

Meet Svetlana

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Complaints

39-year-old female from Belarus presents with three-year history:

- ❖ Burning skin pain
- ❖ Constant metallic taste in her mouth.
- ❖ Major depression
- ❖ Brain fog
- ❖ Poor concentration
- ❖ Cognitive issues
- ❖ Memory loss
- ❖ “Sore Body Syndrome”
 - ❖ Floating pains from head to toe
- ❖ Constant tinnitus
- ❖ Sharp, momentary head pains
- ❖ Muscle fasciculations, especially at night
- ❖ Dry eyes, blurry vision
- ❖ Migratory “pins and needles”
 - ❖ The “running piglet syndrome”
 - ❖ Skin crawling particularly on lower arms and legs
- ❖ “Boring, knife-like” bone pain in left hip
- ❖ Feeling like always has a glove hand/sock on foot Lower extremity skin discoloration

History

Birth: 5/13/1982 in Yelsk, Belarus, USSR (at the time)

Yelsk is in the Periodic Control Zone 180 km (112 miles) Northwest of Chernobyl Blast Site

Emigrated to US in 2002

Hypothyroidism detected at Age 11

Thyroidectomy at age 15

Ulnar Nerve Surgery age 32

Social – cig, rare ETOH, - Drug

Family Hx; GM-Breast Cancer (Predates Chernobyl)

GF-Lung CA (Diagnosed 3 years post Chernobyl)

Mother-CAD, Palpitations

Father-Well

Sister-Hypothyroidism

History

Allergies: Penicillin

Medications: Celexa 40 mg in am

Fluvoxamine CR 100 mg @ bedtime

Venlafaxine 75 mg in am, 75 mg in pm

Mirtazapine 15 mg, 1/d

Doxepin 6 mg 1/d

Gabapentin 300 mg 1 @ bedtime

Levothyroxine 88 mcg 1/d in am on empty stomach

Education: Masters Degree in Business

Employment Prior to Illness: Financial Adviser at Edward Jones

Unemployed at Present. Unable to perform duties for nearly 30 months

History

Symptoms began March 2017.

C/O Breast tenderness, left lower quadrant abdominal pain, heavy irregular menses, and fatty food intolerance with delayed (1-2 hour) postprandial right upper quadrant abdominal pain.

The patient underwent an ultrasound of the abdomen and pelvis. She was found to have a mass on her left ovary which appeared have some bony material in it, a thickened endometrium and gallstones.

Svetlana's diagnosis was dermoid cyst, endometriosis and cholecystitis.

In May 2017 patient had extremely heavy vaginal bleeding. Hemoglobin bleed down to 9.8 (Normal 12-16)

CT Scan was inconclusive. Pt underwent MRI w IV Contrast.

Vaginal thickening of the endometrium. Bizarre appearance of Lt ovarian cysts bone and hair extruding from surface.

Gynecology recommended hysterectomy. Pt refused at first. Next cycle there was a repeat of heavy bleeding, clots and severe left lower quadrant abdominal pain. Pt sought a second opinion.

Pt. traveled to U of San Francisco Medical Center. A repeat MRI w contrast yielded similar results w blood clots noted in vaginal vault. Pt c/o left hip pain on ambulating 24 hours after MRI

History

Pt had a family crisis. Mother had heart attack in June of 2017. Pt. traveled back to “old country” to tend to mother.

Pt was given androgen weighted OC in interim. Pt mother passes away in August of 2017.

Pt returns to US in September of 2017. S/S continue. Pt returns to original OB/GYN

A new MRI w Contrast is ordered to determine changes since original findings. Dermoid cyst is 0.25 cm larger and endometrium now has 14 mm thickening.

Pt underwent hysterectomy and bilateral salpingo-oophorectomy on September 27, 2017. Pt complains of severe fatigue, difficulty concentrating, and burning sensation of lower extremities. She had to sleep with sheets off as she could not tolerate anything touching her skin.

Post op pt began having headaches with “lightning bolt migraines” , visual clouding, SOB, muscle fasciculations, overall weakness. Managed with opioid narcotics, gabapentin.

4 weeks post op: No showed in S/S. Began experiencing hot flashes, night sweats

Previous Diagnosis

I am the Ninth Physician to See Svetlana in the 3 Years Since onset of Symptoms

- (M35.9) Systemic involvement of connective tissue, unspecified
- (R41.3) Other amnesia
- (R41.840) Attention and concentration deficit
- (H54.7) Unspecified visual loss
- (R61) Generalized hyperhidrosis
- (G89.29) Other chronic pain
- (K59.00) Constipation, unspecified
- (T81.9XXS) Unspecified complication of procedure, sequela
- (E78.5) Hyperlipidemia, unspecified
- (G43.909) Migraine, unspecified, not intractable, without status migrainosus
- (G47.00) Insomnia, unspecified
- (E61.1) Iron deficiency
- (R06.02) Shortness of breath
- (I95.9) Hypotension, unspecified
- (J30.2) Other seasonal allergic rhinitis
- (F41.9) Anxiety disorder, unspecified
- (D64.9) Anemia, unspecified
- (J45.909) Unspecified asthma, uncomplicated
- (R61) Generalized hyperhidrosis
- (N89.8) Other specified noninflammatory disorders of vagina
- (R68.82) Decreased libido
- (R35.0) Frequency of micturition
- (R63.5) Abnormal weight gain
- (R63.8) Other symptoms and signs concerning food and fluid intake
- (M25.50) Pain in unspecified joint
- (M62.81) Muscle weakness (generalized)
- (R00.2) Palpitations
- (R32) Unspecified urinary incontinence
- (R45.3) Demoralization and apathy
- (R41.89) Other symptoms and signs involving cognitive functions and awareness
- (R41.840) Attention and concentration deficit
- (R47.89) Other speech disturbances
- (D64.9) Anemia, unspecified
- (R00.2) Palpitation

Physical Exam

Telehealth Visit

5' 3 " 146 lbs. Pulse 72 R 18 T 98.2

Patient Revealed:

Scar on right elbow w Ulnar Nerve Surgery

Reddened, calves and shins.

Thicken discolored skin in ankle, knee, and wrist joints.

