



KryptoPyrrolUria (KPU) and HemoPyrrolLactamUria (HPU) revisited

Abram Hoffer MD discovered this condition in 1958. In the urine of his schizophrenic patients he discovered a compound he named "Mauve factor", later falsely identified as kryptopyrrol, and finally correctly identified as Hydroxy-2,3-Dimethylpyrrolidin-5-on and Hydroxy-Hemopyrrolin-2-on (HPL). These complexes are bound to P-5-P and minerals (Zinc and manganese). Also the urinary porphyrins are elevated, especially Coproporphyrinogen I.

To keep things simple, this condition is today most often referred to as HPU.

Other names used in the literature: Malvaria, Pyrroluria, HemoKryptoPyrrolLactamUria, Mauve



The early KPU literature

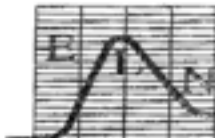
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- **10. Mauve Factor re-identified as 2,4-Dimethyl-3-ethylpyrrole and its Sedative Effect on the CNS Nature 228, 1318 - 1320 (26 December 1970); A.Sohler et al**



Testing

- In the US, several labs test for kryptopyrrole, Vitamin Diagnostics also for HPL
- In Holland, the laboratory of Dr. Kampsteg is the leader in HPU research (www.keac.nl)
- In recent months, many of “my” children with ASD and Lyme disease- and suspected of Mauve on clinical grounds –who previously had tested negative for KPU, tested positive for HPL
- The yield in the US can be greatly improved, if the HPU specimen is collected properly. Unfortunately the US labs do not provide the proper guidelines



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Reportdate 16/01/2009 ¹

Name Dietrich Klinghardt Md
DOB 03/10/1963 Sex Female 11656 98th Ave NE
Patient no 79447 98034 KIRKLAND, WA
Through : VITAMIN DIAGNOSTICS
 : VITAMIN DIAGNOSTICS

Applicant KLINGHART
Date received 31/12/2008
Labno 312835
Date received 31/12/2008
1st printdate 16/01/09


	(1)	Ref. range	Units
<u>Hematologic</u>			
Your reference:	14240		
<u>Urine analysis</u>			
Kryptopyrrol	67.0*	<15	µg/dl

Handwritten:
Faid 1/11/09
PC scheduled 1/21/09 SH

*)outside ref.range ; Performed at ELN

At Vit. Diag. when (#) after testname Final Report Signat.





HPU patients loose supra-physiological amounts of zinc, B6, Biotin and manganese in the urine

- **HPU is caused by the defect of several of the 8 enzymes needed for the synthesis of heme**
- **Heme is needed for liver detox reactions (cytochromes), Cystathionine synthase, Catalase, Heme-hemopexin for MT translation, Guanylate cyclase, Sulfite-reductase, NOS, Pyrrolase.**
- **HPU patients have low serum glutathion levels, high NO levels, low histamine**
- **HPU can be inherited or can be aquired (stress, toxins, infections)**
- **Hoffer: 27/39 early schizophrenics positive**
10/14 criminal / patients with deviant behavior positive
740 patients: all recovered schizophrenics negative, unrecovered 50% positive
- **Down syndrome 70%**
- **Schizophrenia 40-70%**
- **Autism 50%**
- **ADHD 30%**
- **ETOH 20-80%**
- **Lyme disease and co-infections: 80% positive (Klinghardt)**
- **Toxic Patients with mercury and lead retention: 75% (Klinghardt)**
- **I suspect that more then 80% of ASD kids have HPU and should be treated for it**

Symptoms

- **Light / sound / odor intolerance**
- **Hypoglycemia / glucose intolerance/insulin resistance**
- **Pale skin / poor tanning/china doll look**
- **All symptoms of Lyme: buzzing in head, numbness, shaking, short term memory loss, cherry angiomas, stretch marks, insomnia, fatigue**
- **Tremor / shaking / spasms**
- **Environmental and food allergies**
- **Autism/ most symptoms of ASD**
- **Poor breakfast appetite**
- **Cold hands or feet**
- **Eosinophilia**
- **Delayed or early puberty / sensitized hormone receptors**
- **Explosive anger**
- **Anxiety / Withdrawal**
- **Paranoia / Hallucinations**
- **Perceptual disorganization**
- **Stress intolerance**
- **Emotional lability**
- **Nail spots (leukodinia)**
- **Knee and joint pain Pessimism**
- **Depression**
- **Crime and delinquency**
- **Substance abuse**
- **Attention deficit / ADHD**
- **Amenorrhea / irregular periods**
- **B6-responsive anemia**
- **Retention of toxic metals and environmental toxins**
- **Poor dream recall**
- **Acne**
- **Obesity and anorexia**
- **Stretch marks (striae)**
- **Course eyebrows**
- **Abdominal tenderness**
- **Constipation**



Common Lab abnormalities

- High LDL, low HDL
- Low normal alkaline phosphatase (Zn, Mag)
- Low wbc (Zn)
- Low Omega-6 fatty acids in red cell membrane test
- Low taurine in aminoacid profile
- High MCV (B6)
- wbc and rbc Zn, Mn levels may be normal while bone and CNS are severely deficient
- Bone biopsies have been a reliable predictor of HPU (severe Zn, Mn, Ca, Mag and Mo deficiency)
- P-5-P is needed for absorption of **zinc, manganese, magnesium, chromium**
- P-5-P is needed to produce **Niacin** from Tryptophane



Common physical signs in children

- China doll look. 2009: Indigo baby
- Eczema, skin eruptions, fungal infections, herpes virus outbreaks (perioral, index finger)
- Thin fine hair, thin nails, deformed toe nails early after birth which gradually self-correct
- Bloated belly
- Doesn't like to move (knee/hip/ankle pain)
- Frequently gets hurt (Mr.Bump)
- Anal itch/frequent parasites
- Stress intolerant
- Difficulty sleeping



