh. Water 2019; 11: 22-42. https://waterjournal.org/current-volume/seneff-summary/

Deuterium Fractionation is Critical*



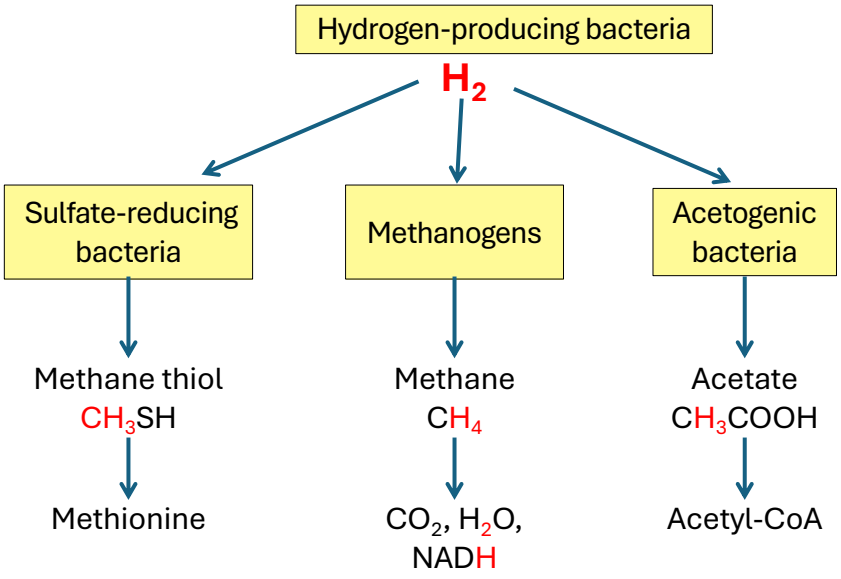
*S. Seneff. Is Deuterium Fractionation a Major Controlling Factor in Human Metabolism and Cancer? An Essential Role for Proline? Preprints 2024, 2024061284.

Hydrogen gas produced by microbes anaerobically from glucose or formate is depleted down to 30 ppm deuterium*

- "Mass spectrometric analyses of the hydrogen produced by growing cells showed a deuterium content of about 30 ppm. (i.e., depleted by a factor of 4.4 to 5.1…)."
- The same was true whether glucose or formate was the substrate.
- The intracellular water and cellular hydrogen were not significantly depleted in deuterium.

*MI Krichevsky et al. JBC 1961 236(9): 2520-2525.

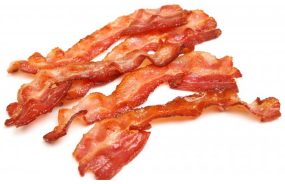
What happens to the hydrogen gas?



Hydrogen Cycling

Ketogenic Diet and DDW: Health Benefits*

- *Deuterium depleted water* (DDW) is essential for mitochondria to function properly
- People whose water supply is naturally depleted in deuterium are healthier
- Deuterium depletion maintains strong hydrogen bond networks in DNA (keeps it stable)
- DDW inhibits tumor progression
- A ketogenic diet is a deuterium-depleted diet



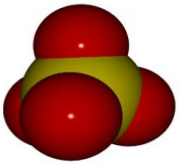
*Laszlo G Boros et al. Medical Hypotheses 2016; 87: 69-74.

Kettle Pond

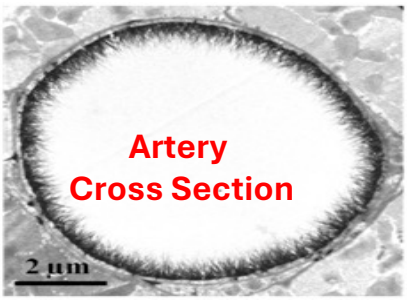
Fog

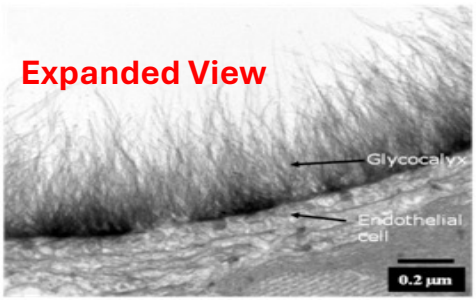
Waterfall

Ocean Waves



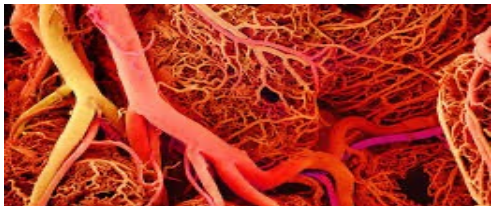
Sulfate and the Glycocalyx



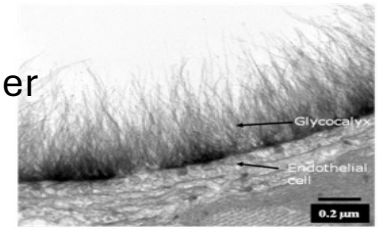


It's All About the Blood

- We are 2/3 water by mass and 99% by molecule count
- Most of the water in the body is gelled
- The big exception is the flowing blood!
- Blood delivers nutrients to and removes waste from all the tissues



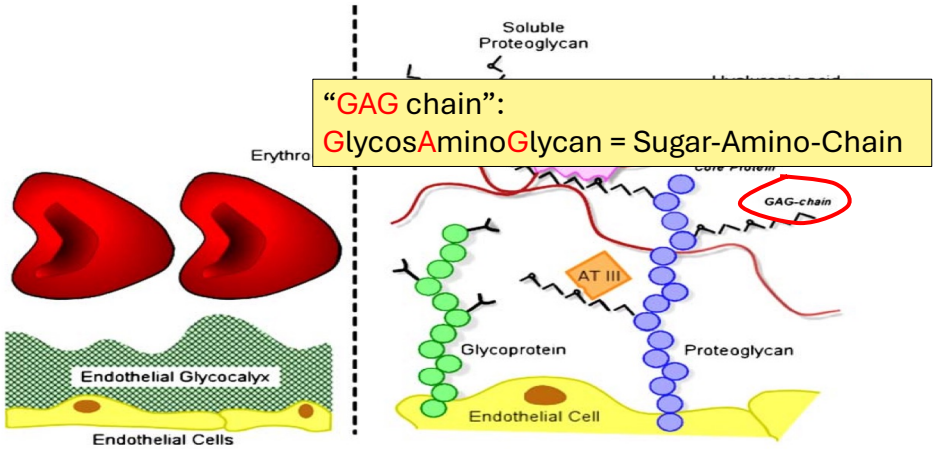
- Gelled water lines the vessel wall and provides slick, frictionless passage of red blood cells through the capillaries
- Sulfate keeps the water gelled along the border
- Sulfate transport is problematic



Sulfate is Crucial to Maintain Structured Water

- Most cells in the body maintain an extracellular matrix formed from proteins with complex sugar chains attached to them
- Sulfate ions bind to the sugars at strategic locations in an irregular but non-random pattern
- The "glycocalyx" that lines the walls of all blood vessels is formed from these sugar-protein complexes
- The sulfomucins lining the interior of the gut barrier are another important example

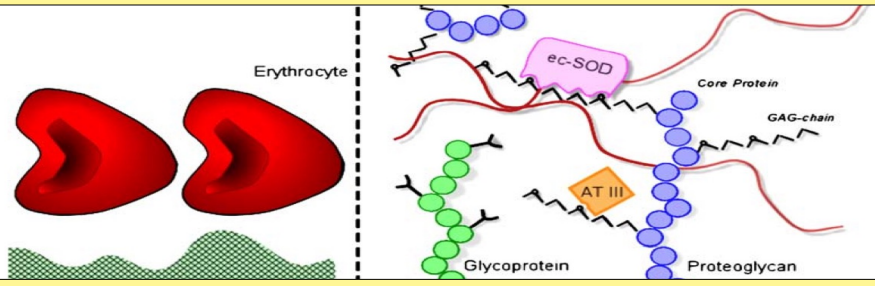
Endothelial Glycocalyx Schematic*



*S Reitsma et al., Pflugers Arch - Eur J Physiol (2007) 454:345–359

Endothelial Glycocalyx Schematic*

Gel layer prevents attack of vessel wall by blood sugars and oxidizing agents.



Cellular signaling mechanisms (e.g., *antioxidant* ec-SOD and *clot-protective* AT III) depend on sulfates to work.