Difficulty flexing and extending joints

Beck Depression Scale- 47/63 = Severe Depression

GAD-7 Score 13/21 = Moderate Depression

Neurotransmitter Exam

Analyte	Result	Unit per Creatinine	L	WRI	H	Reference Interval
Serotonin	61.3	µg/g				60 – 125
Dopamine	176	µg/g				125 – 250
Norepinephrine	33.5	µg/g				22 – 50
Epinephrine	7.1	µg/g				1.6 – 8.3
Norepinephrine / Epinephrine ratio	4.7					< 13
Glutamate	17	µmol/g				12.0 – 45.0
Gamma-aminobutyrate (GABA)	2.9	µmol/g				2.0 – 5.6
Glycine	854	µmol/g				450 – 2200
Histamine	15	µg/g				14 – 44
Phenethylamine (PEA)	60	nmol/g				32 – 84
Creatinine	27.3	mg/dL				30 – 225

Pertinent Labs

Labs:

25 OH Vit D3 26.4,
Testosterone 28, free 2.2,
Progesterone/Estradiol Ratio 174.12 (goal 100-500)
TSH 3.44, fT3 3.2 TPO 1 (goal < 9), reverse T3 10
IGF-1 233
HCT 37.5, MCV 91
Pregnenolone 76 (goal 90-110)
Sed Rate 2; cRP 0.5

Urinary Neurotransmitters: Excess Epinephrine, Low Serotonin, Histamine

1. **Low Serotonin**
 - i. **Contributes to mood concerns including anxiety, OCD, depression, anger and discontentment.**
 - ii. **associated with poor sleep quality and appetite changes**
 - iii. **Associated with chronic fatigue, rheumatoid arthritis, and over-all lassitude.**
2. **High Epinephrine**
 - i. **Results in anxiety, agitation, irritability, insomnia and hypertension.**
 - ii. **Epinephrine levels may be elevated in patients in association with exercise prior to the urine collection.**
3. **Low Histamine**
 - i. **Affects digestion and appetite control, learning, memory, and mood**
 - ii. **Causes drowsiness.**
 - iii. **Modulates neurotransmitter release from neurons.**

Mold Panel/Lyme Panel Negative

Interventions

1. From Serum Labs Added

- Pregnenolone 30 mg 2x/d
- Zinc citrate 30 mg 2x/d
- Vitamin D3 5000 IU 1 @ bedtime
- GABA 400 mg @ bedtime

2. From Neurotransmitters

Low Serotonin

- 5-HTP 50-500 mg
- Rhodiola 100-300 mg
- L-theanine 200 mg 2x/d
- P5P 20 mg (B Complex 100 mg)
- Molybdenum 250 mg-Epsom Salt Bath 3x/ week x 12 weeks

Elevated Epinephrine

- L-theanine 200 mg, 2x/
- Rhodiola 1000-2000 mg/d
- SAME 400 mg/d

Low Histamine

- Fermented foods and dairy products, such as yogurt and sauerkraut
- Dried fruits, avocados, eggplant, spinach, shellfish
- L-Histidine 500 mg 1/d.

Metabolomics Test

Functional Imbalance Scores

Key

0-4 : Minimal Need for Support

5-7 : Moderate Need for Support

8-10 : High Need for Support

Need for Antioxidant Support	Need for Mitochondrial Support	Need for Reduced Exposure	Need for Methylation Support
Oxidative Stress	Mitochondrial Dysfunction	Toxic Exposure	Methylation Imbalance
5	4	1	0
<ul style="list-style-type: none"> Cystine ● Cysteine ● Lipid Peroxides ▲ 8-OHdG ● Taurine ● Citric Acid ● cis-Aconitic Acid ▼ 	<ul style="list-style-type: none"> FIGLU ● Methylmalonic Acid ● Glutaric Acid ▲ Lactic Acid ● Pyruvic Acid ▼ Citric Acid ● cis-Aconitic Acid ▼ Isocitric Acid ● α-Ketoglutaric Acid ● Succinic Acid ● Malic Acid ● Adipic Acid ● Suberic Acid ▲ 	<ul style="list-style-type: none"> Lead ● Mercury ● α-Hydroxyisobutyric Acid ▲ α-Ketophenylacetic Acid ▲ Arsenic ● Cadmium ● Pyroglutamic Acid ● Orotic Acid ▼ Citric Acid ● cis-Aconitic Acid ▼ Isocitric Acid ● Glutaric Acid ▲ 	<ul style="list-style-type: none"> Methylmalonic Acid ● Methionine ● FIGLU ● Sarcosine ● Vanilmandelic Acid ● Arginine ● Glycine ● Serine ● Creatinine ●

Nutrient Need Overview

	Nutrient Need											DRI	Suggested Recommendations	Provider Recommendations
	0	1	2	3	4	5	6	7	8	9	10			
Antioxidants														
Vitamin A												2,333 IU	3,000 IU	
Vitamin C												75 mg	250 mg	
Vitamin E / Tocopherols												22 IU	100 IU	
α-Lipoic Acid													50 mg	
CoQ10													30 mg	
Glutathione														
Plant-based Antioxidants														
B-Vitamins														
Thiamin - B1												1.1 mg	25 mg	
Riboflavin - B2												1.1 mg	50 mg	
Niacin - B3												14 mg	20 mg	
Pyridoxine - B6												1.3 mg	10 mg	
Biotin - B7												30 mcg	100 mcg	
Folate - B9												400 mcg	400 mcg	
Cobalamin - B12												2.4 mcg	100 mcg	
Minerals														
Magnesium												320 mg	500 mg	
Manganese												1.8 mg	6.0 mg	
Molybdenum												45 mcg	75 mcg	
Zinc												8 mg	10 mg	
GI Support														
Digestive Support/Enzymes													0 IU	
Microbiome Support/Probiotics													25 billion CFU	
Amino Acids (mg/day)														
Arginine	0	Methionine	0	<small>Recommendations for age and gender-specific supplementation are set by comparing levels of nutrient functional need to optimal levels as described in the peer-reviewed literature. They are provided as guidance for short-term support of nutritional deficiencies only.</small> <small>The Nutrient Need Overview is provided at the request of the ordering practitioner. Any application of it as a therapeutic intervention is to be determined by the ordering practitioner.</small>										
Asparagine	0	Phenylalanine	0											
Cysteine	0	Serine	0											
Glutamine	259	Taurine	0											
Glycine	1,277	Threonine	0											
Histidine	0	Tryptophan	0											
Isoleucine	0	Tyrosine	0											
Leucine	0	Valine	0											
Lysine	0													

Heavy Metal Test

Toxic Elements		Reference Range
Element	Results in ug/g creatinine	
Lead	0.6	<= 1.4
Mercury	1.01	<= 2.19
Aluminum	15.9	<= 22.3
Antimony	<dl	<= 0.149
Arsenic	23	<= 50
Barium	0.4	<= 6.7
Bismuth	<dl	<= 2.28
Cadmium	0.30	<= 0.64
Cesium	6.8	<= 10.5
Gadolinium	0.114	<= 0.019
Gallium	0.014	<= 0.028
Nickel	1.35	<= 3.88
Niobium	<dl	<= 0.084
Platinum	0.015	<= 0.033
Rubidium	1,377	<= 2,263
Thallium	0.472	<= 0.298
Thorium	<dl	<= 4.189
Tin	1.46	<= 2.04
Tungsten	0.038	<= 0.211
Uranium	<dl	<= 0.026



Heavy Metal Toxicity Symptoms

• *General Symptoms*

- Chronic soft tissue pain
- Chronic fatigue
- Brain fog, mood swings, depression, and/or anxiety
- Chronic “exotic” infections; Fungal, Viral, Parasites
- GI complaints; diarrhea, constipation, bloating, GERD
- Food sensitivities
- Vertigo
- Migraines and/or headaches
- Visual disturbances
- Nervous system “dysfunction.”
 - burning extremities, numbness, tingling, paralysis, and/or an electrifying feeling throughout the body.