Leukodynia

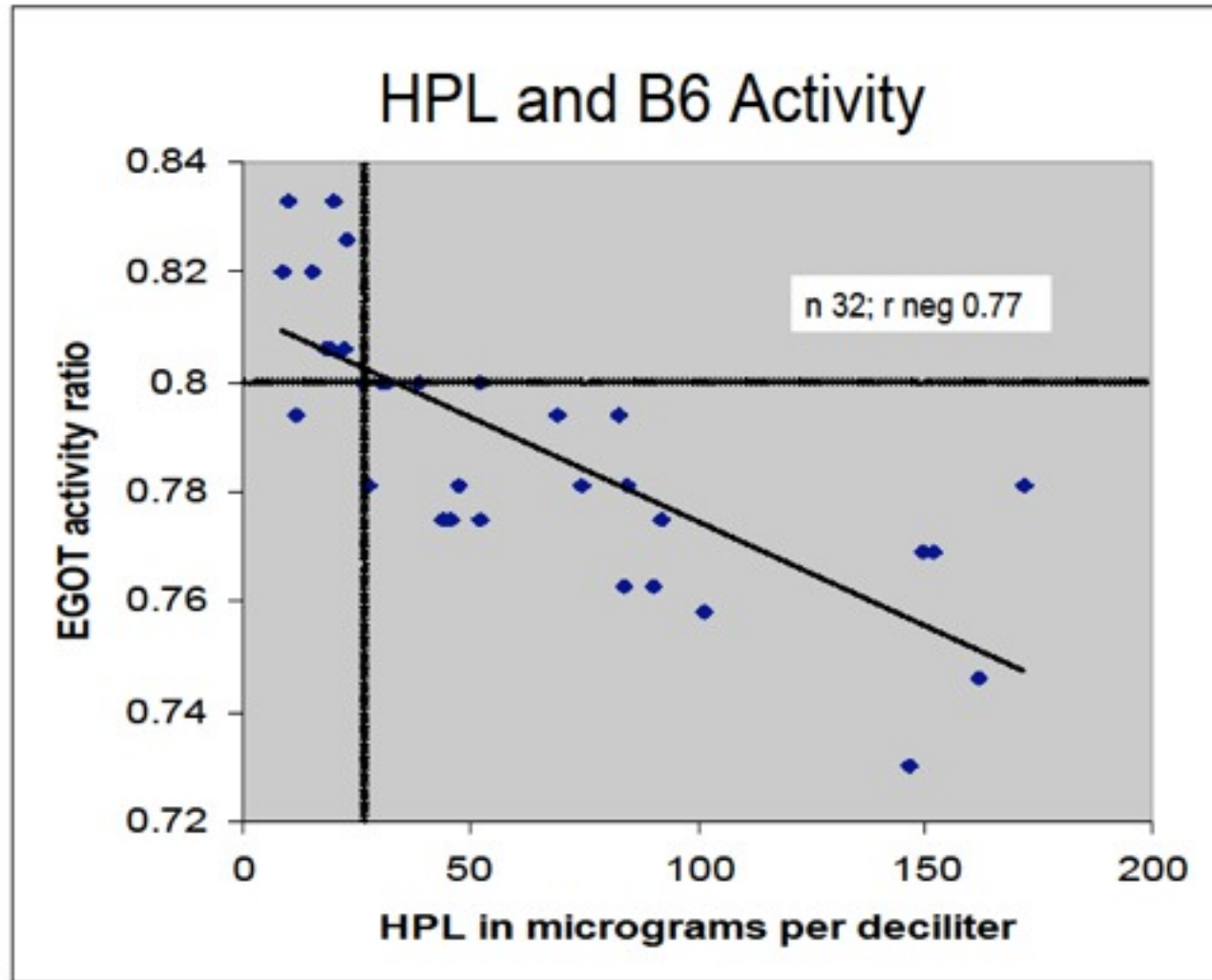
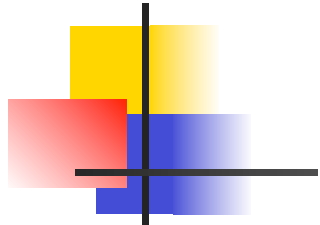


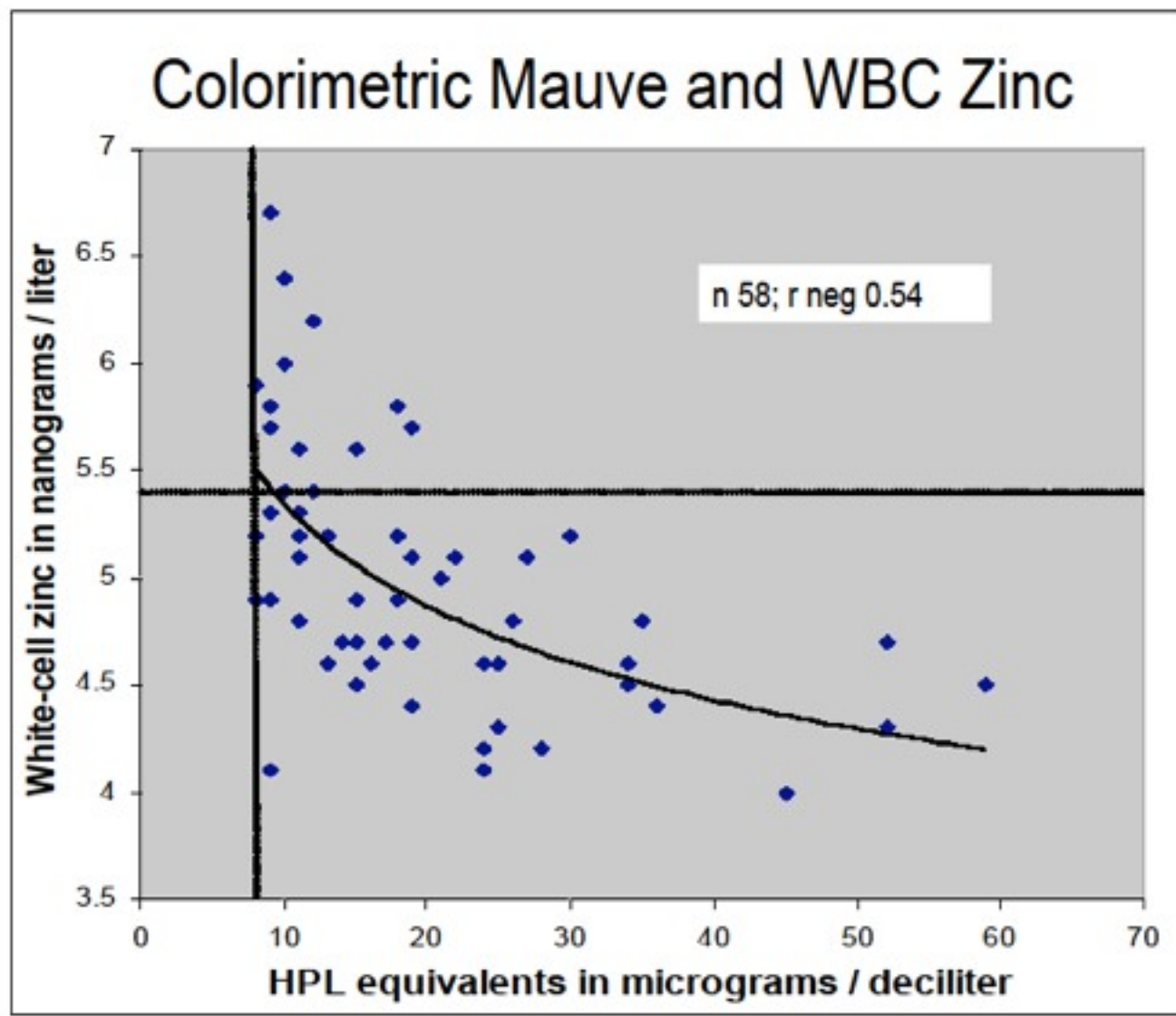
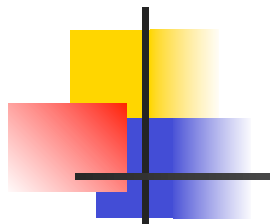
Discerning the Mauve Factor, Part 1 and 2