*S Reitsma et al., Pflugers Arch - Eur J Physiol (2007) 454:345–359

Exclusion Zone: Model of Capillary*

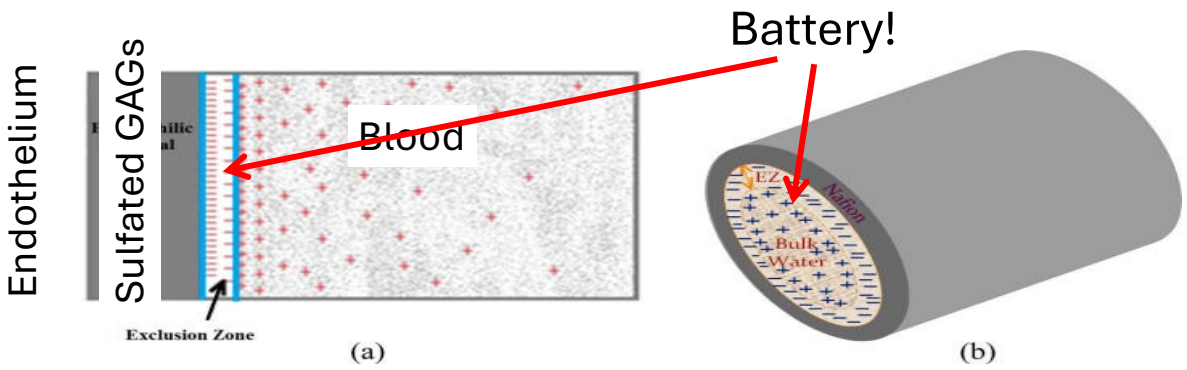
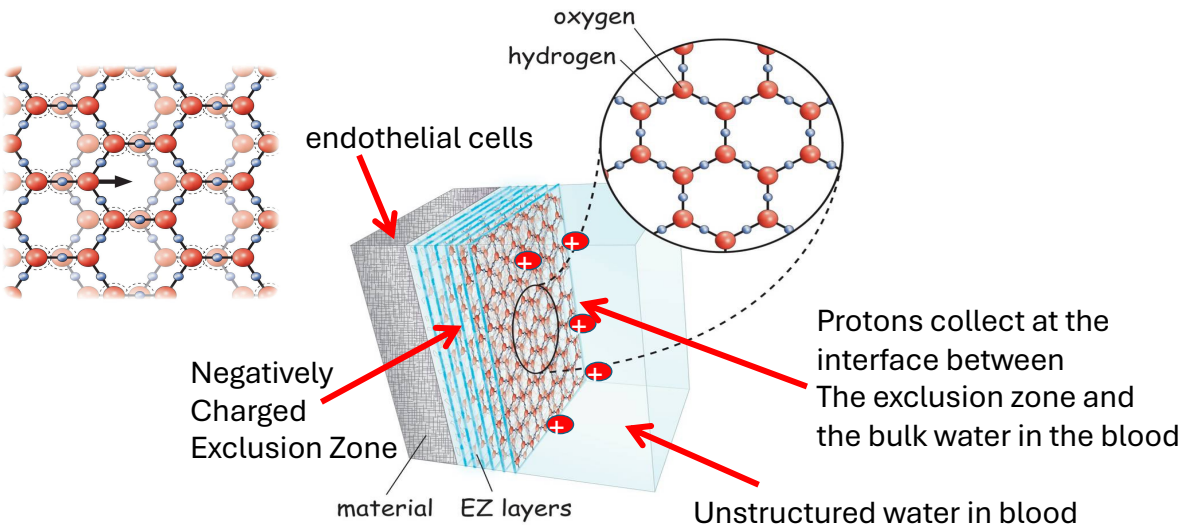


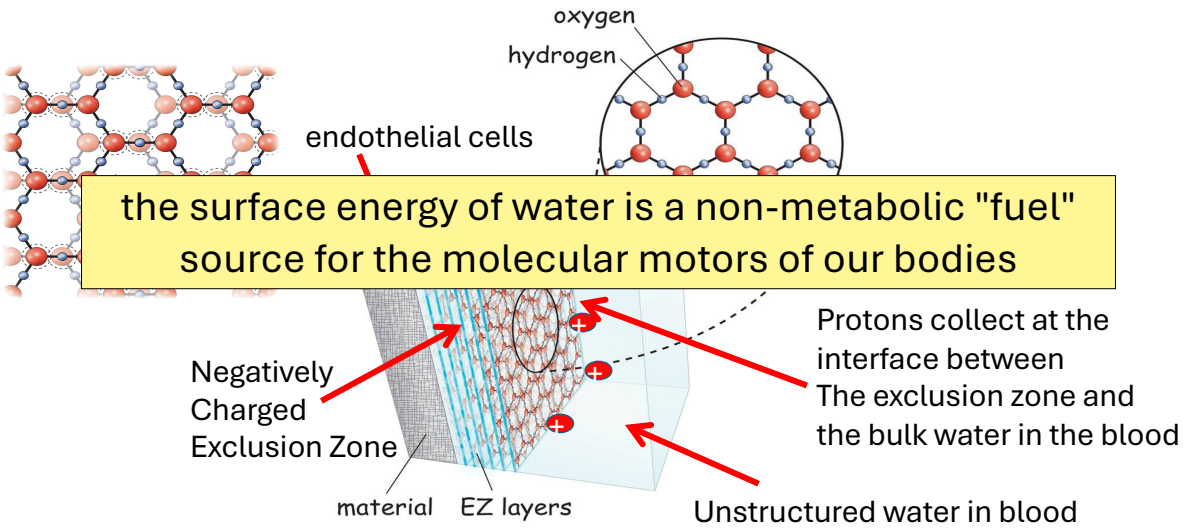
*Figure 9, M. Rohani and G.H. Pollack, Langmuir 2013, 29, 6556–6561

Exclusion Zone*



*http://doublehelixwater.eu/understanding-water-contents/exclusion-zone-form/

Exclusion Zone*



*http://doublehelixwater.eu/understanding-water-contents/exclusion-zone-form/

Glyphosate:
A Pervasive Toxic Herbicide

"Glyphosate Now the Most-Used Agricultural Chemical Ever"*

- Glyphosate usage has increased 50-fold since 1996, when GMO glyphosate-resistant crops were introduced in the US.
- Today, 50 times more glyphosate is allowed by the EPA on corn grain than in 1996
- Half of the American farmers' fields have weeds that are resistant to glyphosate
- New GMO crops offer dual resistance to glyphosate & 2,4-D → Enlist Duo

*Douglas Main, Feb 2, 2016 Newsweekwww.newsweek.com/glyphosate-now-most-used-agricultural-chemical-ever-422419

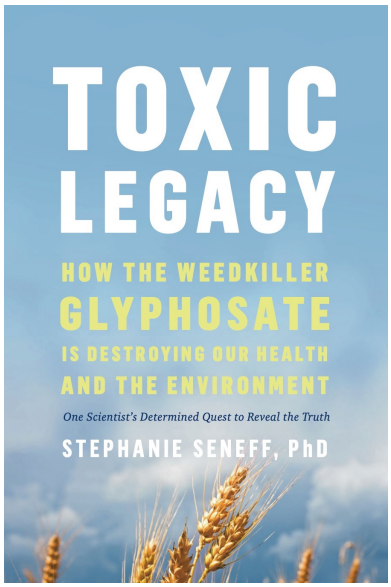
Is Glyphosate Nontoxic?

- Monsanto has argued that glyphosate is harmless to humans because our cells don't have the shikimate biological pathway which is the pathway glyphosate disrupts to kill plants
- However, our gut bacteria DO have this pathway
  - We depend upon them to supply us with essential amino acids produced through that pathway, and with many other nutrients such as vitamins and short chain fatty acids
- Other ingredients in Roundup greatly increase glyphosate's toxic effects
- Insidious effects of glyphosate accumulate over time
  - Most studies are too short to detect damage
- Three successful lawsuits claiming that glyphosate caused non-Hodgkin's lymphoma are bringing public awareness to glyphosate's toxicity

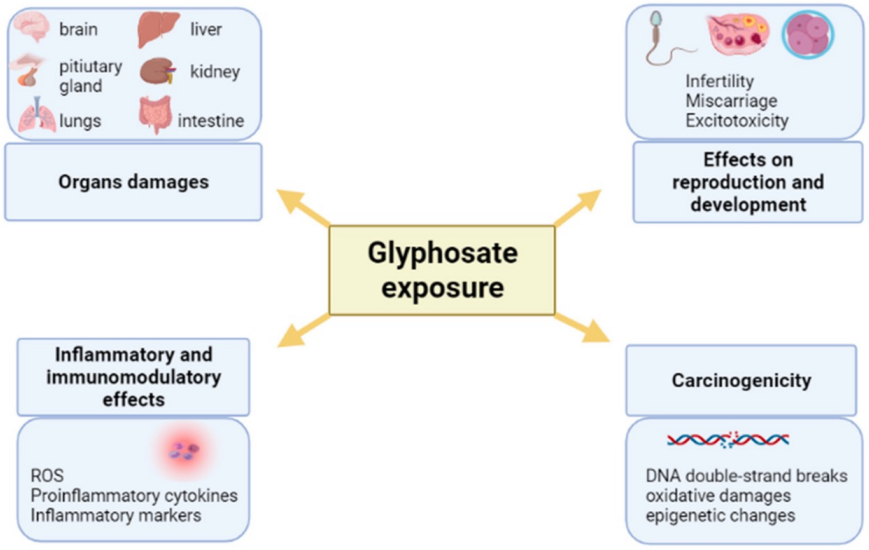
My Book on Glyphosate

- Released by Chelsea Green in July 2021
- Presents extensive data on glyphosate toxicity to animals and humans
- Shows how glyphosate interferes with sulfate homeostasis
- Argues that glyphosate is insidiously, cumulatively toxic through its diabolical insertion into proteins by mistake in place of the coding amino acid glycine
  - This unique feature explains why it is causal in so many diseases

This book was selected by Kirkus Reviews as one of the top 100 non-fiction books of 2021



Glyphosate Toxicity: Summary Graphic*



*M Marino et al. Int J Mol Sci. 2021 Nov 22;22(22):12606.

Contents lists available at ScienceDirect

Neurotoxicology 2019; 75:1-8.

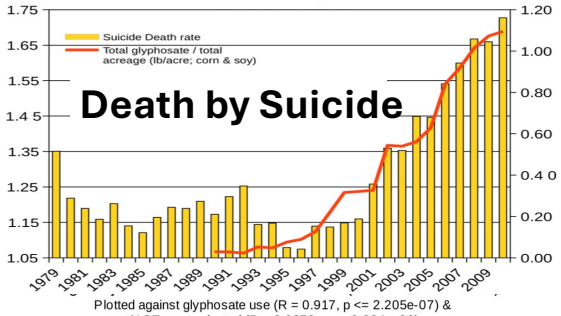
journal homepage: www.elsevier.com/locate/neuro

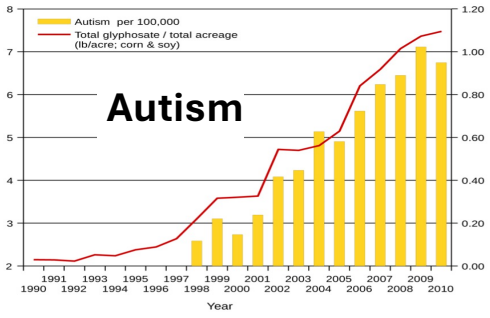
Full Length Article

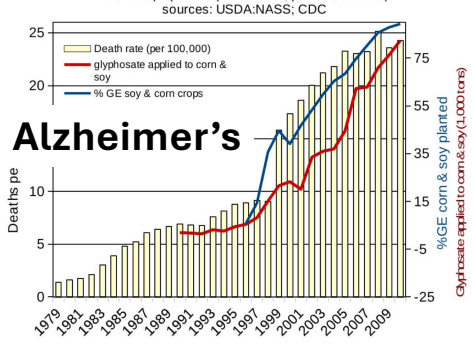
Gut microbiota and neurological effects of glyphosate

Lola Rueda-Ruzafa[a], Francisco Cruz[b], Pablo Roman[c,d,e,*], Diana Cardona[c,e,f]

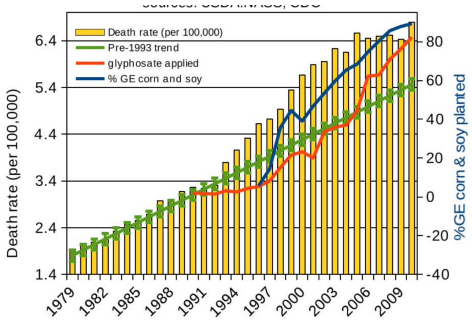
"In this work, we state a possible link between Gly[phosate]-induced *dysbiosis* and cognitive and motor aggravations in neurodegenerative and neurodevelopmental pathologies, such as autism spectrum disorder (ASD). Hence, we review the negative impact that Gly-induced dysbiosis may have on *depression/anxiety, autism, Alzheimer's and Parkinson's diseases*."



