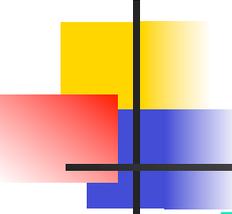


## **KryptoPyrrolUria (KPU) and HemoPyrrolLactamUria (HPU) and ASD**

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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-hemopyrrolin-2-one (HPL). To keep things simple, this condition is today most often referred to as KPU.

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

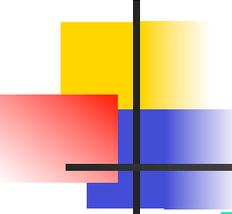


# The early KPU literature

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- 3. Sohler, A., Renz, R. H., Smith, S., and Kaufman, jun., J., *Intern. J. Neuropsychiat.*, 3, 327 (1967).
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- 8. Forrest, F. M., Forrest, I. S., and Mason, A. S., *Amer. J. Psychiat.*, 118, 300 (1961).
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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

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- In the US, several labs test for kryptopyrrole, but not the HPL complex
- In Holland, the laboratory of Dr. Kampsteeg tests for HPL ([www.KEAC.com](http://www.KEAC.com))
- In recent months, all “my” children with ASD - and suspected of Mauve on clinical grounds –who tested negative for KPU, tested positive in the Dutch lab
- The yield in the US can be greatly improved, if the KPU specimen is collected properly. Unfortunately the US labs do not provide the proper guidelines
- I suspect that more then **80% of ASD kids have HPU** and should be treated for it



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**DIAGNOSTICS, Inc.**  
 Rt.35 & Industrial Drive  
 Cliffwood Beach, NJ 07735  
 Phone (732) 583-7773  
 Fax (732) 583-7774

Reportdate 16/01/2009 <sup>1</sup>

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

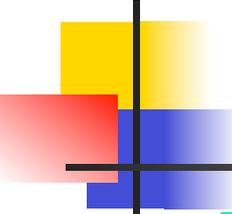
Applicant	KLINGHAR
Date received	31/12/2008
Labno	312835
Date received	31/12/2008
1st printdate	16/01/09

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

*Handwritten notes:*  
 Field 1/15/09  
 PC scheduled 1/21/09 SH

\*)outside ref.range ; Performed at ELN

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

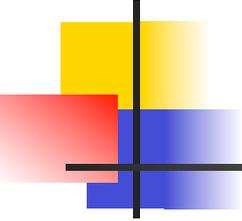


## KPU patients lose supra-physiological amounts of zinc, B6, Biotin and manganese in the urine

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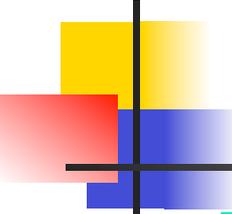
- **KPU is caused by the defect of several of the 8 enzymes needed for the synthesis of heme**
- **Heme is needed for liver detox reactions (cytochromes), Cystathionine synthase, Catalase, Heme-hemopexin for MT translation, Guanylate cyclase, Sulfite-reductase, NOS, Pyrrolase.**
- **KPU patients have low serum glutathion levels, high NO levels, low histamine**
- **KPU can be inherited or can be acquired (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)**

# Symptoms



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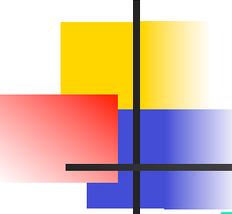
- **Light / sound / odor intolerance**
- **Hypoglycemia / glucose intolerance**
- **Pale skin / poor tanning/china doll look**
- **Tremor / shaking / spasms**
- **Environmental and food allergies**
- **Autism/ most symptoms of ASD**
- **Poor breakfast appetite**
- **Cold hands or feet**
- **Eosinophilia**
- **Delayed or early puberty / sensitized hormone receptors**
- **Stress intolerance**
- **Emotional lability**
- **Explosive anger**
- **Anxiety / Withdrawal**
- **Paranoia / Hallucinations**
- **Perceptual disorganization**
- **Nail spots (leukodysplasia)**
- **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)**
- **Coarse eyebrows**
- **Abdominal tenderness**
- **Constipation**



# Common Lab abnormalities

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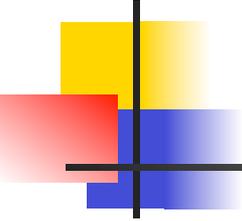
- High LDL, low HDL
- Low normal alkaline phosphatase (Zn, Mag)
- Low wbc (Zn)
- Low Omega-6 fatty acids in red cell membrane test
- Low taurine in aminoacid profile
- High MCV
- wbc and rbc Zn, Mn levels may be normal while bone and CNS are completely deficient
- Bone biopsies have been a reliable predictor of HPU (severe Zn, Mn, Ca, Mag and Mo deficiency)
- High C3a, C4a, MMP-9, low ADH, MSH and VIP