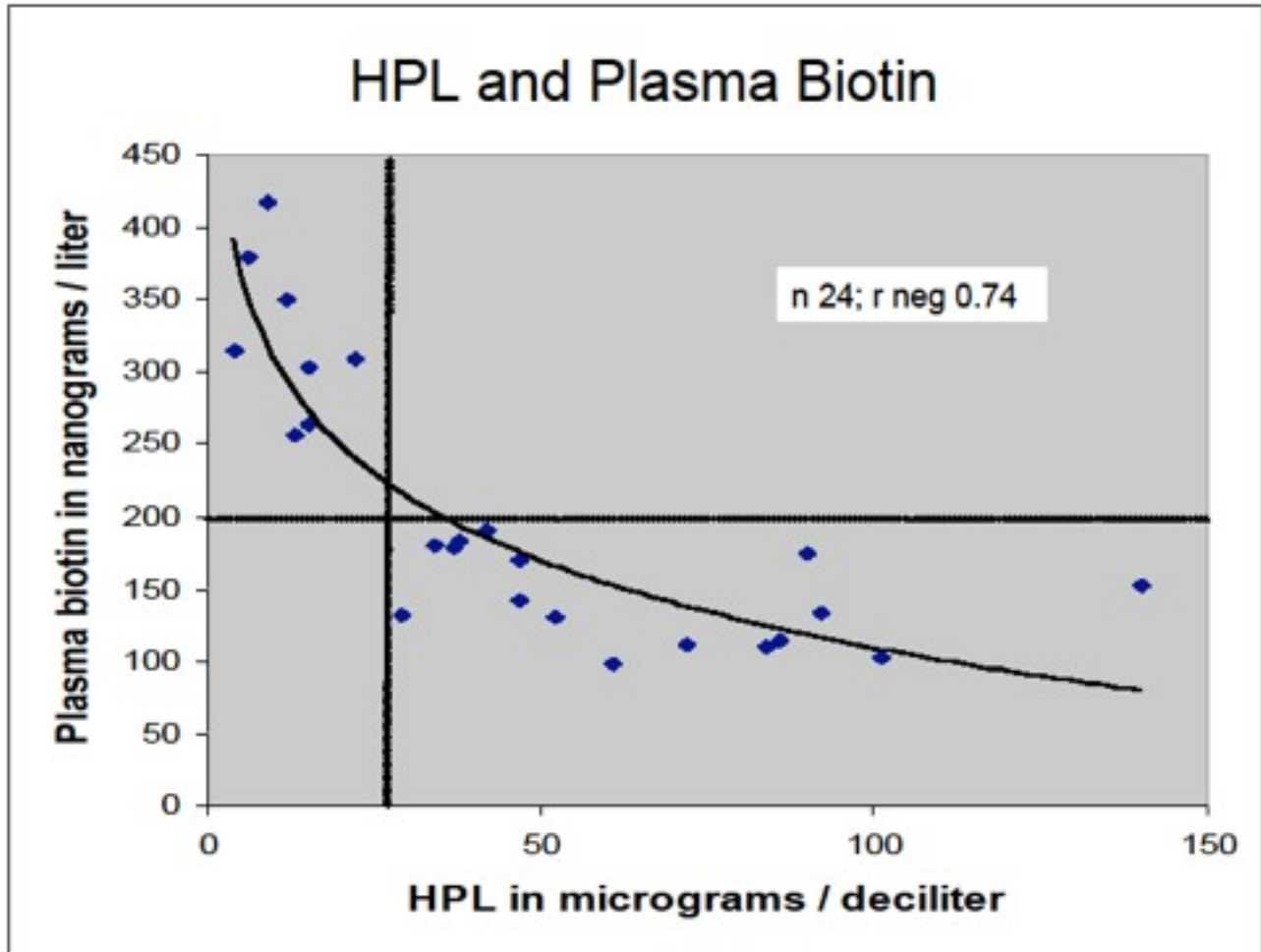
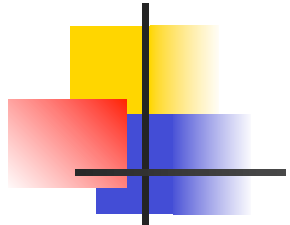
Audhya, Tapan et al, 1: Altern Ther Health Med. 2008 Mar-Apr;14(2): 40-50

In cohorts with mixed diagnoses, 24-hour urinary HPL correlated negatively with vitamin **B6** activity and zinc concentration in red cells ($P < .0001$)

- Above-normal HPL excretion corresponded to subnormal vitamin **B6** activity and subnormal zinc with remarkable consistency
- HPL correlated inversely with plasma **glutathione** and red-cell catalase, and correlated directly with plasma nitric oxide ($P < .0001$)
- HPL is a valuable biomarker for oxidative stress
- HPL is known to cause heme depression, which lowers zinc, increases nitric oxide, and **increases oxidative stress**
- Administration of prednisone reportedly provoked HPL excretion in animals (model for **stress**)
- KPU causes **leaky gut** syndrome: urinary HPL examined in relationship to urinary indicans, presumptive marker for intestinal permeability. Urinary HPL associated with higher levels of indicans ($P < .0001$)