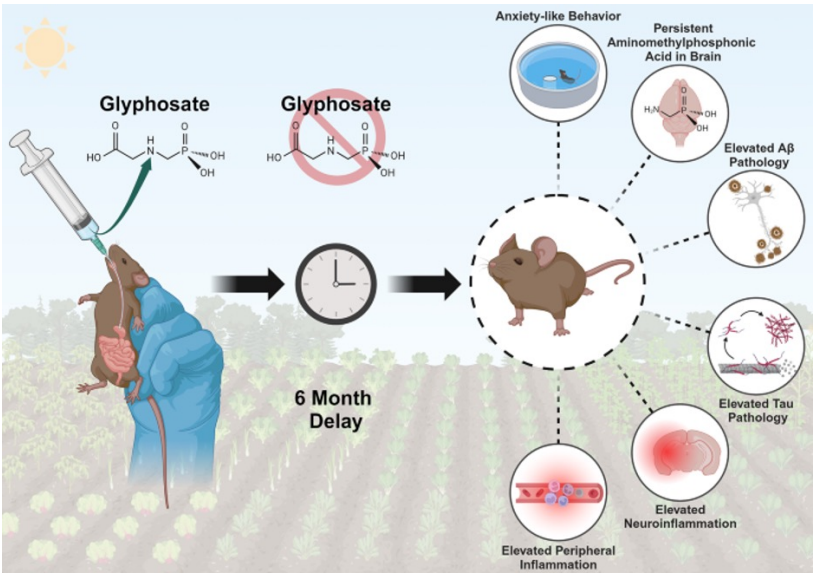




Parkinson's disease



Glyphosate causes Alzheimer's in mice*



A newly published paper (2024) shows that glyphosate induces neuroinflammation in the brain and an increase in phosphorylated tau and amyloid beta, indicators of Alzheimer's disease

*SK Bartholomew et al., J Neuroinflammation 21, 316 (2024).

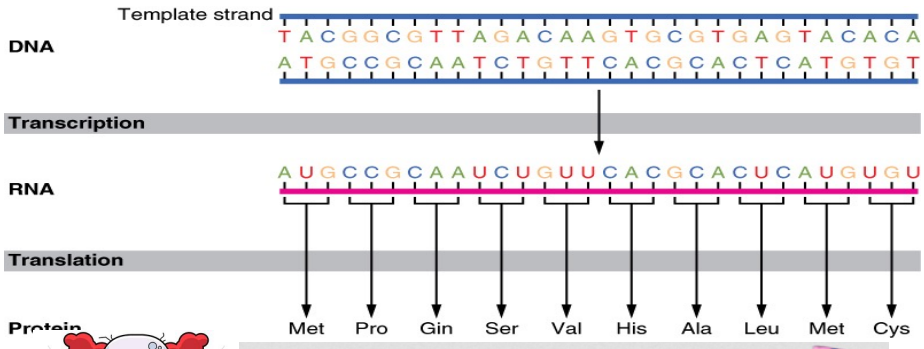
Glyphosate Impairs NAD(P)(H) Pathways*

- NAD(P)(H) is a major carrier of deuterium-depleted protons
- *NAD(P)(H) is derived from tryptophan*
  - Tryptophan is a major product of the shikimate pathway, blocked by glyphosate in plants and microbes
- Glyphosate inhibits *NADH dehydrogenase*, which directly supplies deuterium-depleted protons to the ATPase pumps in the mitochondria
- Glyphosate inhibits *glucose 6 phosphate dehydrogenase* (G6PD), which restores NADPH from NADP+
- Glyphosate inhibits *succinate dehydrogenase*, the only enzyme that participates in both the citric acid cycle and oxidative phosphorylation in the mitochondria
  - Succinate dehydrogenase deficiency is linked to many cancers

*S Seneff, Toxic Legacy, Chelsea Green Publishers, July 2021.

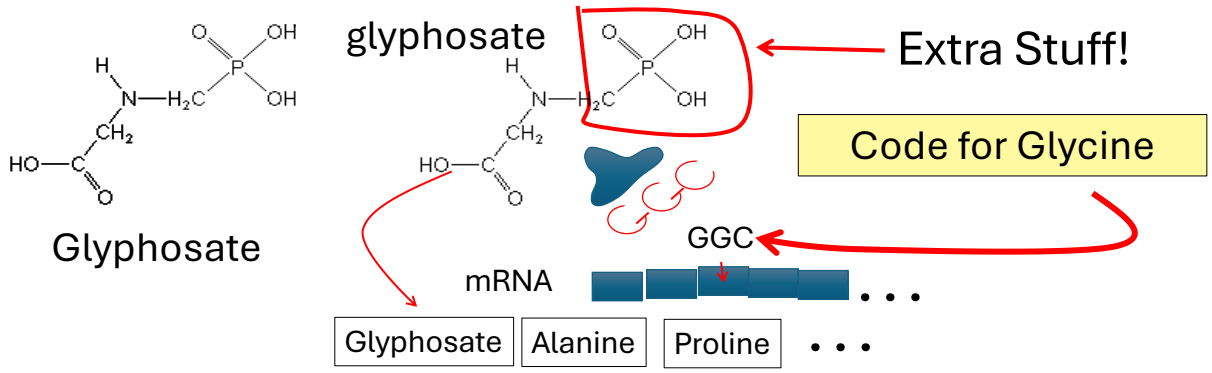
Glyphosate Substitution for Glycine during Protein Synthesis

The Basics of Protein Synthesis



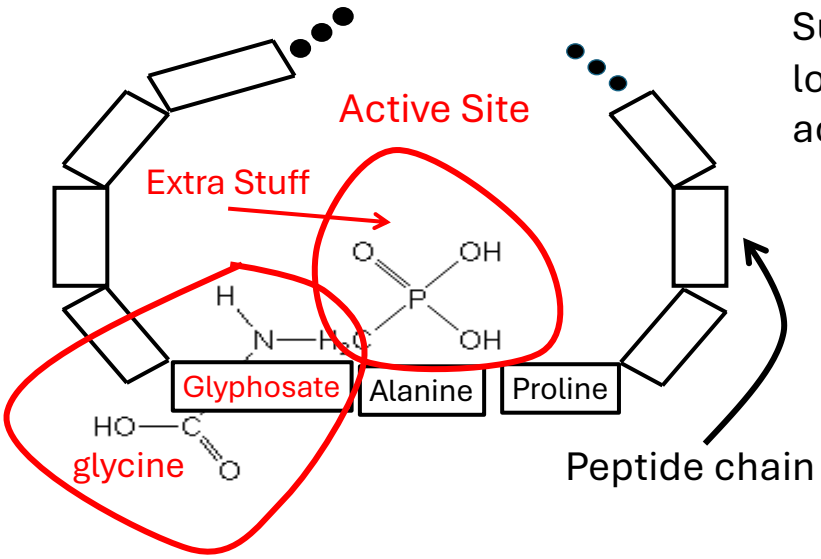
Glyphosate

What if Glyphosate could Insert itself into Proteins during Synthesis???



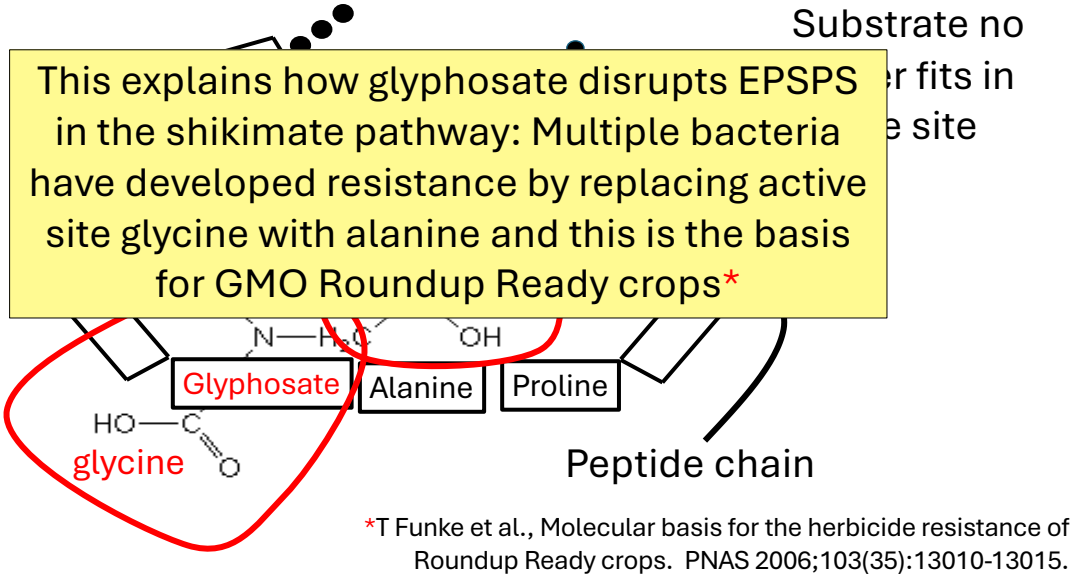
-- Any proteins with conserved glycine residues are likely to be affected in a major way

Extra Piece Sticks Out at Active Site



Substrate no longer fits in active site

Extra Piece Sticks Out at Active Site



*T Funke et al., Molecular basis for the herbicide resistance of Roundup Ready crops. PNAS 2006;103(35):13010-13015.