# Common physical signs

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- 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

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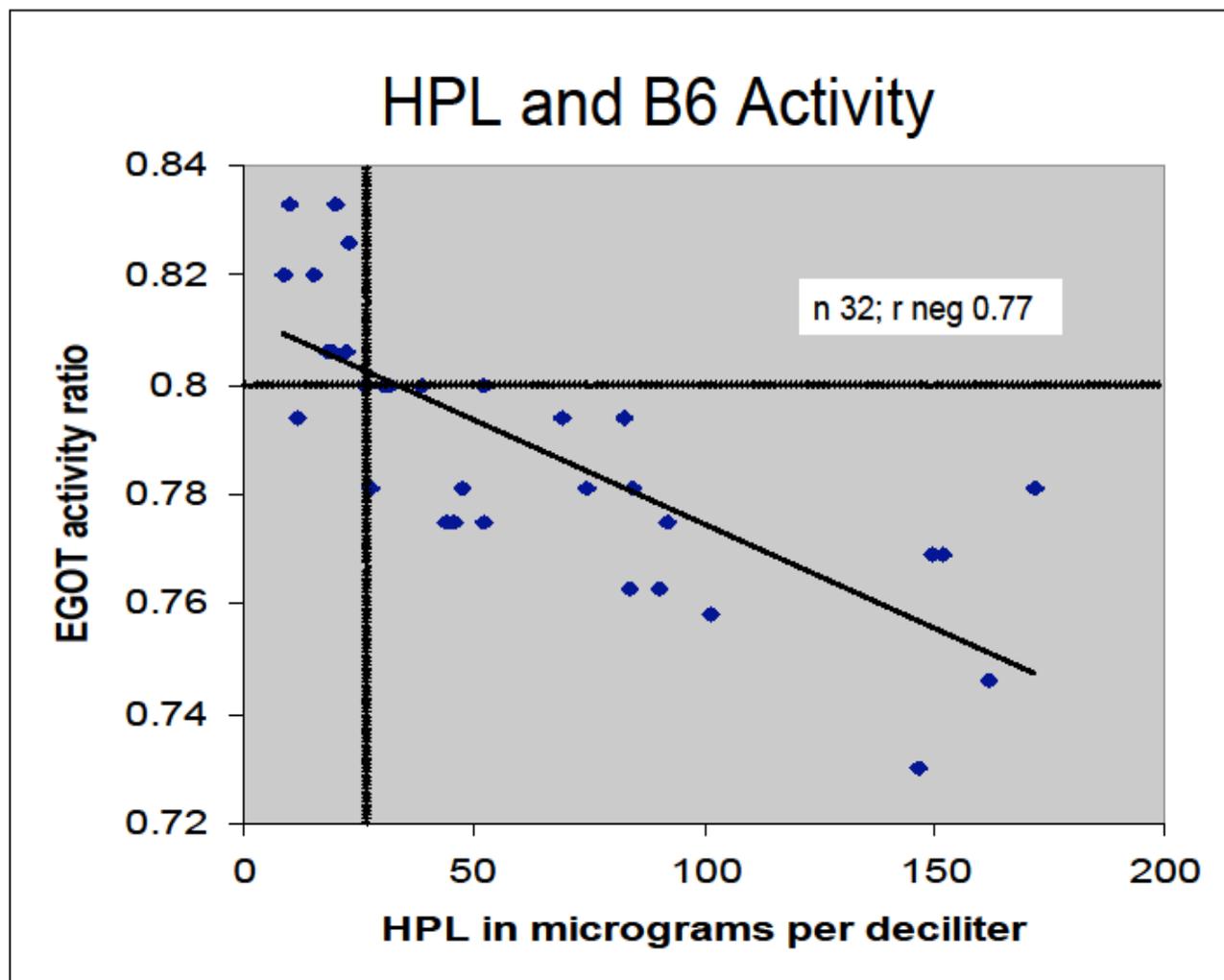
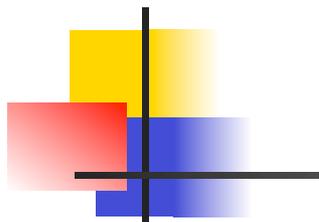