Svetlana’s Symptoms

- ❖ “Sore Body Syndrome”
 - ❖ Floating pains from head to toe
- ❖ Brain fog, poor concentration , memory loss, depression
- ❖ Constant tinnitus
- ❖ Sharp, momentary head pains
- ❖ Muscle fasciculations, especially at night
- ❖ Dry eyes, blurry vision
- ❖ Migratory “pins and needles”
- ❖ The “running piglet syndrome”
- ❖ Skin crawling particularly on lower arms and legs
- ❖ “Boring, knife-like” bone pain in left hip
- ❖ Feeling like always has a glove hand/sock on foot Lower extremity skin discoloration
- ❖ Burning skin pain
- ❖ Constant metallic taste in her mouth.

What is Gadolinium ?

1. A silvery white metal, atomic number 64, f block on the periodic table, used as contrast material to distinguish (normal and) abnormal structures on MRI scans.
1. In of itself, gadolinium is toxic. It is attached to a chelating agent. The chelating agent (allegedly) renders the toxic gadolinium harmless.
1. Renally impaired patients who undergo IV contrast MRI's and also were recently exposed to a pro-inflammatory state, i.e. surgery, sepsis, or vascular injury (DVT for example) are susceptible to a scleromyxedema-like cutaneous disease.
1. Gad I s contraindicated in patients with GFR < less than 30 mL per minute per 1.73 m².
1. Immediate hemodialysis or initiating hemodialysis for the sole purpose of removing gadolinium-based contrast agents does not protect against nephrogenic systemic fibrosis.

1. Cowper SE, Robin HS, Steinberg SM, Su LD, Gupta S, LeBoit PE. Scleromyxedema-like cutaneous diseases in renal-dialysis patients. *Lancet*. 2000;356(9234):1000–1001.

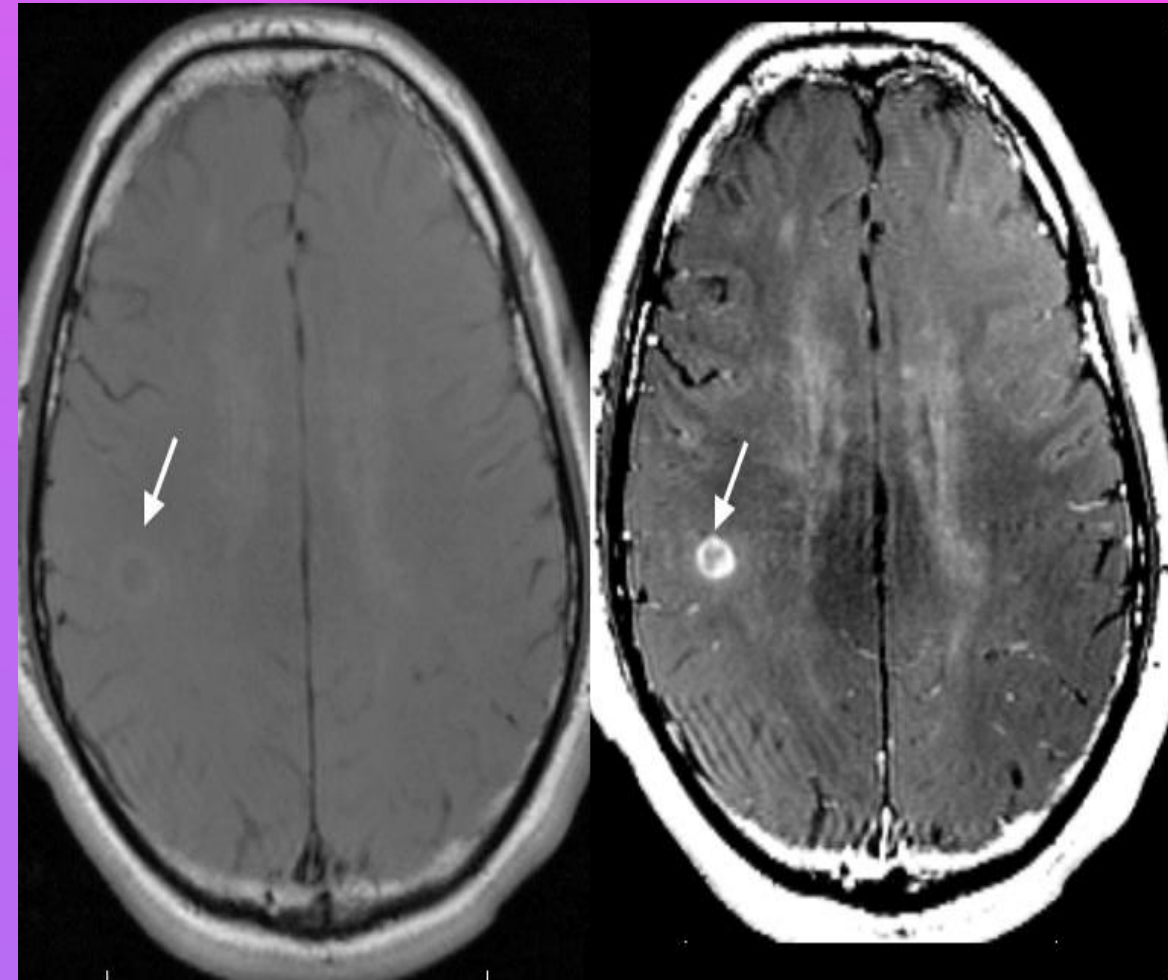
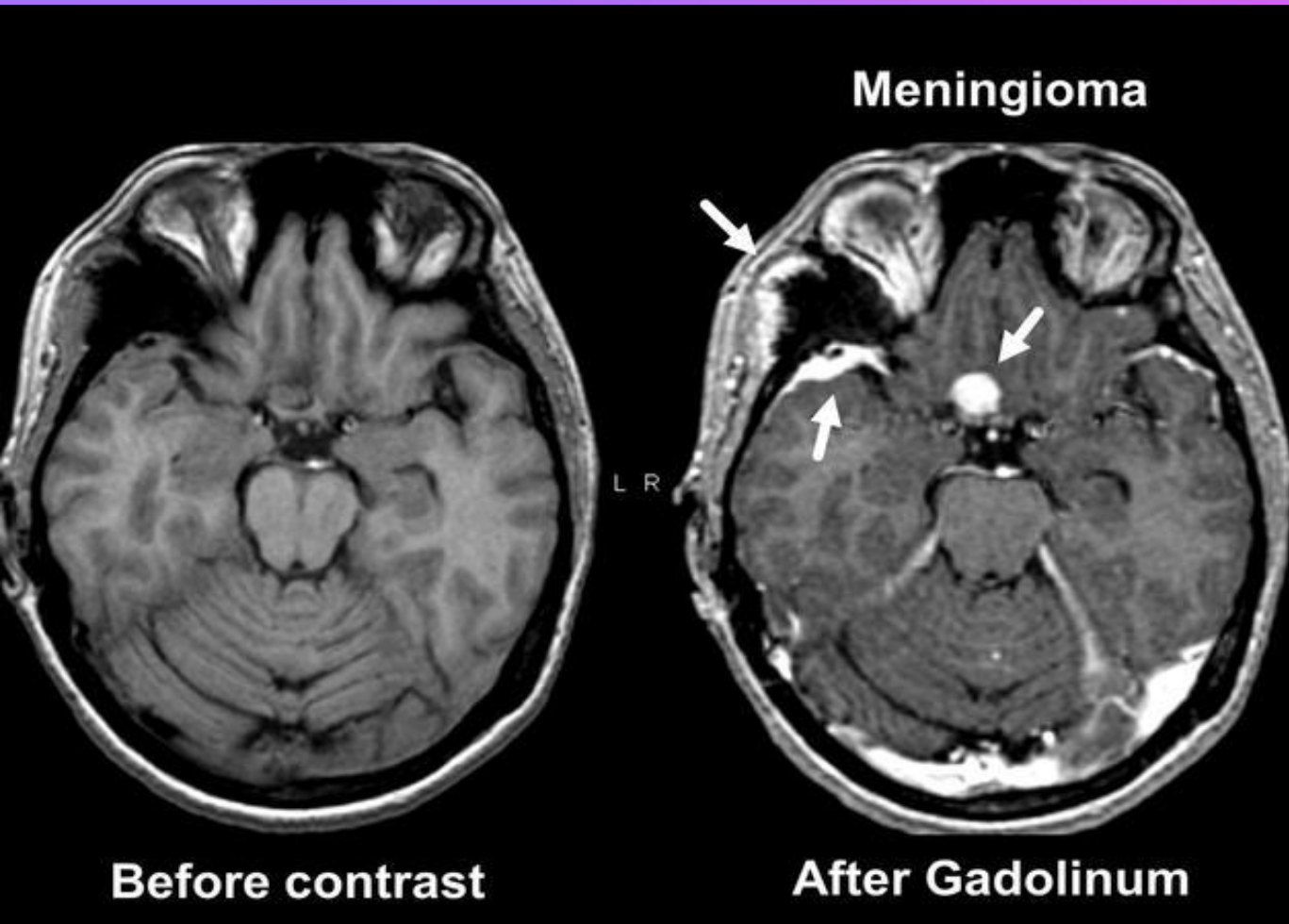
2. Ting WW, Stone MS, Madison KC, Kurtz K. Nephrogenic fibrosing dermopathy with systemic involvement. *Arch Dermatol*. 2003;139(7):903–906.