Inhibition of EPSPS by glyphosate: Resistant E coli mutant*

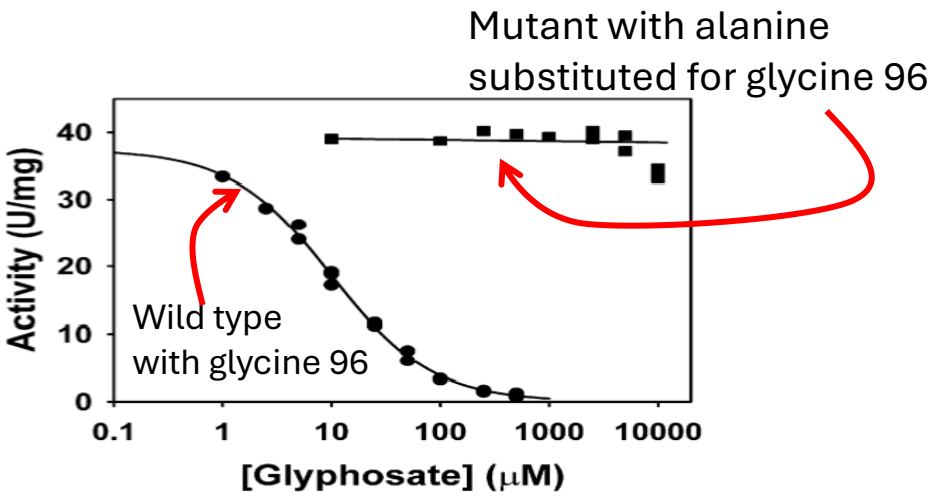


*Figure 3, S Eschenburg et al. Planta 2002;216:129-135.

Only Glyphosate Works!*

"More than 1,000 analogs of glyphosate have been produced and tested for inhibition of EPSP synthase, but minor structural alterations typically resulted in dramatically reduced potency, and no compound superior to glyphosate was identified."

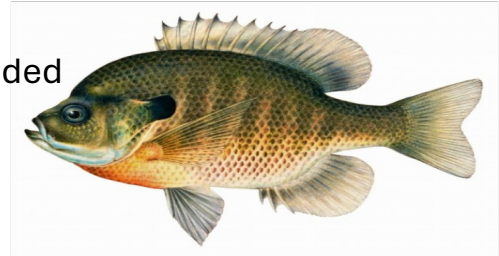
Hypothesis:

These other molecules failed to work as an amino acid analogue of glycine, **because they were not amino acids**

*T Funke et al. PNAS 2006; 103(35): 13010-13015.

Quote from Monsanto Study (1989)*

- Study exposed bluegill sunfish to carbon-14 radiolabelled glyphosate
- Measured radiolabel in tissues greatly exceeded measured glyphosate levels
- Proteolysis recovered more glyphosate
  - 20% yield → 70% yield



"Proteinase K hydrolyses proteins to amino acids and small oligopeptides, suggesting that a significant portion of the 14C activity residing in the bluegill sunfish tissue was tightly associated with or *incorporated into* protein."

*WP Ridley and KA Chott. Monsanto unpublished study. August 1989.

Some Predicted Consequences*

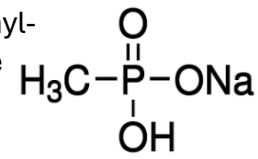
- Impaired cholesterol sulfate synthesis → heart disease
- Autism
- Impaired collagen → osteoarthritis
- Steatohepatitis (fatty liver disease)
- Obesity and adrenal insufficiency
- Hypothyroidism
- Impaired iron homeostasis and kidney failure
- Insulin resistance and diabetes
- Cancer

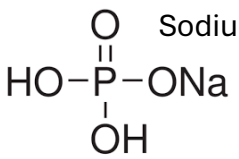
*A. Samsel and S. Seneff. Journal of Biological Physics and Chemistry 2016;16:9-46.

Hypothesis: Glyphosate Disrupts Proteins that Bind Phosphate

- Glyphosate is a glycine molecule with a methylphosphonate unit attached to the nitrogen atom
- Glyphosate kills weeds by suppressing EPSP synthase in the shikimate pathway
- Glyphosate blocks EPSP synthase binding to the phosphate in PEP
- The binding site for PEP has a highly conserved glycine residue

Sodium Methyl-phosphonate





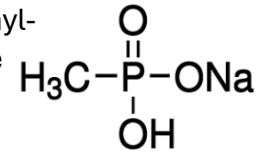
Sodium Phosphate

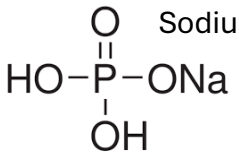
Hypothesis: Glyphosate Disrupts Proteins that Bind Phosphate

- Glyphosate is a glycine molecule with a methylphosphonate unit attach
- Glypho n the shikim
- Glypho hate in PEP
- The bir esidue

Many enzymes that glyphosate has been shown to suppress contain a "glyphosate susceptibility motif": they bind phosphate at a site where there is at least one highly conserved glycine residue

Sodium Methyl-phosphonate



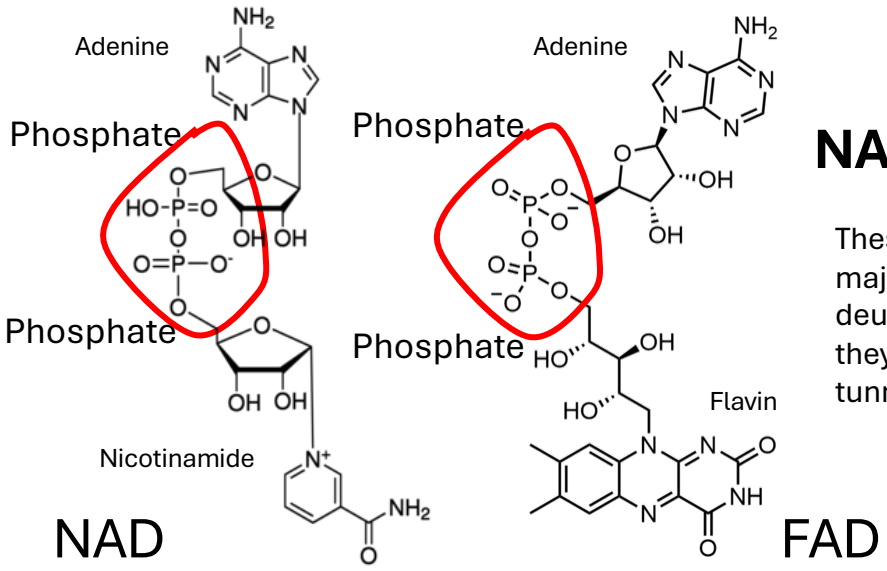


Sodium Phosphate

Does Glyphosate Disrupt FAD Binding in Dehydrogenases?

- Dehydrogenases play a major role in supplying deupleted protons to the mitochondrial ATPase pumps
- Many dehydrogenases are *flavoproteins.* They bind flavin-adenine dinucleotide (FAD) at a site with at least one highly conserved glycine residue. FAD facilitates the transfer of protons and electrons
- A region near the carboxyl-terminal segment of FAD-binding dehydrogenases contains a highly conserved glycine-aspartate pair
- Mutation of Gly-478 to alanine in a Bacillus NADH dehydrogenase caused complete loss of activity, due to loss of binding capacity to FAD*
- Gly-478 is preceded by alanine, a small amino acid, leaving room for glyphosate's methylphosphonate unit

*Masato Shiraki and Noriyuki Kayama. Current Microbiology 2003; 46: 432–434.



NAD and FAD

These dinucleotides are major carriers of deupleted protons and they support proton tunneling in enzymes

Colitis and Colon Cancer

The Big Picture

- Sulfate homeostasis involves three critical enzymes:
  - Sulfite oxidase converts sulfite to sulfate
  - Phosphoadenosyl phosphosulfate (PAPS) is the universal sulfate donor
  - PAPS synthase is the enzyme that synthesizes PAPS from sulfate and ATP
  - Sulfotransferases transfer sulfate from PAPS to many other molecules
- *Glyphosate likely suppresses all of them*
- Decreased PAPSS expression is associated with colon cancer
- In a mouse model of colitis, PAPSS deficiency was associated with inflammation in the gut and a leaky gut barrier
- Glyphosate usage on core crops over time correlates strongly with inflammatory bowel disease

THE JOURNAL OF BIOLOGICAL CHEMISTRY
Vol. 273, No. 16, Issue of April 17, pp. 9450–9456, 1998
Printed in U.S.A.