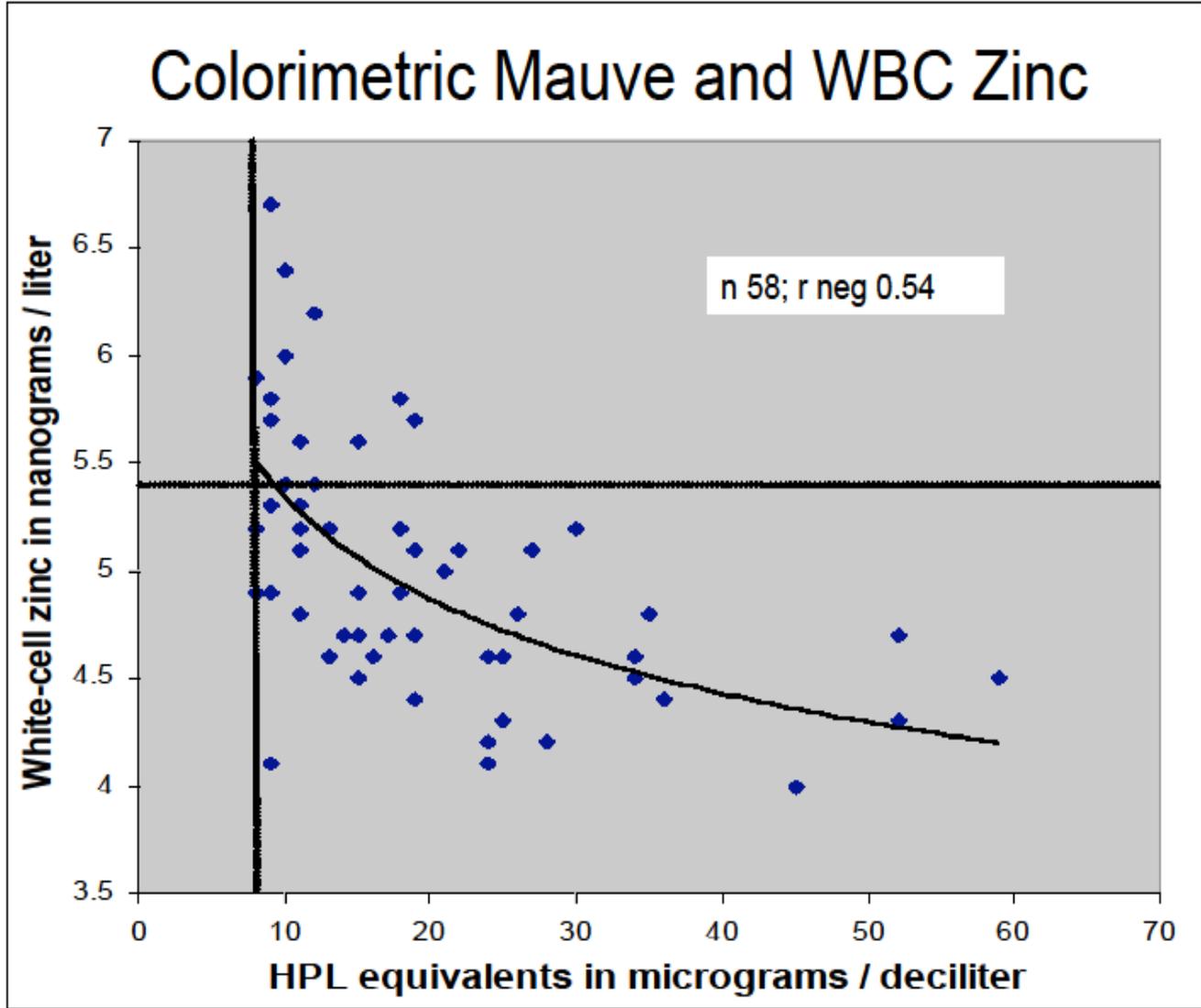
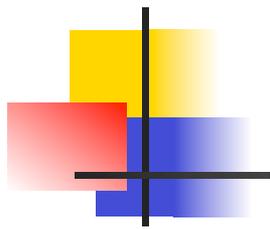
## Discerning the Mauve Factor, Part 1 and 2

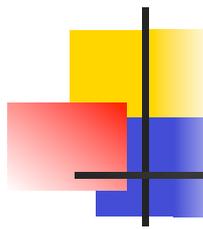
Audhya, Tapan et al, 1: Altern Ther Health Med. 2008 Mar-Apr;14(2): 40-50