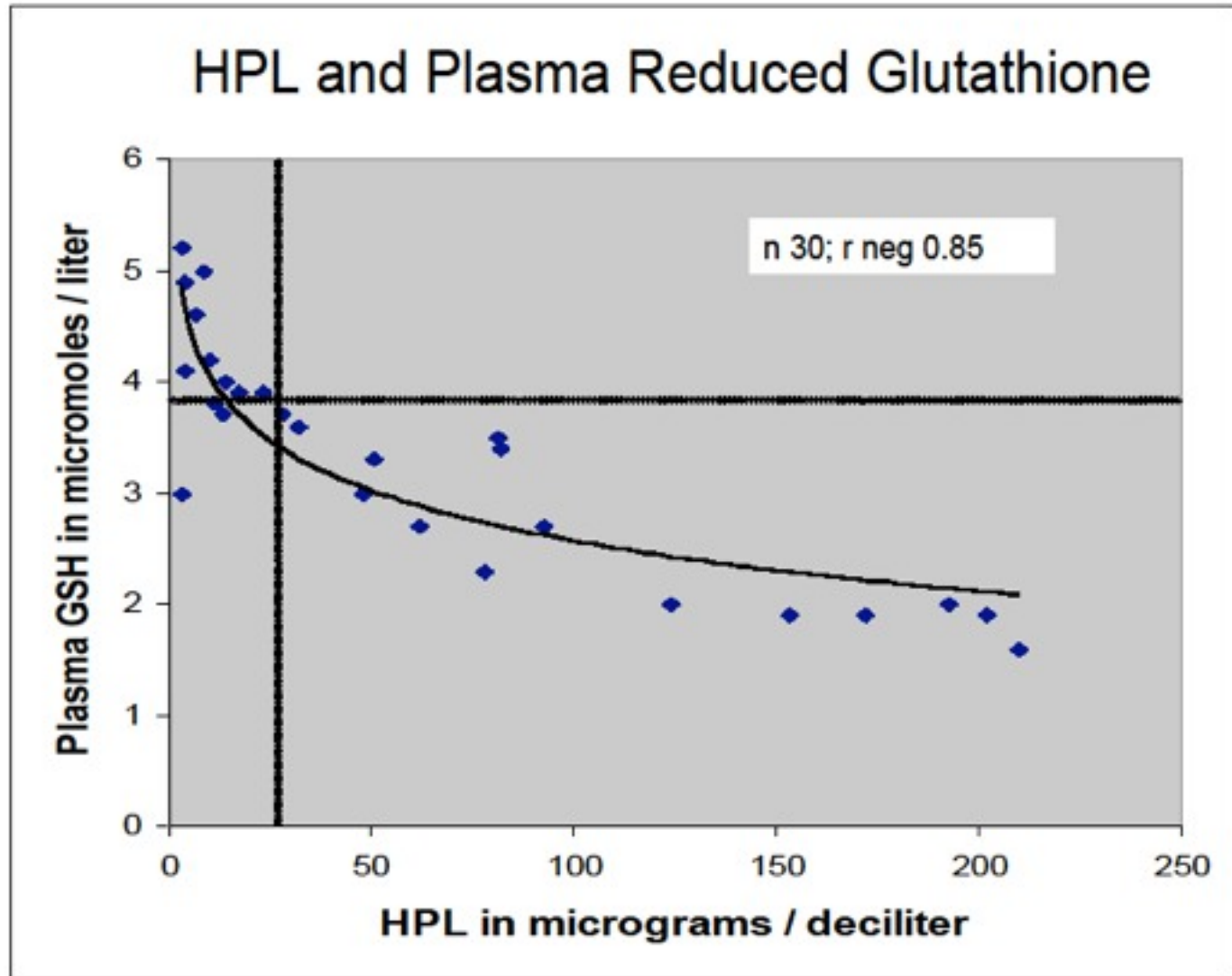


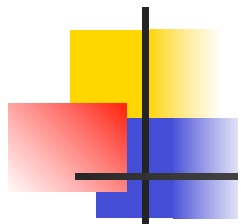




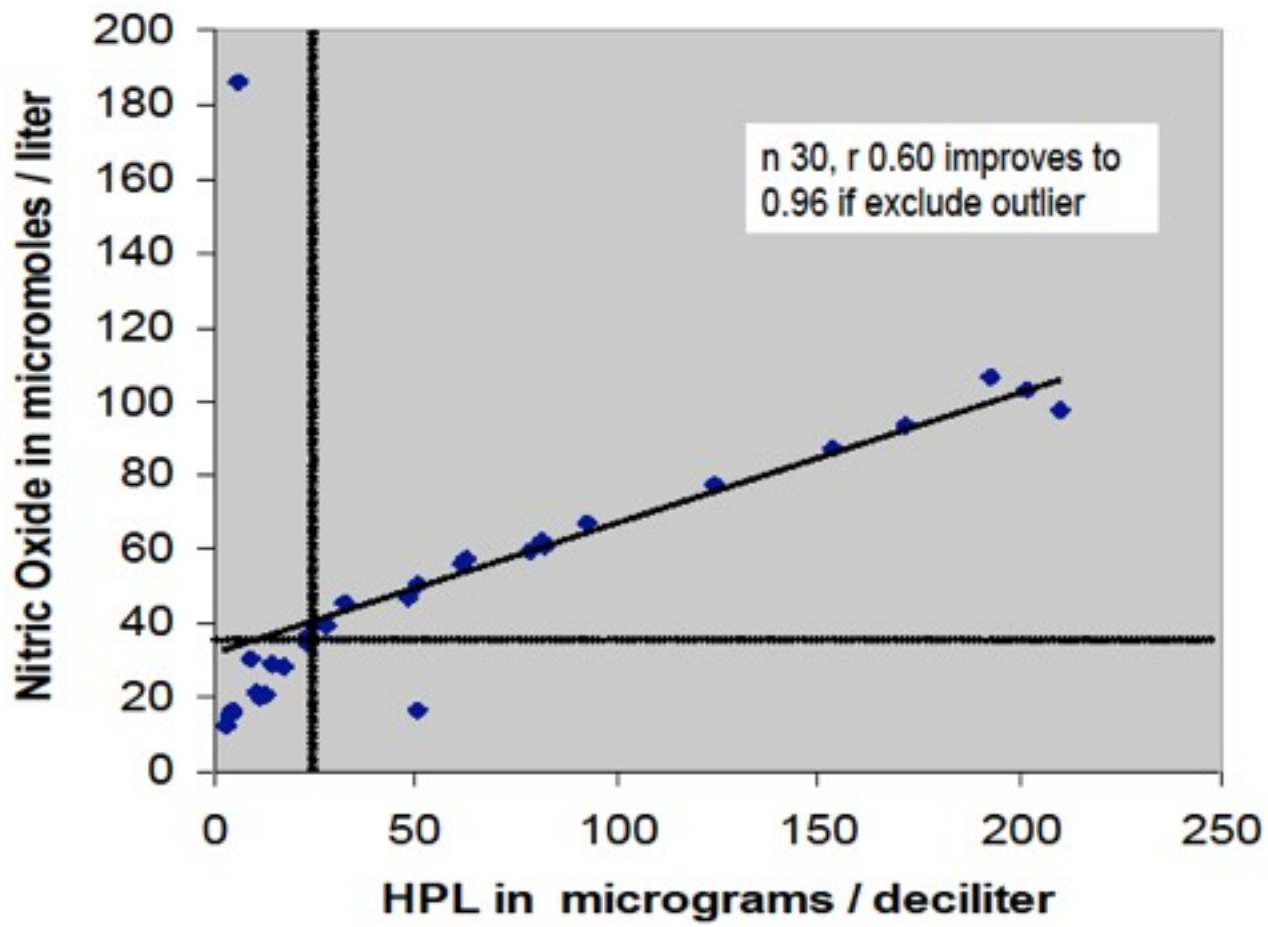


HPL and Plasma Reduced Glutathione



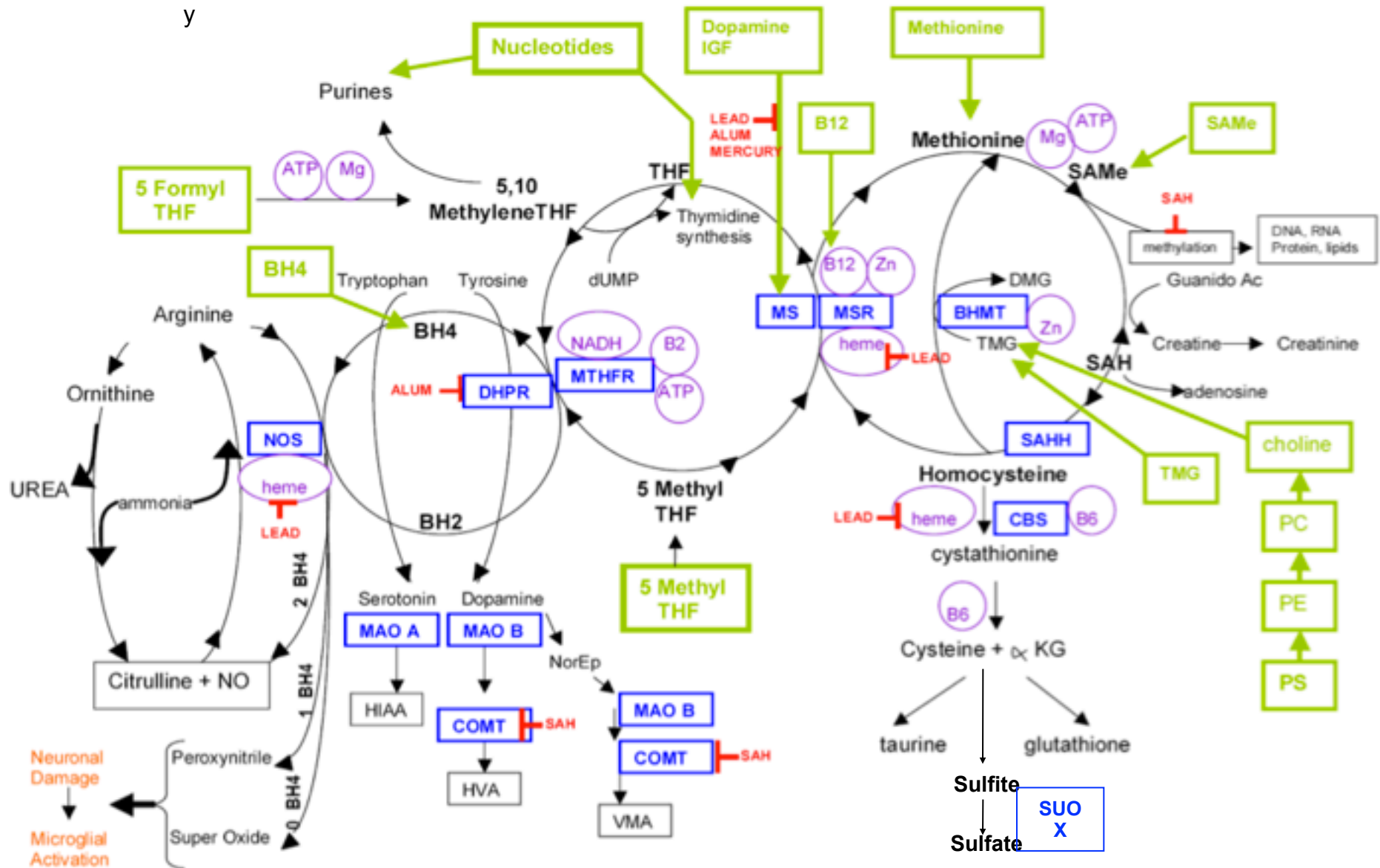


HPL and Plasma Nitric Oxide



Pathways With Enzymes, Cofactors, Supplements & Blocking Metals/SAH

y





Diagnosis

- When to suspect HPU: diagnosis of Lyme disease, Autism and other disorders on the spectrum, Rett syndrome (100% positive), Asperger, CFIDS, FMS, heavy metal toxicity
- 24-hr urine test for HPU (Vitamin Diagnostics).
 - Do not take vitamins (especially B's and minerals) five days prior to the test
 - Exposure to normal daily stresses is needed (no stress- avoidance or rest)
 - Use cleaned large orange or milk juice-carton for collection (then filling the transport tube).
 - Add 500 mg of ascorbic acid per liter of urine to stabilize pyrrols
 - Wrap aluminum foil around collection-container and transport-tube to prevent light induced pyrrol breakdown
 - Keep collection container in fridge
 - Pour into collection tube, briefly freeze to break up tetrapyrrols, then send (Mo-Wed)



Treatment (adult dosages)

a.m. before breakfast:

- **Zinc** 250 mg/day for 3-4 months (as picolinate, gluconate, citrate or sulfate) Later in the treatment less zinc may be needed for maintenance
- Manganese 20-50 mg/day
- MicroMinerals 1 tbsp (BioPure)
- **Biotin** 10 mg