Deletion and Site-directed Mutagenesis of the ATP-binding Motif (P-loop) in the Bifunctional Murine Atp-Sulfurylase/Adenosine 5′-Phosphosulfate Kinase Enzyme*

(Received for publication, December 9, 1997, and in revised form, February 4, 1998)

Andrea T. Deyrup‡, Srinivasan Krishnan‡, Brian N. Cockburn§, and Nancy B. Schwartz¶‖

- Phosphadenosyl phosphosulfate (PAPS) is the universal sulfate donor
- *PAPS synthase* carries out two catalytic reactions: it is both a sulfurylase and a kinase
- It binds to two ATP molecules (three phosphates in each)
  - Its P-loop is a common motif found in proteins that bind to ATP and GTP
- The sequence "GLSGAGKT" from 59 to 66 in the P loop of human PAPS synthase matches the GxxGxGKT motif characteristic of binding to ATP
  - When G59 (the first glycine) is mutated to alanine, sulfurylase activity is reduced to 8% residual activity
  - Substituting alanine for G64 reduced kinase activity down to only 6% residual activity

Sulfite Oxidase and the Sulfotransferases

Sulfite oxidase (SuOx)*

- Depends on molybdenum as catalyst (glyphosate chelation could make it unavailable)
- Changing glycine at residue 473 with aspartate destroys enzyme activity
  - Leads to severe impairment in ability to bind sulfite and 5-fold reduction in catalysis
  - Aspartate has similar properties as glyphosate, being bulky and negatively charged
- Defective SuOx leads to severe birth defects and neurological problems resulting in early death

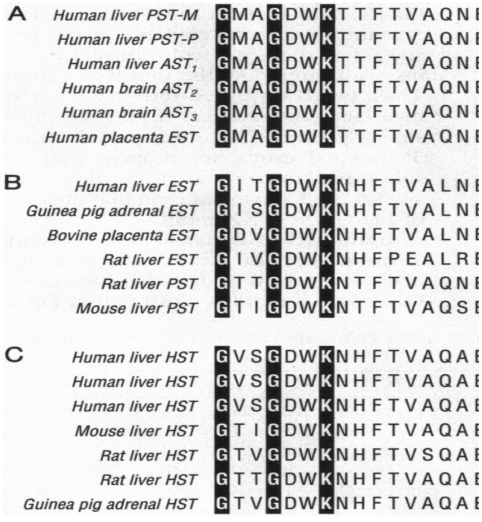
The sulfotransferases**

- GxxGxxK motif required for binding PAPS (activated sulfate)

*H.L. Wilson et al., Biochemistry 2006, 45, 2149-2160 2149.
**K. Komatsu et al., Biochemi and Biophys Res Comm 1994;204(3): 1178-1185.

GxxGxxK Motif in Sulfotransferases*

- Sulfotransferases are crucial to attach sulfate ions to multiple bioactive molecules
- **Steroids** (cholesterol, estrogen, testosterone, vitamin D, …)
- **Glycosaminoglycans** (chondroitin sulfate, heparan sulfate, …)
- **Polyphenols, aromatics** (curcumin, resveratrol, tryptophan, …)
- **Neurotransmitters** (dopamine, serotonin, melatonin, …)



*H Chiba et al. Proc. Natl. Acad. Sci. USA 1995; 92:8176-8179.

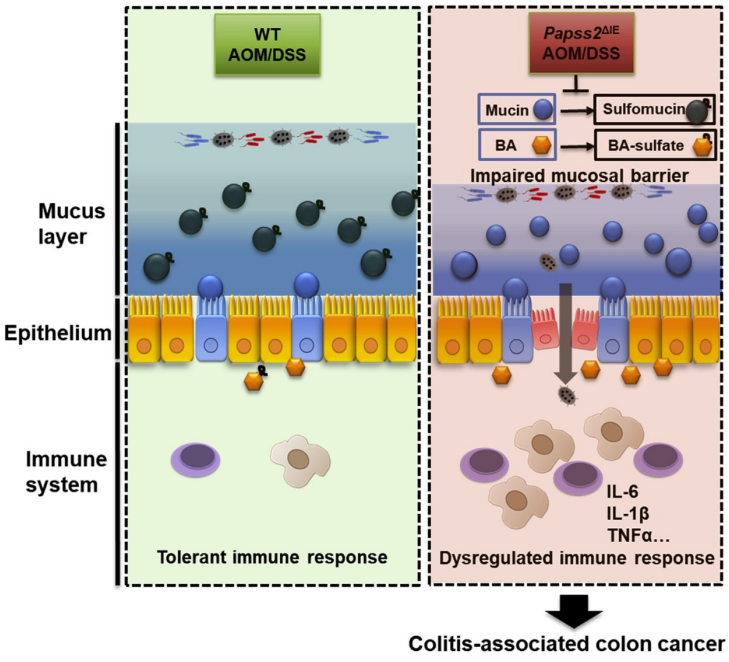
Gastroenterology 2021;161:271–286

Intestinal Sulfation Is Essential to Protect Against Colitis and Colonic Carcinogenesis

Pengfei Xu,[1] Yue Xi,[1,2] Junjie Zhu,[1] Min Zhang,[1] Zigmund Luka,[3] Donna B. Stolz,[4] Xinran Cai,[1] Yang Xie,[1] Meishu Xu,[1] Songrong Ren,[1] Zhiying Huang,[2] Da Yang,[1] John D. York,[3] Xiaochao Ma,[1] and Wen Xie[1,5]

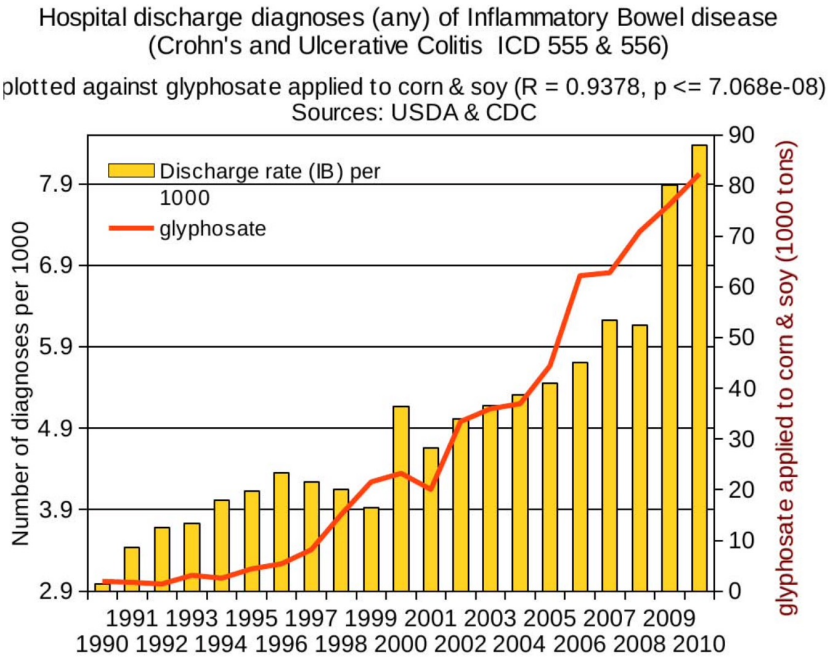
- Colon cancer is the third most common cancer and the third leading cause of death due to cancer
- PAPSS expression is decreased in both mice and humans with colon cancer, and is correlated with higher mortality
- Associated with:
  - Reduced intestinal sulfomucin content
  - Deficiency in the formation of bile acid sulfates

AOM/DSS = azoxymethane/dextran sodium sulfate



Mouse model of colitis: Mice with deficiency in PAPSS had a leaky gut barrier and an acute inflammatory response

*Pengfei Xu et al., Gastroenterology 2021; 161: 271-286.



Correlation between inflammatory bowel disease and glyphosate usage on core crops*

*Figure 20
N Swanson et al. Journal of Organic Systems, 9(2), 2014.

Histamine Intolerance

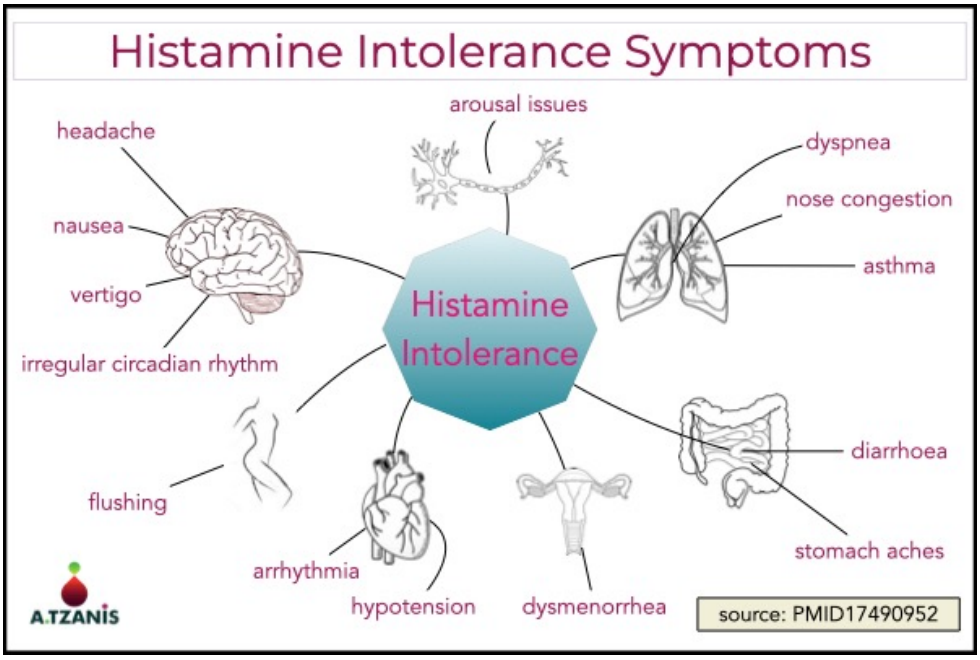
The Big Picture

- Mast cells release histamines in response to allergens
- Histamines are metabolized primarily by histaminase in the gut
- Histamine sensitivity results when histaminase is defective (suppressed)
  - A large number of uncomfortable symptoms arise from histamine intolerance
  - Glyphosate likely suppresses histaminase
- *Hypothesis:* Mast cell activation is induced when the gut lumen contains too much deuterium due to insufficient sulfate in the sulfomucins
- *Hypothesis:* The metabolites of histamine can trap deuterium and permanently sequester it

MAST CELL ACTIVATION SYNDROME

There is an epidemic of chronic disease in this country. Millions of Americans suffer from multiple diagnoses given by various doctors. For these diagnoses, they are put on an array of medications in an attempt to "stabilize" their condition. They often do not improve and their health may continue to decline over time. These patients are sometimes told their symptoms are imagined, or "psychosomatic." Until the root cause of the chronic disease is found, these patients will continue to go from doctor to doctor in search of answers they will most likely never get. But what if there was a unifying condition that could explain all of their symptoms and diagnoses? What if there was a root cause that could be identified and then treated?