What is Gadolinium ?

6. >300 million enhanced MRI Scans performed between 1986 through 2016
7. 8.8 million Gad enhanced procedures in US in 2016
8. Gad-enhanced scans detect inflammation increased blood flow.
9. Indications for Enhanced Scans
 - Brain injuries
 - Spinal cord injuries
 - Inflammation of solid organs such as the kidney and liver
 - Inflammation or cancerous cells in bone, muscle and connective tissue
 - Inflammatory bowel disease
 - Inflammatory joint disease
 - Some types of angiograms (imaging of the blood vessels in the heart)
 - Blood vessel problems

Levine D, McDonald RJ, Kressel HY. Gadolinium Retention After Contrast-Enhanced MRI. *JAMA*. 2018;320(18):1853–1854. doi:10.1001/jama.2018.13362

The Case FOR IV Contrast



What is Gadolinium ?

9. Types of Gad Contrast

Linear-Open Chain Surrounds Gadolinium

Brands-Eovist, Magnevist, Multihance, Omniscan, Optimark(discontinued)

2.5 x GAD deposited in cells vs. Macrocyclic Agents

Macrocyclic—

Brands-Dotarem, Gadavist, ProHance

10. Package Insert Side Effects-(Rate listed 0.07 % to 2.4 %)

- Headache
- Nausea
- Dizziness
- Injection site reactions such as pain, irritation, burning, or a cold sensation
- Altered taste (dysgeusia)
- Feeling warm

<https://www.drugwatch.com/gadolinium/>

Nephrogenic Systemic Fibrosis

1. Predisposing factors: Linear, nonionic, less stable GBCAs, stage V chronic renal failure.
2. Disappeared largely in 2007 w removal of Magnevist (ionic linear agent) from renal patients
3. Mean onset from time of exposure to symptoms 11.5 days



1. Skin Lesions present as “Peau d’orange, pruritic, erythematous plaques with associated induration and edema
2. Lesions are usually bilateral on extremities, and trunk. Joint contractures are common. Rare on face.
3. CD34+ fibrocytes are stimulated and released in the setting of chronic inflammatory diseases
4. Respiratory failure with internal organ involvement
5. Mortality rate 31%

Gadolinium Deposition Disorder (GDD)

- Reports of symptoms similar to Nephrogenic Systemic Fibrosis emerged in the late 2000's
- Following IV contrast, Gad leaves behind residue w preferentially in:
 - Bone, Kidney, Brain
 - Residue left even with an intact blood-brain barrier, preserved renal function, and normal hepatic clearance

□ Symptoms of GDD

“A” Symptoms

Brain fog
Head pain
Eye symptoms: Dry eye, blurred vision
Muscle fasciculations
“Pins and Needles” Skin crawling, esp. lower arms and legs
 (“Running Piglet Syndrome” or stocking and glove feeling of limbs)
“Boring” Bone pain, Joint pain.
BURNING SKIN PAIN – *Muy Importante*
Skin discoloration, thickening, doughiness
A metallic sensation in taste, smell, and overall body odor