- **Chromium** 454 (B.i.i.) 1 cap before each meal (3/day)
- BioPure has the only combination product, which makes the treatment easier

after breakfast

- Arachidonic acid from Omega-6 oils: **ghee**, evening primrose, borage oil, black current oil
- fish oil

p.m. before bedtime:

- **P-5-P** 50 mg, **B-6** 25 mg (up to 800 mg B6)
- **Magnesium glycinate** 600 mg (up to 1600 mg), calcium citrate 1200 mg
- psychiatric and neurological symptoms: **Niacin** 500 mg tid
- to improve bile quality/neurotoxin elimination/normalizing brain rhythms: **Taurine** 500 mg tid. before meals



other considerations

- high gamma vit E: 400 i.u per 40 lbs weight
- Zinc depletes copper levels. Some patients are or become copper deficient. There is much misinformation regarding copper in the current nutritional teachings. Beware. Monitor with red cell mineral test and replace if indicated (3-6 mg/day)
- Food allergies: all HPU patients are chromium deficient. Use Chromium 454 from B.i.i. (non-yeast source - great to chew for ASD kids)
- Brain allergies/sulfur intolerance: use Molybdenum
- Always have metal- detox agents on board (see next page)
- Initially zinc in high doses causes nausea (sign of hypochlorhydria) – carboanhydrase is zinc deficient enzyme. Give zinc several times per day in smaller doses and with vinegar in water. This symptom disappears in 2- 4 months




HPU leads uncontained growth of microorganisms and parasites.