Dr. Tania Dempsey
https://drtaniadempsey.com/mast-cell-activation-syndrome-mcas-a-hidden-epidemic/

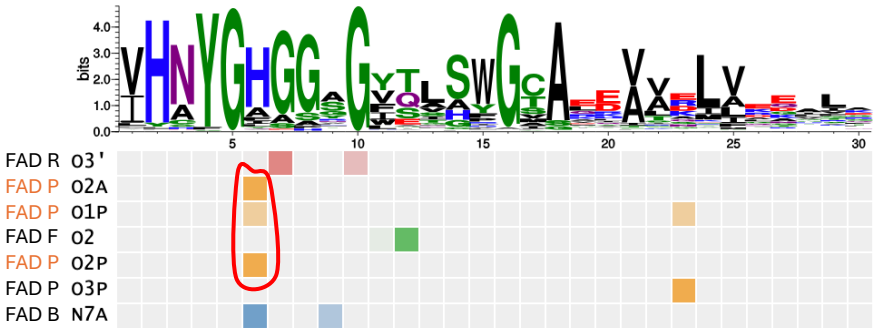


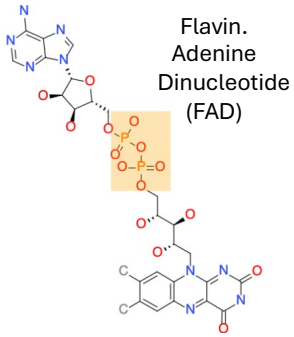
*https://www.atzanis.com/fix-histamine-intolerance/

Histamine! YGHGGGWG Motif in Histaminase

- Histaminase has a fantastic "glyphosate susceptibility motif"
  - It contains 5 glycine residues
  - It is a motif known to be found in proteins that bind flavin adenine dinucleotide (FAD)

... IHNYGHGGYGLTIHWG...
YGHGG G WG





Histaminase: Rat Study*

- Diamine oxidase (DAO; histaminase) is found in high concentrations in the intestinal mucosa
- The intestinal mucosa are the primary source of plasma DAO
- A decrease in plasma DAO reflects an increase in mucosal damage
  - Circulating levels of DAO can serve as a marker of mucosal damage
- A deficiency in histaminase is a primary cause of histamine intolerance **
- Heparin infusion increases expression of DAO
  - Heparin is the most highly sulfated molecule in the body

*GD Luk et al. J Clin Invest. 1980 Jul;66(1):66-70.
**L Maintz and N Novak. Am J Clin Nutr. 2007 May;85(5):1185-96.

Hist

"The ingestion of histamine-rich food or of alcohol or drugs that release histamine or block DAO may provoke diarrhea, headache, rhinoconjunctival symptoms, asthma, hypotension, arrhythmia, urticaria, pruritus, flushing, and other conditions in patients with histamine intolerance."**

- Diam
  high
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- A dec
  - Ci
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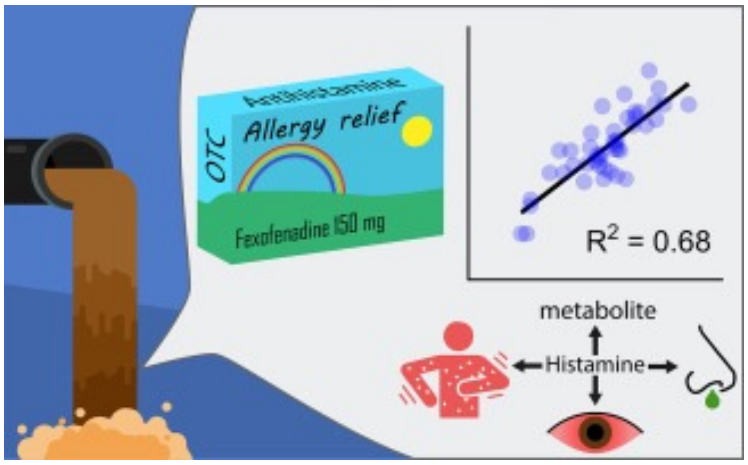
  intole
- Heparin infusion increases expression of DAO
  - Heparin is the most highly sulfated molecule in the body

ge

*GD Luk et al. J Clin Invest. 1980 Jul;66(1):66-70.
**L Maintz and N Novak. Am J Clin Nutr. 2007 May;85(5):1185-96.

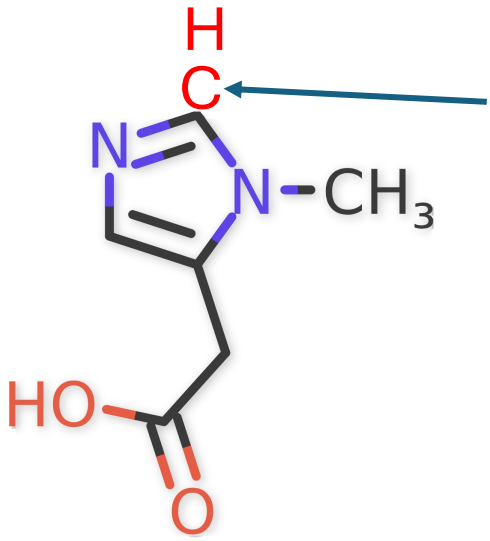
Histamine metabolite MIAA in wastewater*



- Authors found a high correlation between the amount of fexofenadine (Alleve) in wastewater and the amount of MIAA (metabolite of histamine)
- Technique allows researchers to assess disease risk for allergic diseases in the population served by the sewer system

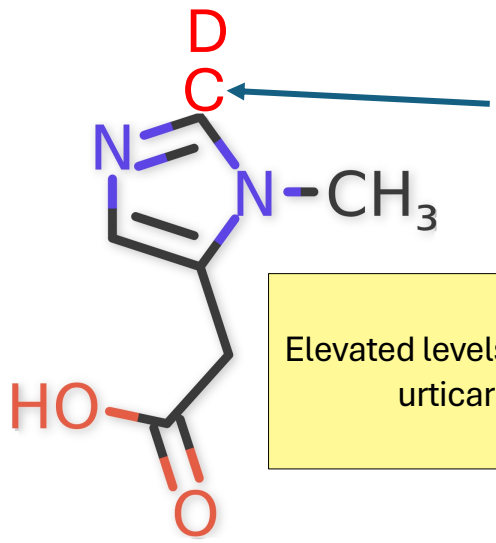
*Phil M Choi et al. Environment International 120 (2018) 172–180.

MIAA: methylimidazole acetic acid



- This carbon atom (C2) in the imidazole ring easily picks up deuterium from the water, due to its neighboring two nitrogen atoms
- Once it has trapped deuterium, it doesn't let go

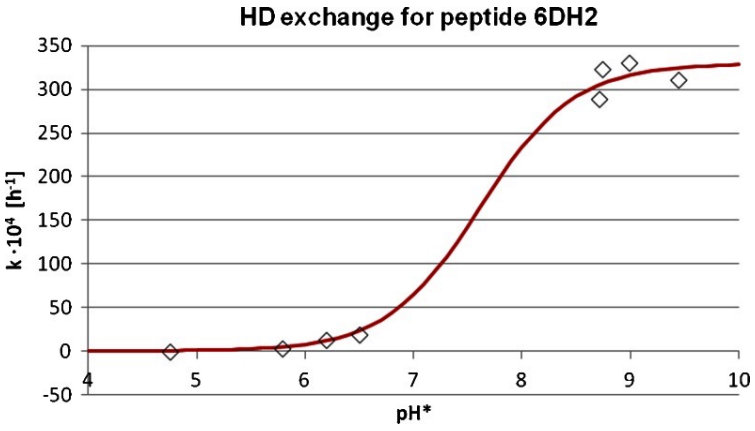
MIAA: methylimidazole acetic acid



- This carbon atom (C2) in the imidazole ring easily picks up deuterium from the water, due to its neighboring two nitrogen atoms
- Once it has trapped deuterium, it doesn't let go

Elevated levels in the urine are associated with mastocytosis, urticaria, atopic dermatitis, and allergic rhinitis

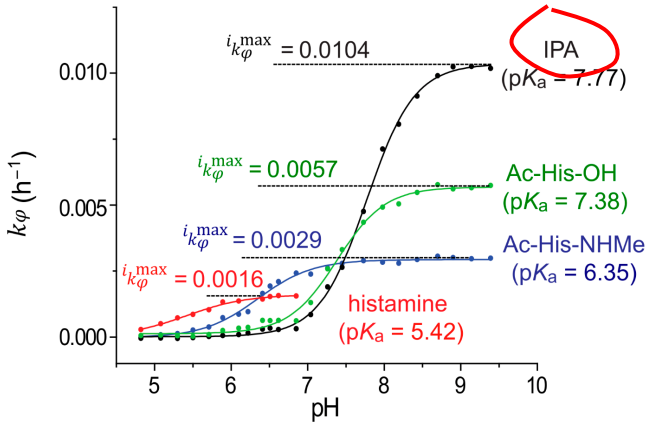
pH dependence of H-D exchange in imidazole ring*



6DH2 = Asp-Ala-Ala-His-Ala-Phe-OH

*M Cebo et al. Anal Bioanal Chem. 2014 Dec;406(30):8013-20.

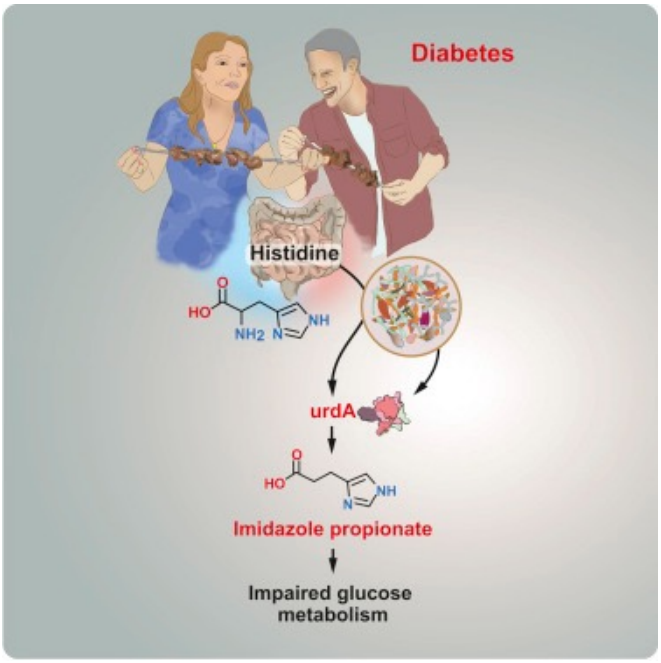
HDX (Hydrogen/Deuterium Exchange) for various metabolites of histamine/histidine*



IPA = Imidazole Propionate

Hypothesis: Histamine metabolites can trap deuterium when the gut lumen becomes too basic. They essentially trap and remove deuterium "landmines"

*M Miyagi et al. Biology (Basel). 2024 Jan 9;13(1):37.