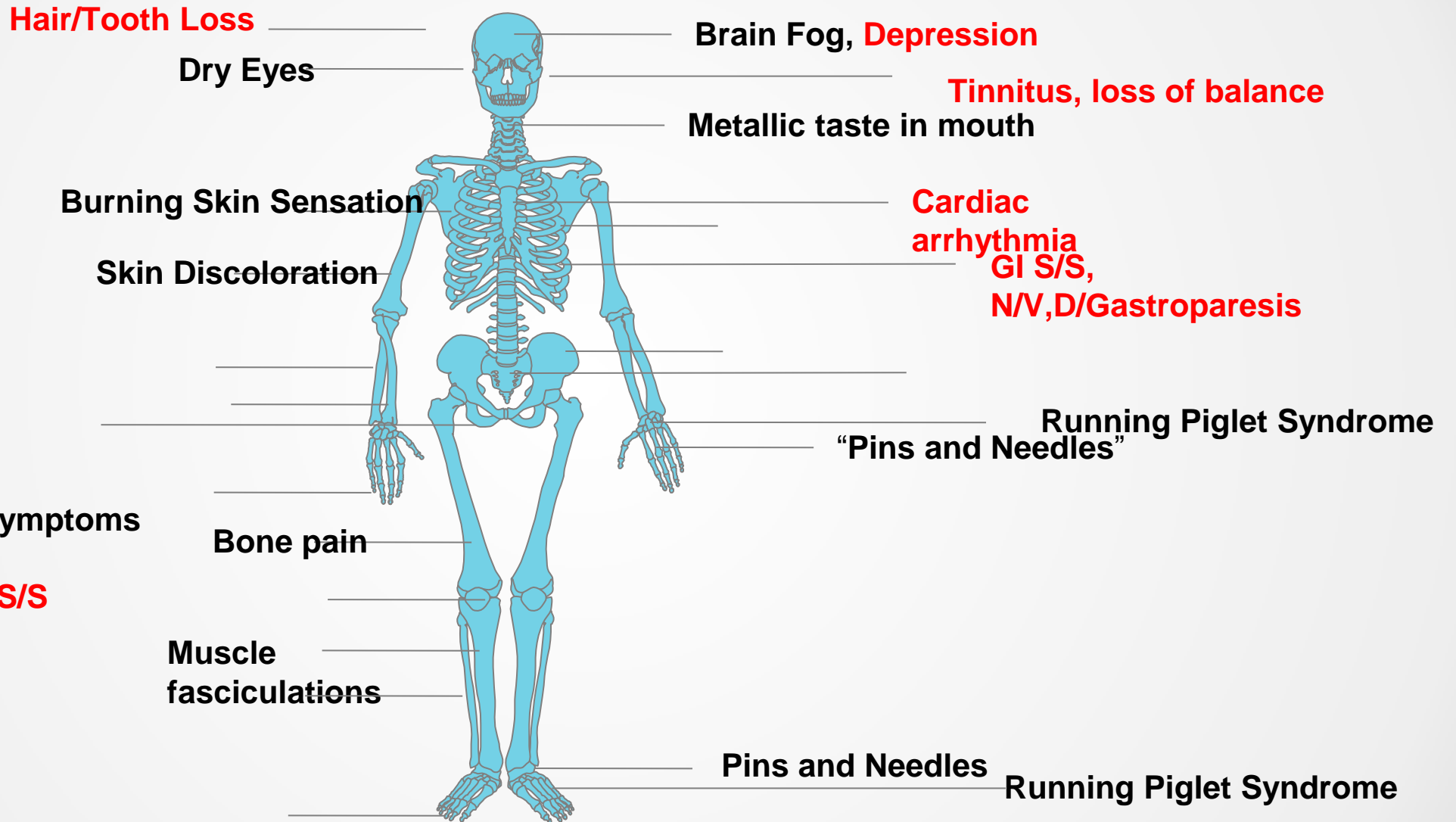
“B” Symptoms

Cardiac arrhythmia
GI Symptoms-Nausea/vomiting/gastric stasis or diarrhea
Tinnitus
Loss of balance
Depression
Hair loss/teeth loss

1. Thomsen H.S. Nephrogenic systemic fibrosis: history and epidemiology. *Radiol Clin North Am.* 2009; 47: 827-831

2. Richard C. Semelka, et., al., Gadolinium deposition disease: Initial description of a disease that has been around for a while, *Magnetic Resonance Imaging*, Volume 34, Issue 10, 2016, Pages 1383-1390, ISSN 0730-725X, <https://doi.org/10.1016/j.mri.2016.07.016>. (<https://www.sciencedirect.com/science/article/pii/S0730725X16301035>)

Gadolinium Deposition Disease S/S



Gadolinium Deposition Disorder (GDD) vs. Svetlana

Symptoms of GDD

- BURNING SKIN PAIN** –*Muy Importante*
- Brain fog
- A metallic sensation in taste, smell, and overall body odor
- Depression
- Head pain
- Eye symptoms: Dry eye, blurred vision
- Muscle fasciculations
- “Pins and Needles” Skin crawling, esp. lower arms and legs (“Running Piglet Syndrome” or stocking and glove feeling of limbs)
- “Boring” Bone pain, Joint pain.
- Skin discoloration, thickening, doughiness
- Cardiac arrhythmia
- GI Symptoms-Nausea/vomiting/gastric stasis or diarrhea
- Tinnitus
- Loss of balance
- Hair loss/teeth loss

Svetlana

- ❖ Burning skin pain
- ❖ Brain fog
- ❖ Constant metallic taste in her mouth.
- ❖ Major depression
- ❖ Sharp, momentary head pains
- ❖ Poor concentration
- ❖ Cognitive issues
- ❖ Migratory “pins and needles”
- ❖ The “Running Piglet Syndrome”
- ❖ Skin crawling particularly on lower arms and legs
- ❖ Memory loss
- ❖ “Sore Body Syndrome”
 - ❖ Floating pains from head to toe
- ❖ Constant tinnitus
- ❖ Muscle fasciculations, especially at night
- ❖ Dry eyes, blurry vision
- ❖ “Boring, knife-like” bone pain in left hip
- ❖ Feeling like always has a glove hand/sock on foot Lower extremity skin discoloration

Gadolinium Deposition Disorder

Are the Symptoms “Mass Hysteria” or Can they be Predicted”

Remember Finasteride!

GBCAs are strongly associated with high signal intensity on unenhanced T1 weighted images in:

Dentate Nucleus (DN)

Location: Within the deep white matter of each cerebellum

Function: Planning, initiation, planning, and control of voluntary motion

Dorsal region: Skeletal muscle function

Ventral Region: Nonmotor function-conscious thought, visuospatial
Language, Cognition

Special Structure: House Purkinje cells; GABAergic neurons; inhibiting neurotransmitter

Associate Maladies: Cerebellar ataxia, Maple Syrup Dx., Alzheimer’s Dx
Autism, Essential tremor

Globus Pallidus (GP)

Location: Structure in the Basal ganglia

Function: Regulates voluntary movement; Inhibitory-balances cerebellum (excitatory movement)
“Fine tunes” movement, cognition, emotion