- In HPU positive clients, always consider biotoxin producing bowel microbes (C.diff, etc.), parasites, mold and chronic Lyme
- Viruses are opportunistic and not the cause - only a symptom. They come on board when the defenses are down
- Garlic is the holy grail of any biological Lyme treatment
- Supernatant probiotic from B.ii. treats C.diff. (or oral Vancomycin)
- Organic high alliin freeze dried garlic (BioPure) releases 13 mg of allicin when it is dissolved (unmatched by any other product)
- Most ASD children not only tolerate, but start craving garlic – when they are on the HPU treatment for a few months and stable on it. Even the ones that should not, based on their genetic profile
- Start sneaking it into each meal in small amounts, then increase. Full adult dose for Lyme: 3 caps dissolved in water 3- 4 time per day
- Use the Coca pulse test to differentiate allergic from die-off reactions

HPU leads to bioaccumulation of toxins

(no HPU treatment without metal detox)

- 
- To turn on phase-1, 2 and 3 detox:
 - a. **MicroSilica** (silica molecules spiked with sulfhydryl groups) – 1-4 doses per day at 100 mg each
 - b. sound-wave enhanced chlorella 15 tbl t.i.d. with meals (BioPure)
 - c. Valkion singlet oxygen energy: water and inhalation

 - To mobilize metals from their binding sites, provide glutathion precursors and binding-peptides:
 - a. nanonized chlorella 5-6 sprays b.i.d (Matrix Metals, BioPure)
 - b. energized cilantro tincture 15 drops t.i.d

 - To shuttle metals from intracellular environment to the liver: **Phospholipid Exchange** – charged EDTA, lipoic acid, phospholipids, magnesium 1 tbsp twice daily (BioPure). Enhances absorption of all nutrients given at same time

 - Matrix transport of mobilized metals and facilitated kidney excretion:
 - a. **Matrix electrolyte** 2-8 tbsp in daily water (BioPure) and M-water w. glucose (Agave, Honey, Maple)
 - b. substitute HPU related chronic trace mineral losses with mono- atomic elements: MicroMinerals (BioPure): 2 tbsp in daily water



The healing crisis

- Watch out for the detox crisis 2-6 weeks into the treatment, and then other waves of it months into it.
- Do not underestimate it!
- Use the strongest available detox agents during that time: DMSA 100- 200 mg every 2-3 hours for several days, during less acute phases 200 mg at bedtime every other night
- Transdermal or i.v./i.m. DMPS (3-6 mg/kg)- even daily for a few days, then once/2 weeks
- i.v. ZnDTPA: 1 vial slow i.v. Every 4-6 hours for 2 days or until crisis is over
- i.v. Vit C (50-75 gms), **colonics** and lymphatic drainage
- Massive amounts of **chlorella**, zeolite or best: MicroSilica
- Laser detox, if energetic testing is available (best: ART)

Chlorella and Metal Binding

Cadmium

- Hagino et al.: Effect of chlorella on fecal and urinary cadmium excretion in Itai-itai. Jap. J. Hyg. 30: 77, 4/1975
- Nagano, T./Suketa, Y., et al.: Absorption and excretion of chlorella ellipsoidea cadmium-binding protein and inorganic cadmium in rats. Jpn. J. Hyg., 38: 741-747, 1983
- Carr, H.P., Carino, F.A., et al.: Characterization of the cadmium-binding capacity of chlorella vulgaris. Bull. Environ. Contam. Toxicol., 60: 433-440, 1998

Uranium

- Horikoshi, T./ Nakajima, A., et al.: Uptake of uranium by various cell fractions of chlorella vulgaris. Radioisotopes 28: 485-488, 1979
- Nakajima, A; Horikoshi, T; Sakagushi, T.: Recovery of uranium by immobilised micro-organisms. Evr. J. Appl. Microbiol. Biotech, 16: 88-91, 1982.