Microbially Produced Imidazole Propionate Impairs Insulin Signaling through mTORC1*

- Imidazole propionate (IPA) levels are increased in association with type 2 diabetes
- It is produced by certain gut microbes that are increased in diabetic patients
- It inhibits insulin signaling by activating the mTORC pathway

*A Koh et al. Cell 2018 Nov 1;175(4):947-961.e17.

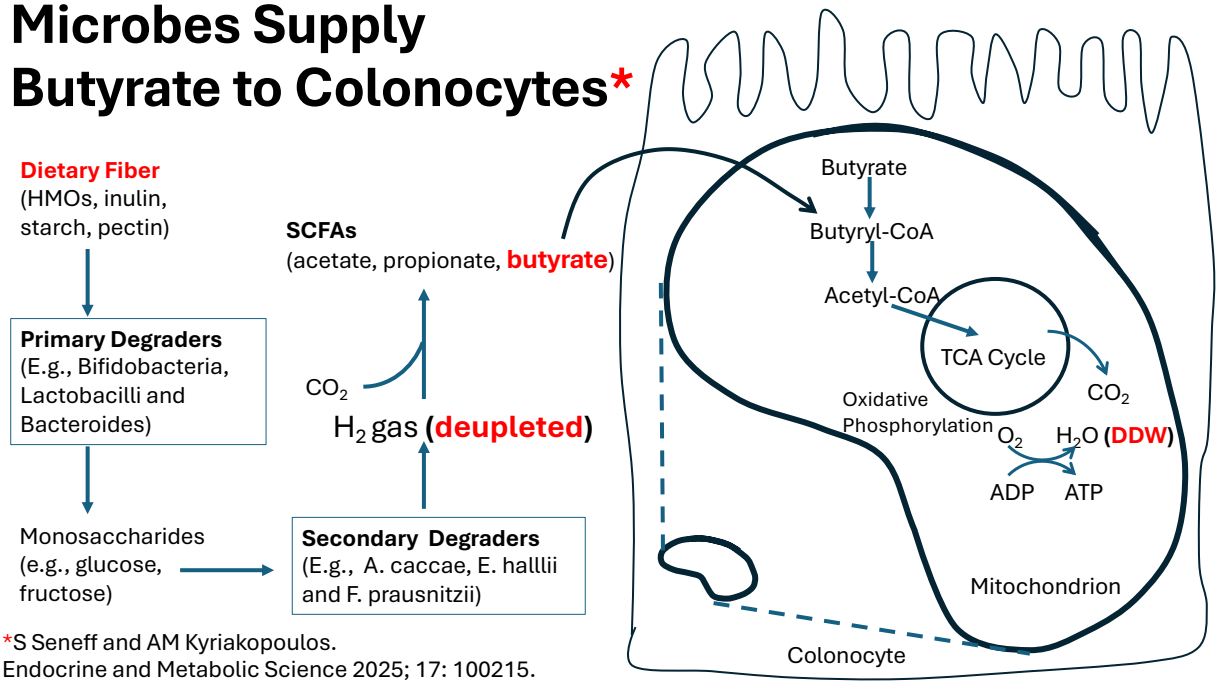
Explanation of Gut Disruption Leading to IPA Overproduction

"In addition, because UrdA [the enzyme that produces IPA] is active at neutral pH (Bogachev et al., 2012) and the proximal colon has an acidic pH, increases in pH, *possibly resulting from decreased production of short-chain fatty acids and increased protein fermentation in the gut* (Windey et al., 2012), may increase production of imidazole propionate."*

- Glyphosate causes an increase in the pH of the gut, which greatly reduces the production of short chain fatty acids by acid-loving microbes**
- Glyphosate also increases the production of ammonia (which raises the pH) from protein fermentation**

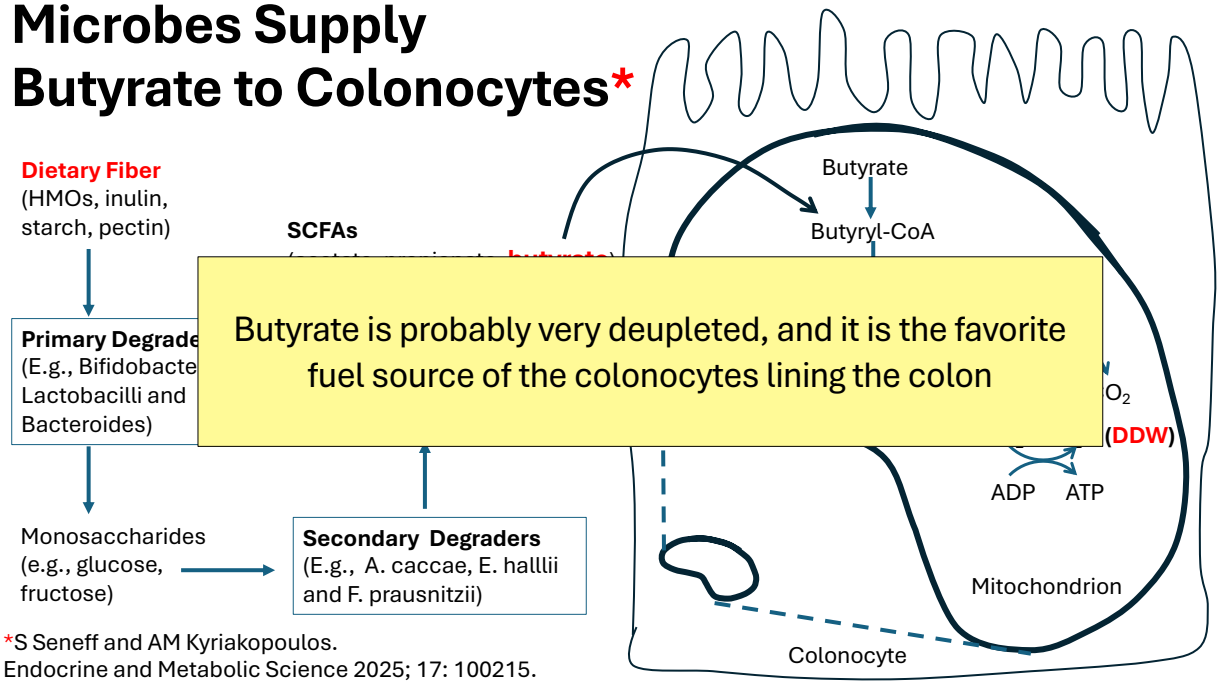
*A Koh et al. Cell 2018 Nov 1;175(4):947-961.e17
**Stephanie Seneff, Toxic Legacy, 2021, Chapter 3.

Microbes Supply Butyrate to Colonocytes*



*S Seneff and AM Kyriakopoulos.
Endocrine and Metabolic Science 2025; 17: 100215.

Microbes Supply Butyrate to Colonocytes*



*S Seneff and AM Kyriakopoulos. Endocrine and Metabolic Science 2025; 17: 100215.

Recapitulation

- Mast Cell Activation Syndrome was first recognized as a disease in 2007
  - Associated with excessive inflammation and allergic reactions
  - Mast cells release abundant histamines into the gut lumen
  - Histamines act as signaling molecules to induce diarrhea, abdominal pain, and nausea
- Histaminase metabolizes histamines into metabolic products that may be able to trap deuterium and remove it from the gut
  - Suppressed histaminase causes histamine intolerance
  - Histaminase has a very strong glyphosate susceptibility motif
- Gut microbes metabolize histidine to imidazole propionate (IPA), and elevated levels are linked to diabetes
- Glyphosate induces an environment in the gut that is conducive to IPA-producing bacteria

Impaired Fatty Acid Metabolism

Why So Many Picky Eaters?

- **Observation:** Many children in America, especially autistic children, are very picky eaters.
- **Question:** Are there enzymes that could be suppressed by glyphosate to cause this condition?



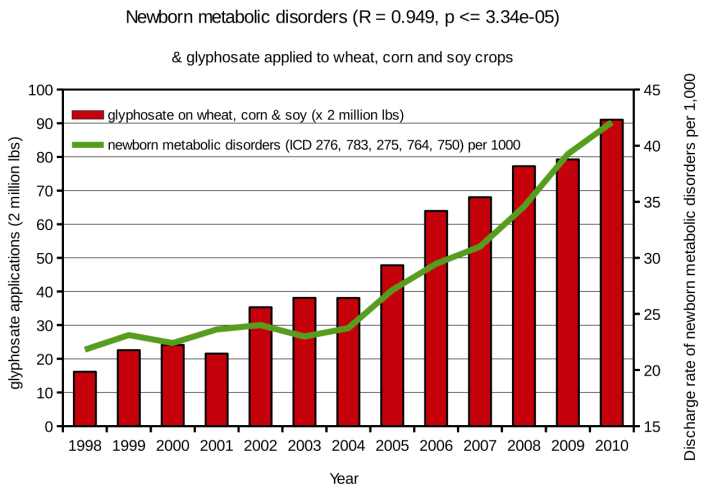


Figure 32: Hospital discharge rates for newborn metabolic disorders compared to glyphosate applications to wheat, corn and soy crops. The metabolic disorders include: disorders of fluid electrolyte and acid-base balance (ICD 276); underweight, feeding problem & fetal malnutrition (ICD 783); disorders of mineral metabolism (ICD 275); slow fetal growth and fetal malnutrition (ICD 764); other congenital anomalies of upper alimentary tract (ICD 750). The Pearson correlation coefficient is R=0.949.