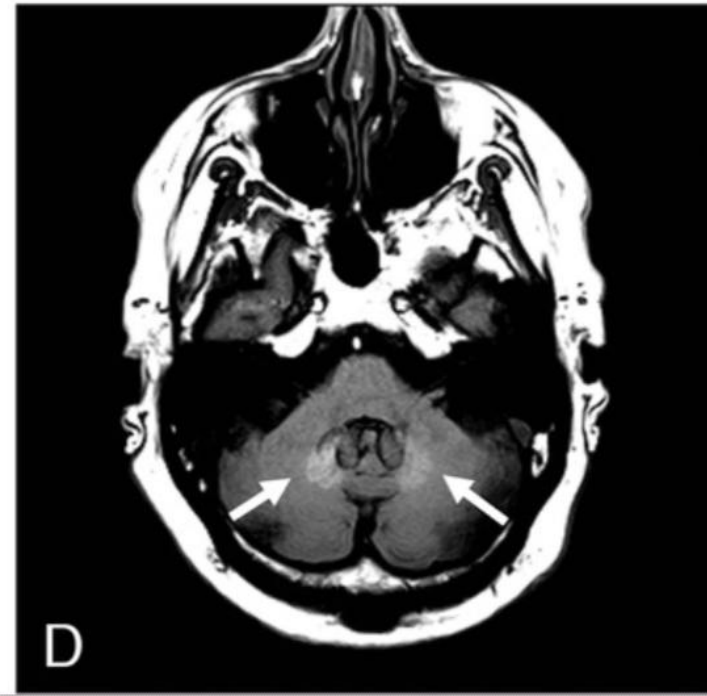
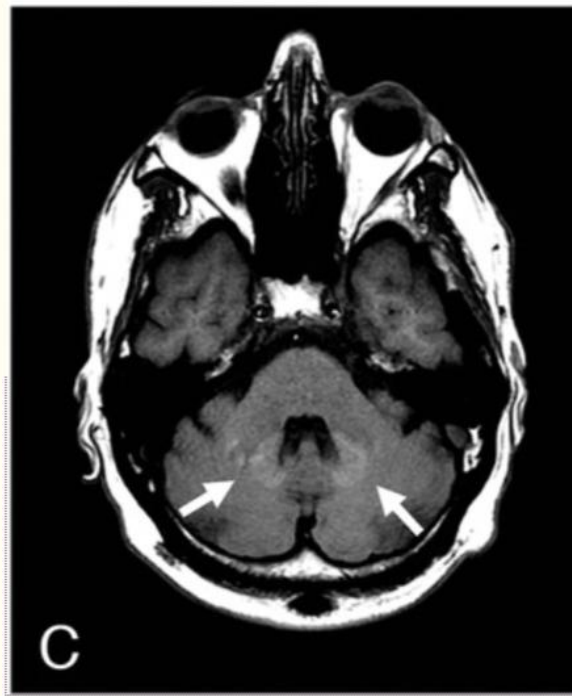
Neurotransmitter: GABA

Associated Maladies: Motor dysfunction of dystonia; Parkinson’s Dx.

Sultan, F., Hamodeh, S., & Baizer, J. S. (2010). THE HUMAN DENTATE NUCLEUS: A COMPLEX SHAPE UNTANGLED. [Article]. Neuroscience, 167(4), 965–968.

Koeppen AH. The neuropathology of the adult cerebellum. Handb Clin Neurol. 2018;154:129-149

GADOLINIUM DEPOSITION IN DENTE NUCLEUS



Dec. 2011

June 2013

Sept. 2016

June 2018

Smith, Tyler E et al. "Gadolinium Deposition in Neurology Clinical Practice." *The Ochsner journal* vol. 19,1 (2019): 17-25. doi:10.31486/toj.18.0111

Gadolinium Deposition Disorder

□ Disorders of Metabolism Associated with Gadolinium

- Calcium channel blockade
- Inhibition of mitochondrial function
- Inhibition of Ca²⁺-activated enzymes
- Induction of oxidative stress.

□ Inflammatory Markers of GDD Toxicity

⊛ Pro-inflammatory cytokines

- Interleukin-6 (IL-6) , Interleukin-2
- Interferon- γ (IFN- γ)
- TNF- α , TGF- β

⊛ Pro-fibrotic cytokines

- IL-4
- Transforming growth factor- β (TGF- β)
- Cytokine IL-13 (both fibrogenic and with mixed pro-and anti-inflammatory actions)
- Growth factor vascular endothelial growth factor (VEGF)

⊛ Other Cytokines

- IL-8, IL-18, IL-23, IL-31, TGF- α , growth related oncogene alpha (GRO- α), and leukemia inhibitory factor (LIF)

Thomsen H.S. Nephrogenic systemic fibrosis: history and epidemiology. *Radiol Clin North Am.* 2009; 47: 827-831

Maecker, Holden T et al. "An initial investigation of serum cytokine levels in patients with gadolinium retention." *Radiologia brasileira* vol. 53,5 (2020): 306-313. doi:10.1590/0100-3984.2019.0075

Cytokine Changes in Dr. C's Study Areas

Autism

- IGFBP-1.
- Interleukin-6 (IL-6)
- TNF- α
- Interferon- γ (IFN- γ)

• TBI

- IL-1 β
- IL-6
- CCL2

Gadolinium Deposition Disease

- Interleukin-6 (IL-6) , Interleukin-2
- Interferon- γ (IFN- γ)
- TNF- α , GF- α ,TGF- β
- IL-8, IL-18, IL-23, IL-31

Post Finasteride Syndrome

- IL-1 β ,
- IL-6
- TNF- α

References for Cytokines

□ Autism

- Xu, Ningan & Li, Xiaohong & Zhong, Yan. (2015). Inflammatory Cytokines: Potential Biomarkers of Immunologic Dysfunction in Autism Spectrum Disorders. *Mediators of inflammation*. 2015. 531518. [10.1155/2015/531518](https://doi.org/10.1155/2015/531518).
- [Kolevzon A, Bush L, Wang AT, Halpern D, Frank Y, Grodberg D, Rapaport R, Tavassoli T, Chaplin W, Soorya L, Buxbaum JD. A pilot-controlled trial of insulin-like growth factor-1 in children with Phelan-McDermid syndrome. *Mol Autism*. 2014 Dec 12;5\(1\):54. doi: 10.1186/2040-2392-5-54. eCollection 2014. Erratum in: *Mol Autism*. 2015; 6:31.](https://doi.org/10.1186/2040-2392-5-54)
- Wei, Hongen, et al. "IL-6 is increased in the cerebellum of autistic brain and alters neural cell adhesion, migration, and synaptic formation." *Journal of neuroinflammation* vol. 8 52. 19 May. 2011, doi:10.1186/1742-2094-8-52

□ Gadolinium Deposition Disorder

- Maecker, Holden T et al. "An initial investigation of serum cytokine levels in patients with gadolinium retention." *Radiologia brasileira* vol. 53,5 (2020): 306-313. doi:10.1590/0100-3984.2019.0075
- Pałasz A, Czekaj Toxicological and cytophysiological aspects of lanthanides action. *Acta Biochim Pol* 2000;47:1107–14 pmid:11996100

□ TBI

- Sun, Yingxiang et al. "Elevated Serum Levels of Inflammation-Related Cytokines in Mild Traumatic Brain Injury Are Associated With Cognitive Performance." *Frontiers in neurology* vol. 10 1120. 23 Oct. 2019, doi:10.3389/fneur.2019.01120

□ Post Finasteride Syndrome

- Hamadi, N., Sheikh, A., Madjid, N. *et al.* Increased pro-inflammatory cytokines, glial activation and oxidative stress in the hippocampus after short-term bilateral adrenalectomy. *BMC Neurosci* 17, 61 (2016). <https://doi.org/10.1186/s12868-016-0296-1>
- Silvia Diviccaro, Silvia Giatti, Francesca Borgo, Matteo Barcella, Elisa Borghi, José Luis Trejo, Luis Miguel Garcia-Segura, Roberto Cosimo Melcangi, Treatment of male rats with finasteride, an inhibitor of 5alpha-reductase enzyme, induces long-lasting effects on depressive-like behavior, hippocampal neurogenesis, neuroinflammation and gut microbiota composition, *Psychoneuroendocrinology*, Volume 99, 2019, Pages 206-215,ISSN 0306-4530, <https://doi.org/10.1016/j.psyneuen.2018.09.021>.