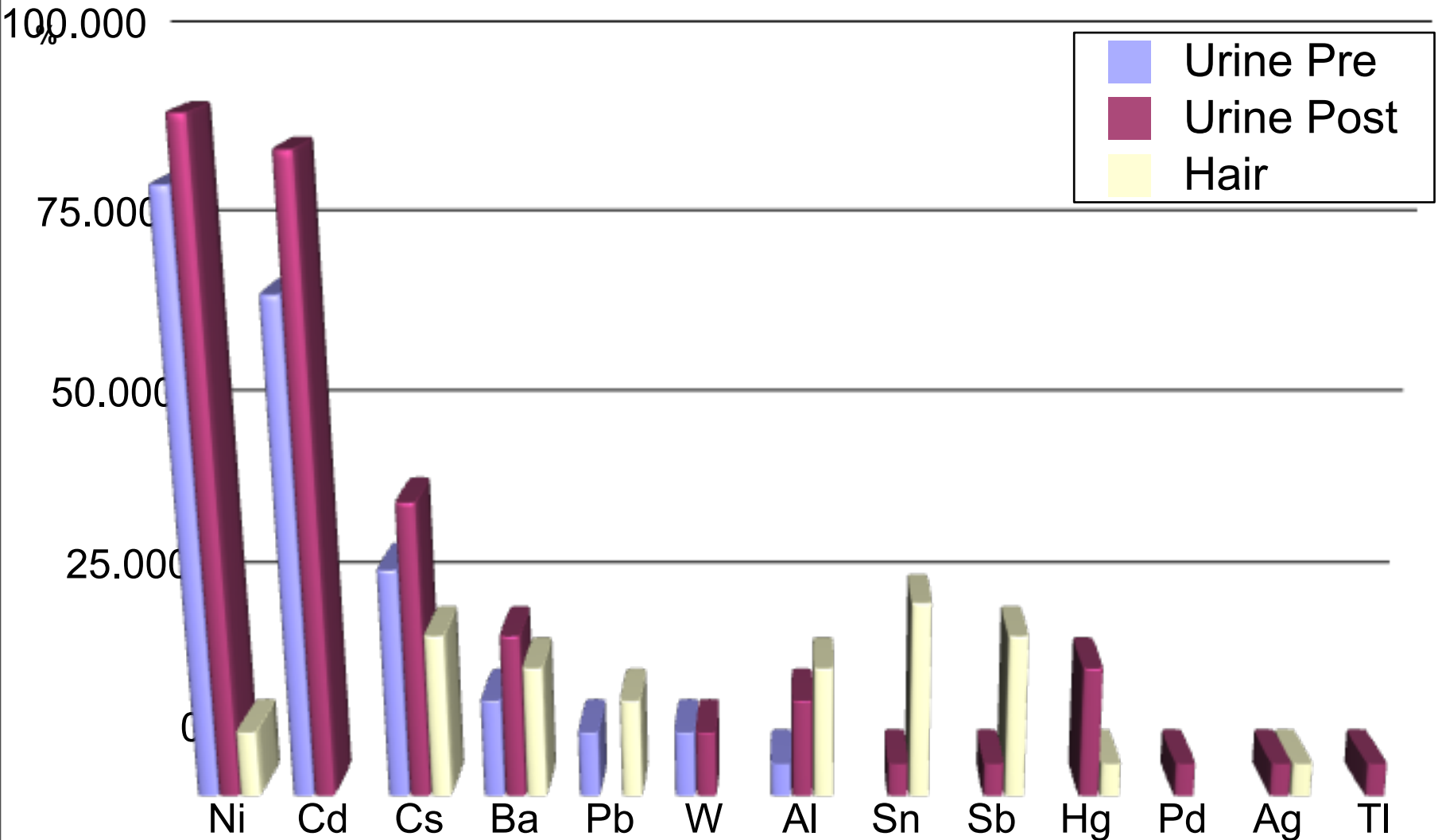
Lead

- Protective effects of chlorella vulgaris in lead exposed mice infected with Listeria monocytogenes M.Queiroz et al International Immunopharmacology 3 (2003) 889-900

Mercury

- Shieh, Y.J.; Barger, J: Uptake of mercury by chlorella and its effect on potassium regulation. Planta, 109: 49-60, 1973
- Klinghardt, D. :Algenpraeparat hilfreich bei der Amalgamausleitung
Erfahrungsheilkunde Band 48, Heft 7, Juli 1999
- D.Klinghardt and J. Mercola: Mercury toxicity and systemic elimination agents D.Klinghardt and J. Mercola, J of Nutritional and environmental Medicine (2001) 11, 53-62
- Parachlorella beyerinckii CK-5 is found to accelerate excretion of methyl-mercury both into feces and urine:
"Japan Society for Bioscience, Biotechnology and Agro-chemistry"(JSBBA: <http://www.jsbba.or.jp>) Meeting in Nagoya City, Japan, March 29~30, 2008 .

Toxic metal ions in urine and hair after provocation with a single dose of 15 drops energized cilantro tincture (20 patients, Margarita Griesz-Brisson MD, PhD)





HPU is a frequent co-factor in patients with:

1. heavy metal toxicity (detox pathways are overwhelmed and ineffective, lack of glutathione)
2. Lyme disease (microbes induce KPU enzymes to deplete white cells of zinc and weaken their fighting abilities)
3. Many -if not most - neurological illnesses (common in MS, Parkinson, Depression, Autism)

When KPU is correctly diagnosed and the recommended substitution of supplements is included in the treatment of any chronic illness, outcome can be dramatically improved



Observations, clinical tips and unresolved issues

Many HPU patients are copper intolerant, but also copper deficient in various body compartments (wbc, cranial nerves, frontal lobe/dopamine, etc.)

- Zinc may have a synergistic effect with mercury and may temporarily increase toxic symptoms
- Zinc is a sulfhydryl affinitive metal and binds to the same metal complexing agents as mercury by competition (DMSA, DMPS, OSR)
- Supplementing zinc liberates many 2-valent toxic metals, such as Hg, Cd, Al, Pb. These start moving and may cause damage on the way out. The clients need metal capturing agents on board (CVE, cilantro, anti-oxidants) and support with other detox strategies (colonics, i.v. chelation, phospholipid exchange, DMSA, etc.)
- Zinc is part of many metallo-proteinases. These are activated in Lyme disease and cancer. Disulfiram is an effective antidote.
- The HPU protocol improves hormonal status. Patient may become symptomatic (hyperthyroid, no more need for progesterone etc.)
- The kidneys often need support with drainage remedies (Matrix electrolyte, M-Water)



Recent Literature

- Graham 1979: HPL acutely depresses hepatic microsomal heme and p450 levels
- Ames 2002: Experimental heme depression lowers intracellular zinc, induces NOS and increases oxidative stress
- Audhya T et al: Discerning the Mauve Factor, Part I. *Altern Ther Health Med.* 2008 Mar-Apr;14(2):40-50.
- Part II: *Altern Ther Health Med.* 2008 May-Jun;14(3):56-62



cases

- Monica L., 5 year old with Rett syndrome. Has not been able to walk for 3 years. No language. Frequent seizures. Has been on DAN type protocol for 2 years and slightly improved.
- Presentation: she is in wheel chair, bend over, collapsed. No eye contact. Constant stims (rubs fingers together and grinds teeth loudly)
- Lab: HPU pos. (32) – after poor collection
- Treatment: HPU protocol. Homeopathic IGF-1. L-DOPA 0.5mg/kg. Mom calls after 6 weeks: increased seizure activity, everything worse. We add 100 mg MicroSilica 3 times per day to protocol, for 3 days she also gets 50 mg DMSA every 3 hours during the day. After 1 week no more seizures. We stop DMSA and keep her on 50 mg MicroSilica twice daily. In next 4 ½ months she makes an 80% improvement according to mom. She walks into the practice 6 months after 1st visit, interacts friendly with the health team, smiles, responds to cues and cooperated with all aspects of the exam. The wheel chair is in a storage unit
- March 09: started Quintessence/Lyme nosode/Rizol Zeta. May 09 Western Blot. Pos. for Lyme (IgG, IgM CDC criteria)