Trends in newborn metabolic disorders over time compared to the rise in glyphosate usage on core crops*

Includes feeding problems, poor weight gain, slow fetal growth, congenital anomalies in the gut, and fetal malnutrition

$p < 0.0000334$

*J Hoy et al. Poult Fish Wildl Sci 2015; 3: 132.

Long-chain 3-hydroxyacyl-CoA dehydrogenase (LCHAD) deficiency*

- This dehydrogenase plays an essential role in the metabolism of long chain fatty acids
- Deficiencies in this enzyme lead to severe disease
  - Feeding difficulties; dislikes of many foods; nausea and vomiting; lack of energy; low blood sugar; weak muscle tone; delayed development; liver problems; light sensitivity
  - Neonates with the severe phenotype present within a few days of birth with hypoglycemia (low blood sugar), hepatomegaly (enlarged liver), encephalopathy (brain dysfunction), and often cardiomyopathy (heart problems)

Glyphosate has been shown to suppress dehydrogenase enzymes in many studies on human cells, E coli and soil bacteria

*medlineplus.gov/genetics/condition/long-chain-3-hydroxyacyl-coa-dehydrogenase-deficiency

Neuropsychological Development in Patients with Long-Chain 3-Hydroxyacyl-CoA Dehydrogenase (LCHAD) Deficiency

A. Strandqvist • C. Bieneck Haglind • R.H. Zetterström • A. Nemeth • U. von Döbeln • M. Halldin Stenlid • A. Nordenström

Conclusion:

"Patients with an LCHAD deficiency appear to have a specific cognitive pattern, presenting as intellectual disability and specific autistic deficiencies or a normal IQ with weaknesses in auditive verbal memory and adaptive and executive functions." *

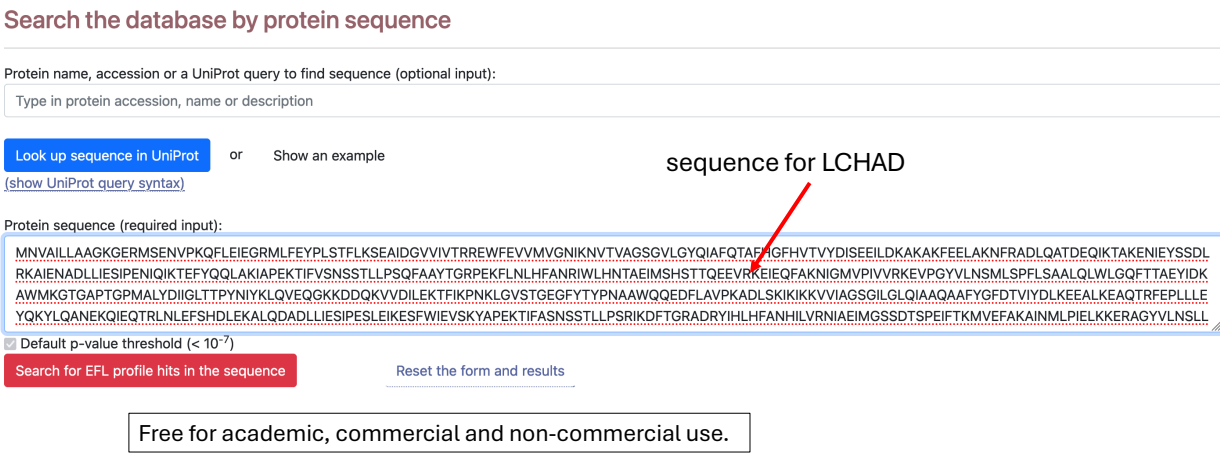
*A Strandqvist et al. JIMD Rep. 2016;28:75-84.

"Human serum lipidomics analysis revealed glyphosate may lead to lipid metabolism disorders and health risks"*

- Glyphosate production workers from three chemical factories in China were compared to controls
- Lipidomics analysis revealed significantly elevated levels of acylcarnitines in the workers
- Elevated acylcarnitines are an indicator of impaired fatty acid oxidation in the mitochondria
- A critical enzyme in long chain fatty acid oxidation is LCHAD (long chain 3-hydroxyacyl CoA dehydrogenase)

*Feng Zhang et al. Environment International 171 (2023) 107682

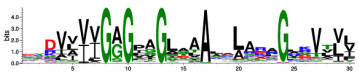
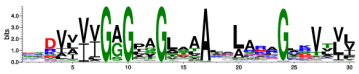
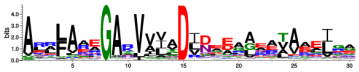
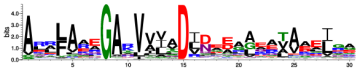
Nucleotide Binding Database*

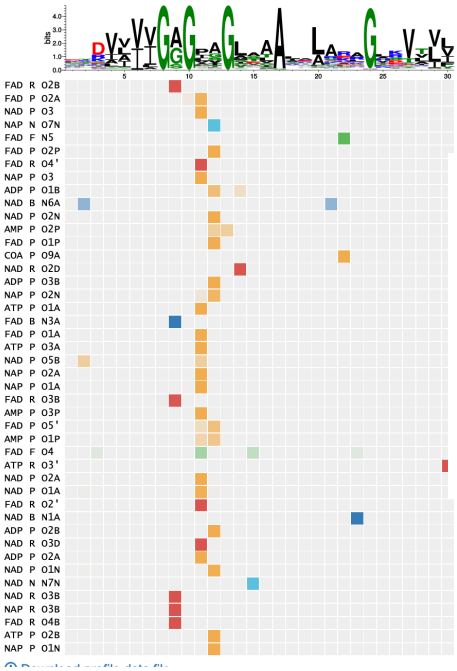


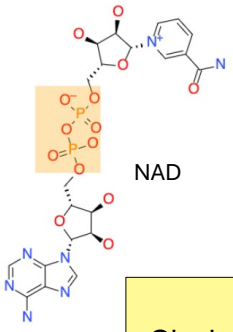
Free for academic, commercial and non-commercial use.

*Zheng, Z., Goncearenco, A., Berezovsky, I.N. 2015. TBD
Bioinformatics Institute (BII), A*STAR, Singapore

Many glycine residues in LCHAD bind to phosphate!!

Profile name	Binds moieties	Profile logo	Hit from	Hit to
GxGxxG	B R P F N		309	338
GxGxxG	B R P F N		4	33
GxGGxG	P		304	333
GAVD	B R		20	49
GAVD	B R		325	354

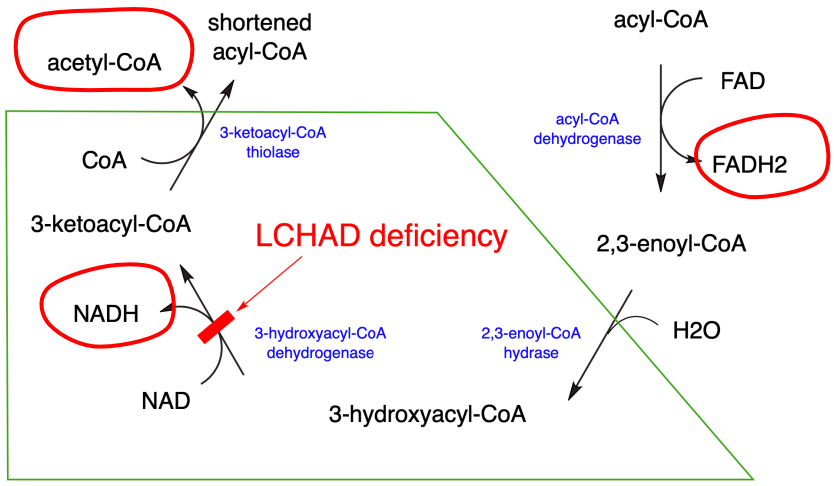




GxGxxG Sequence Motif binds to many phosphate-containing molecules

Glyphosate suppresses EPSP synthase at a site that binds phosphate where glycine is highly conserved

LCHAD is Essential for Fatty Acid Oxidation



- Fatty acids are naturally low in deuterium
- Each round through this pathway peels off two carbons from the fatty acid chain to release acetyl-CoA
- LCHAD deficiency blocks long chain fatty acid oxidation in the mitochondria

“Glyphosate Excretion is Associated With Steatohepatitis and Advanced Liver Fibrosis in Patients With Fatty Liver Disease”*

- Non-alcoholic fatty liver disease (NAFLD) is the most common chronic liver disease in developed countries, and it can progress to a more severe form, non-alcoholic steatohepatitis (NASH)
- Fatty liver disease increases risk to cirrhosis and liver cancer
- Rats develop fatty liver disease after low-dose exposure to glyphosate

"We report that glyphosate excretion is significantly higher in patients with NASH compared to patents without NASH. In addition, we also report a significant dose-dependent increase of glyphosate exposure with increase in fibrosis stages."

*Paul J Mills et al. Clin Gastroenterol Hepatol. 2020 Mar;18(3):741-743.

Recapitulation

- LCHAD is essential for metabolizing long chain fatty acids
- Genetic defects in LCHAD are associated with severe developmental problems and autism-like behaviors
- LCHAD has four sequences containing glycine where the protein binds phosphate (high glyphosate susceptibility)
- Glyphosate has been shown experimentally to disrupt fatty acid metabolism in the mitochondria
- Non-alcoholic fatty liver disease (NAFLD) is an epidemic today and is associated with high levels of glyphosate in the urine
- *Fatty acids are a low-deuterium nutrient, so impaired metabolism leads to excessive mitochondrial deuterium & mitochondrial dysfunction*

Summary

- Deuterium (heavy hydrogen) is a natural element with biophysical and biochemical properties distinctly different from hydrogen
- ***Hypothesis:*** Deuterium management in the body involves sequestering D in gelled water lining the gut and the vascular barrier
  - Deupleted protons are released into the gut lumen and the circulating blood
- Glyphosate suppresses many dehydrogenases and enzymes involved in sulfation, impairing gel formation and derailing deuterium homeostasis
- Colitis and colon cancer are associated with defective sulfomucins
- ***Hypothesis*:** Histamine release may be a mechanism to defuse deuterium “land mines” in the gut
- Peer-reviewed papers show that lipid oxidation in mitochondria is suppressed by glyphosate
  - Lipids are low-deuterium nutrients