The "Big Boys" Don't Like Us Messing with Their Turf

Stanford Test

Genova Test

MAYO MEDICAL LABORATORIES
MISCELLANEOUS ORDER

TEST NAME:

GADOLINIUM

24 HOUR

URINE

RESULT:

Gadolinium, 24 Hr, U <0.1 mcg/24 h <1.1

Collection Duration 24 h

... [Show More](#)

Toxic Elements		Reference Range
Element	Results in ug/g creatinine	
Lead	0.6	<= 1.4
Mercury	1.01	<= 2.19
Aluminum	15.9	<= 22.3
Antimony	<dl	<= 0.149
Arsenic	23	<= 50
Barium	0.4	<= 6.7
Bismuth	<dl	<= 2.28
Cadmium	0.30	<= 0.64
Cesium	6.8	<= 10.5
Gadolinium	0.114	<= 0.019
Gallium	0.014	<= 0.028
Nickel	1.35	<= 3.88
Niobium	<dl	<= 0.084
Platinum	0.015	<= 0.033
Rubidium	1,377	<= 2,263
Thallium	0.472	<= 0.298
Thorium	<dl	<= 4.189
Tin	1.46	<= 2.04
Tungsten	0.038	<= 0.211
Uranium	<dl	<= 0.026

The "Big Boys" Don't Like Us Messing with Their Turf

Doctors Data Test

Genova Test

ROL: 40 DOD: 03/10/2001

Toxic Metals; urine 24 hour

TOXIC METALS			TOXIC METALS				
	RESULT µg/g Creat	REFERENCE INTERVAL	RESULT µg/24hr	REFERENCE INTERVAL	WITHIN REFERENCE	OUTSIDE REFERENCE	
Gadolinium (Gd)	0.09	<0.8	0.11	<0.6			

URINE CREATININE							
	RESULT mg/24hr	REFERENCE INTERVAL	-2SD	-1SD	MEAN	+1SD	+2SD
Creatinine	1170	600-2100					

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Lead	0.6	<= 1.4
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Opinion

Stanford Test Doctor's Data

MAYO MEDICAL LABORATORIES
MISCELLANEOUS ORDER

TEST NAME: **GADOLINIUM
24 HOUR
URINE**

RESULT:

Gadolinium, 24 Hr, U <0.1 mcg/24 h <1.1
Collection Duration 24 h
... [Show More](#)

AGE: 40 DOB: 06/10/1961

Toxic Metals; urine 24 hour

TOXIC METALS			TOXIC METALS			
	RESULT µg/g Creat	REFERENCE INTERVAL	RESULT µg/24hr	REFERENCE INTERVAL	WITHIN REFERENCE	OUTSIDE REFERENCE
Gadolinium	(Gd) 0.09	<0.8	0.11	<0.6		

URINE CREATININE							
	RESULT mg/24hr	REFERENCE INTERVAL	-2SD	-1SD	MEAN	+1SD	+2SD
Creatinine	1170	600-2100					

The reference range for Mayo is <1.1 and the lower limit is 0.1 mcg/24h at GDX our reference range is .019. As you can see, our detection is less than Mayo clinic. Our ranges ionnaire healthy-qualified cohort.

Remedy Protocol

1. AIP Diet

a. Allowed

- **All fruits - limit 10-20g fructose/day or 2-3 pieces of fruit.**
- **Coconut products - coconut oil, manna, creamed coconut, coconut aminos, coconut milk (with no additives), unsweetened shredded coconut.**
- **Oils/fats - olive oil, coconut oil, avocados, lard, avocado oil, bacon fat, cultured ghee (free of casein and lactose), and palm oil.**
- **Fermented foods - coconut yogurt, kombucha, water and coconut kefir, fermented vegetables (such as sauerkraut and kimchi). Fermented foods contain probiotics that help gut health.**
- **Bone broth**
- **Meats - grass fed meats (beef and bison) and wild caught fish are recommended. Aim for having fish 3 times/week.**
- **Teas - non-seed herbal teas, green tea.**
- **Vinegars - apple cider, coconut, red wine, balsamic (make sure vinegars have no added sugar).**
- **Sweeteners - you may use honey and maple syrup sparingly (1 tsp/day)**
- **Fresh herbs - all fresh and non-seed herbs are allowed (basil, thyme, mint, oregano, rosemary, ginger, turmeric, cinnamon, savory, edible flowers)**
- **Binders - grass fed gelatin and arrowroot starch are permitted, if needed. Be careful with the starch if you have adrenal issues.**
- **Vegetables - all except nightshades or legumes *more details on nightshades and legumes under "Foods Not Allowed**

Remedy Protocol

1. AIP Diet

b. Not Allowed

- Nuts and seeds - including nut/seeds oils like sesame seed oil, flax, chia, pumpkin, cocoa and coffee
- Beans/legumes - no beans of any kind (including soy) or legumes except snap peas or string green beans.
- Nightshades - eggplant, tomatoes, onion, potatoes (only sweet potatoes allowed), goji berries, sweet and hot peppers
- Grains - corn, wheat, buckwheat, rye, oats, tapioca, etc.
- Sweeteners - sugar, xylitol, stevia, mannitol, aspartame, Sucralose
- Dried fruits
- Dairy products
- Processed foods
- Alcohol
- Chocolate
- Eggs (especially egg whites)
- Gums/additives - guar gum, carrageenan, Tara gum, Gellan gum, Gum Arabic, benzoic acid, MSG, sulfates/sulfites, nitrates/nitrites
- Oils/fats - vegetable oils, butter, ghee, canola oil and other seed oils, palm-kernel oil.
- Herbs/spices from seeds or nightshades - mustard seed, cumin, coriander, fennel, cardamom, fenugreek, caraway, nutmeg, dill seed, cayenne, paprika and chili peppers
- NSAIDS - aspirin or ibuprofen

No gluten, no grains, no legumes, no dairy, no sugar, and no alcohol

Stage 2 Remedies

IV Chelation (+ Control “Immune Host Response”)