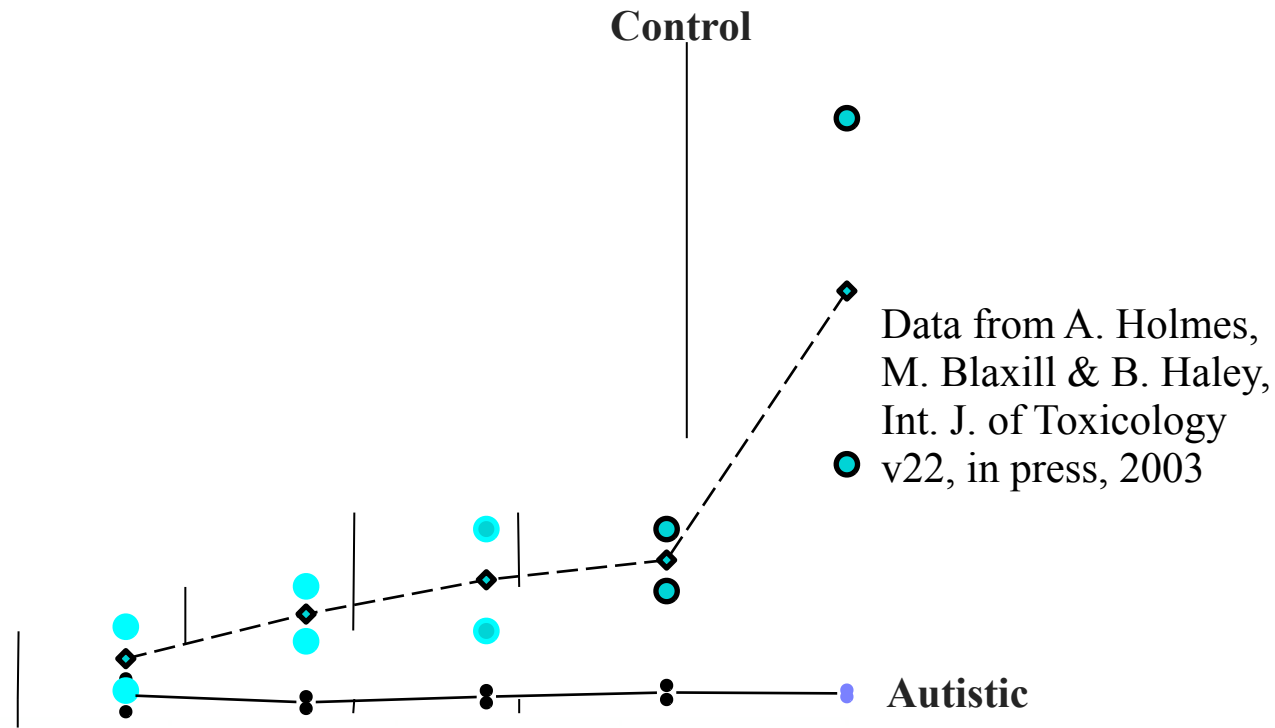
cases

- 7 year old autistic boy. All over the place, aggressive. No language, uncooperative. Weekly seizures. Difficult to manage at home, even though parents try. Hyper and hypopigmented skin sections. Striae on hips. Poor dental status. Narrow upper dental arch.
- Lab ordered: KPU (pos.78), 6 weeks into Phase 2: Western Blot (pos. IgM) and pos PCR for Bartonella
- Phase 1: HPU protocol plus MicroSilica 100 mg b.i.d., Phospholipid Exchange 1 tbsp at bedtime. Severe bouts of anger, depression, attacks mom twice (never did that before) starting after 5 weeks, ending after 9. Becomes peaceful and follows instructions for first time. No more seizures. Hair analysis now shows high levels of lead and mercury (never before)
- Phase 2: start Lyme treatment with Quintessence 12 dropperfull/day, Artemisinin 5 cap t.i.d 2 days each week, Rizol Gamma and Zeta (15 drops each t.i.d) and Oxo (1 cap after each meal)
- 6 weeks into Phase 2 starts saying his first words. Is interested. First time real eye contact with parents since he is 18 months old. He keeps making good progress over next year while working this protocol. Major forward leap after he gets a 3-way appliance to expand the upper jaw. He is now in school (special ed) and doing amazingly well at age 9 (has full age-appropriate vocabulary).

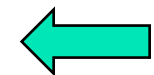
Autistic children fail to excrete Mercury

Mercury Birth Hair Levels Vs. Amalgam Fillings In Autistic and Control Groups

**Hair Hg level
(mcg/g)**



Number of amalgams:	0-3	4-5	6-7	8-9	≥10
Control: autistic ratio:	2.64	6.93	6.70	6.32	17.91
N:	15	22	29	30	43





Principles of treatment of chronic infections

- Diet: ART based is best. All patients are on GFCF diet
- Month 1:
 - Gut biofilm protocol: green clay, BioSil (silica breaks mucus bonds and restructures the matrix) and Interfase (up to 5 caps tid)
 - Start basic biomedical protocol:
 - **folinic acid and Hydroxy B12 (cellular detox)**
 - **Di-methyl glycine (cellular detox, especially chemicals)**
 - **Trial of methyl B12 injections (5 mg biw)**
- Month 2:
 - start **HPU protocol** if lab positive or good clinical evidence.
 - 20 day Alinia course (parasites, giardia, amoebas, H.pylori, clostridia, Babesia, some effects on Bartonella and Borrelia).
 - start **Detox protocol** simultaneously
- Month 3: start **“Lyme” protocol**



Other considerations

- Increase mitochondrial activity and ATP with Valkion
- Increase brain metabolism with Health Light
- Homeopathic laser detox for vaccines and chemicals
- Immunemodulation with KH6 method
- Low dopamine levels: Children: L-DOPA for language and movement skills (0.5 mg/kg/day – compounded as sublingual lozenge). Consider at bedtime 4-6 caps “Bitter Orange” (octopamine), in adults Mucuna powder (BiuPure) -1 tbsp/day
- Lab: urine organic acids for chemicals and toxins (Gold profile from Great Plains Lab) with specific detox suggestions – or 48 day detox pack (HBN)
- Genetic testing with Amy Yasko type analysis

The H-Dilution Method

(J.Monro, B.Shelton,T.Randolph, Reinhold Voll, Bill Rea, Napoleon and Korsakoff)

How to make an auto-nosode and/or energetic supplement (works for any condition that involves derailed immune responses, genetic glitches, malabsorption and other metabolic problems):

- To make energetic supplement, start with drops or ground-up supplement (i.e. 1 drop methyl B12). To make immune tonic, collect specimen (best is tongue scrapings). Stretch with just enough clean water so it's a liquid. This is your H0 mother tincture.
- Dilute with 5 parts water (5:1) and secuss 50 times. This is your H1.
- Empty bottle to 1/6th of previous content, fill with water. Secuss 50 times. This is your H2
- Continue until H-4. Use Matrix Elektrolyte for next step -instead of water – this sterilizes the content osmotically. This is your H5. Next step with water again. This is your H6, which will be your main treatment for months. Fill into a tincture bottle. Keep this bottle wrapped in alu foil away from electric equipment in a cool place
- H7: to ease into the treatment, take a small amount of H-6 into a second small tincture bottle, add 5 parts water and secuss. This is now an H7. Give 7 drops 4-6 times per day under the tongue. After 1 week – if there is no Herx, discard and use the H6 bottle. Redo this process every 6 weeks. Stay with H6, unless you use ART to fine tune the final dilution
- H6: most supplements need to be given only energetically, not in true biochemical form. This allows for better absorption and utilization of this nutrient. Most patients do really well with the H6
- General rule, if energetic testing is not available: if you start with a toxin or allergen, use H7 (in the most sensitive persons a higher dilution may be needed initially). If you start with something good (supplement, medication), use H6. For rapid initiation of detox, use LBR – laser biofield restructuring