1. IV Chelation

1. **DTPA (300,000 x more stable with Gad than EDTA)**
 1. **Stability of chelating agent is key to removal without redistributing Gad in body**
 1. **DTPA holds much more Gas than EDTA**
 2. **Redistribution in body rate: DTPA 1 %; EDTA 30 %**
 2. **All chelating agents remove and cause re-equilibration. Weak chelators also redistribute.**
 1. **FLARE(i.e.) Immune Host Response From removal of Gad-within hours to 1 week post Rx**
 - From Re-equilibration (weeks 4 to 12)
 - From Redistribution (Weak chelators EDTA, DMSA)-within hours, lasts 1 week
 1. **No FLARE = Misdiagnosis-There is no Gad**
1. **Predicted Reaction**
 1. **Due to amount removed**
 2. **No chelation for at least 90 days post Gad injection**
2. **Chelation Schedule**
 1. **One GBCA injection, treatment 3 months to 1 year after initiation of GDD, 5 Rs. 80 % improve**
 2. **Individuals with more complex circumstances, 15 Ca/Zn-DTPA Rx. 80% + better at Rx. # 15.**
 3. **Extreme illness: 20+ GBCAs Unknown number: probably 20+ Rx., Improvement in range 60%-70%.**
3. **Chelation Doses**
 1. **Day 1**
 1. **Ca-DTPA (0.5 gm) IV push over 1 minute at the beginning of infusion, along w NSS over 90 minutes ending with a second -CA-DTPA (0.5 gm) with 10 minutes of saline left**
 2. **Day 2 (24 hour interval)**
 1. **Zn-DTPA, 0.5 gm push over 1 minute with normal saline (over a 90 minute period), ending with another 0.5 gm DTPA dose with 10 minutes left of saline infusion.**
1. **A total of 1 gm of DTPA is administered at each treatment.**
2. **This sequence will be administered 5-15 times, approximately 1 month apart.**

Stage 2 Remedies

IV Chelation (+ Control “Immune Host Response”)

1. FLARE Reaction

- i. Hypersensitivity reaction to GAd manipulation
- ii. Stimulation of the immune system in response to increased mobilization of recreated GBCA
- iii. Begins day 2- dissipates by day 5
- iv. Exacerbation in the 24 hours after Ca-DTPA CT of preexistent GDD symptoms or onset of new but related to preexistent symptoms

1. FRAME Drug Response

- i. Medical
- ii. Radiology Hypersensitivity Protocol
 1. Prednisone: 50 mg by mouth at 13 hours, 7 hours, and 1 hour before contrast media injection; and
 2. Diphenhydramine (Benadryl®): 50 mg by mouth 1 hour before contrast medium

i. Steroid Dose Pack

<https://rafimaging.com/physicians/pre-medication-protocol/>

Stage 2 Remedies

IV Chelation (+ Control “Immune Host Response”)

1. FRAME Functional Medicine Response

a. Cytokine Targets

1. Interleukin-6 (IL-6) , Interleukin-2
2. Interferon- γ (IFN- γ)
3. TNF- α , GF- α ,TGF- β
4. IL-8, IL-18, IL-23, IL-31

a. Remedies

1. Low Dose Naltrexone

- a. (IL)-1 β , IL-1Ra, IL-2, IL-4, IL-5, IL-6, IL-10, IL-12p40, IL-12p70, IL-15, IL-17A, IL-27, interferon (IFN)- α , transforming growth factor (TGF)- α , TGF- β , tumor necrosis factor (TNF)- α , and granulocyte-colony stimulating factor (G-CSF).

2. Quercetin

- a. Inhibition of NO, TNF- α , IL-1 β , IL-6, NF- κ B and interferon (IFN)- γ production. Increased IL-10 secretion

3. Rutin

- a. TNF- α

4. Luteolin

- a. IL-1 β , IL-6, IFN- γ and TNF- α

5. Omega 3 FA

- a. TNF- α , IL-1 β , NF- κ B and IL-6

6. Resveratrol

- a. TNF- α , NF- κ B, anti NO activity

Stage 2 Remedies

IV Chelation (+ Control “Immune Host Response”)

1. FRAME Functional Medicine Response

a. Cytokine Targets

1. Interleukin-6 (IL-6) , Interleukin-2
2. Interferon- γ (IFN- γ)
3. TNF- α , GF- α ,TGF- β
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a. Remedies

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- a. (IL)-1 β , IL-1Ra, IL-2, IL-4, IL-5, IL-6, IL-10, IL-12p40, IL-12p70, IL-15, IL-17A, IL-27, interferon (IFN)- α , transforming growth factor (TGF)- α , TGF- β , tumor necrosis factor (TNF)- α , and granulocyte-colony stimulating factor (G-CSF).

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3. Rutin

- a. TNF- α

4. Luteolin

- a. IL-1 β , IL-6, IFN- γ and TNF- α

5. Omega 3 FA

- a. TNF- α , IL-1 β , NF- κ B and IL-6

6. Resveratrol

- a. TNF- α , NF- κ B, anti NO activity

7. Nicotine

- a. IFN γ , TNF α , IL-1 β and IL-2

8. NAC

- a. IL-6, IL-8, NF- κ B

Stage 2 Remedy References

1. Parkitny, Luke, and Jarred Younger. "Reduced Pro-Inflammatory Cytokines after Eight Weeks of Low-Dose Naltrexone for Fibromyalgia." *Biomedicines* vol. 5,2 16. 18 Apr. 2017, doi:10.3390/biomedicines5020016
2. Leyva-López, Nayely et al. "Flavonoids as Cytokine Modulators: A Possible Therapy for Inflammation-Related Diseases." *International journal of molecular sciences* vol. 17,6 921. 9 Jun. 2016, doi:10.3390/ijms17060921
3. Lidan Xiong, Quercetin and Quercitrin Attenuates the Inflammatory Response and Oxidative Stress in LPS-Induced RAW264.7 Cells: In Vitro Assessment and a Theoretical Model, *BioMed Research International*, Volume 2019, 8 pages
4. Mejia et al., 2014; Cure et al., 2020; Rudnicka et al., 2020; National Institutes of Health, 2020b
5. Martínez, G. J., Robertson, S., Barraclough, J., Xia, Q., Mallat, Z., Patel, S., et al. (2015). Colchicine acutely suppresses local cardiac production of inflammatory cytokines in patients with an acute coronary syndrome. *J Am Heart Assoc* 4, e002128. doi:10.1161/JAHA.115.002128

Stage 2 Remedies

IV Chelation (+ Control “Immune Host Response”)

1. FRAME Functional Medicine Response

a. Other Medications

i. IL-2

1. Metformin
2. Cyclosporine
3. Tacrolimus

ii. IL-6

1. Testosterone
2. Verapamil
3. Bumetanide
4. LDN

iii. TNF-alpha

1. Spironolactone
2. LDN
3. Spearmint Tea
4. Infliximab

iv. IL-18

1. Colchicine

Neuroprotek

Contains:

Luteolin, Quercetin, Rutin.

Serving Size: 1 Softgel Capsule

Servings Per Container: 60

Amount Per Serving % Daily Value**

Calories (Unsaturated Fatty
Acids)* 3

Proprietary Blend

containing:

Luteolin	100 mg	†
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Quercetin	70 mg	†
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Rutin	30 mg	†
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** Percent Daily Values are based on a 2000 calorie diet.

† Daily Value not established

* 45% Volume Olive Pomace Oil

Brain Care II

B is for Brain

DHA:

Tocopherol:

Ascorbyl Palmitate:

Quercetin:

N-Acetyl-Cysteine:

EGCG:

B Vitamins

PQQ

CoQ 10

Thank You !

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