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

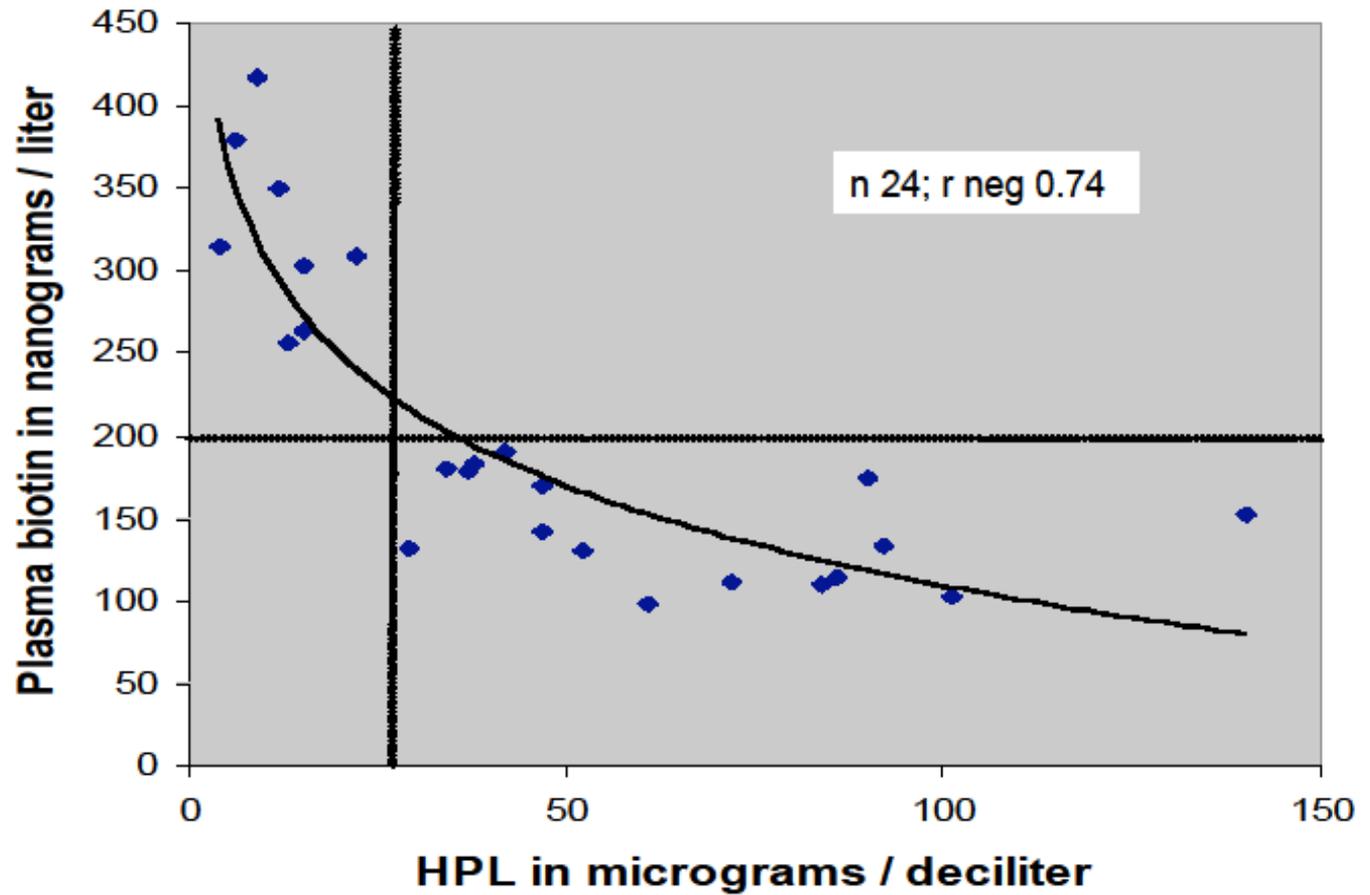
- Above-normal HPL excretion corresponded to subnormal vitamin **B6** activity and subnormal zinc with remarkable consistency
- HPL correlated inversely with plasma **glutathione** and red-cell catalase, and correlated directly with plasma nitric oxide ( $P < .0001$ )
- HPL is a valuable biomarker for 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 ( $P < .0001$ )

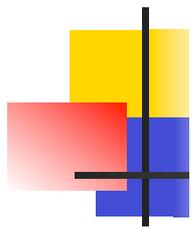




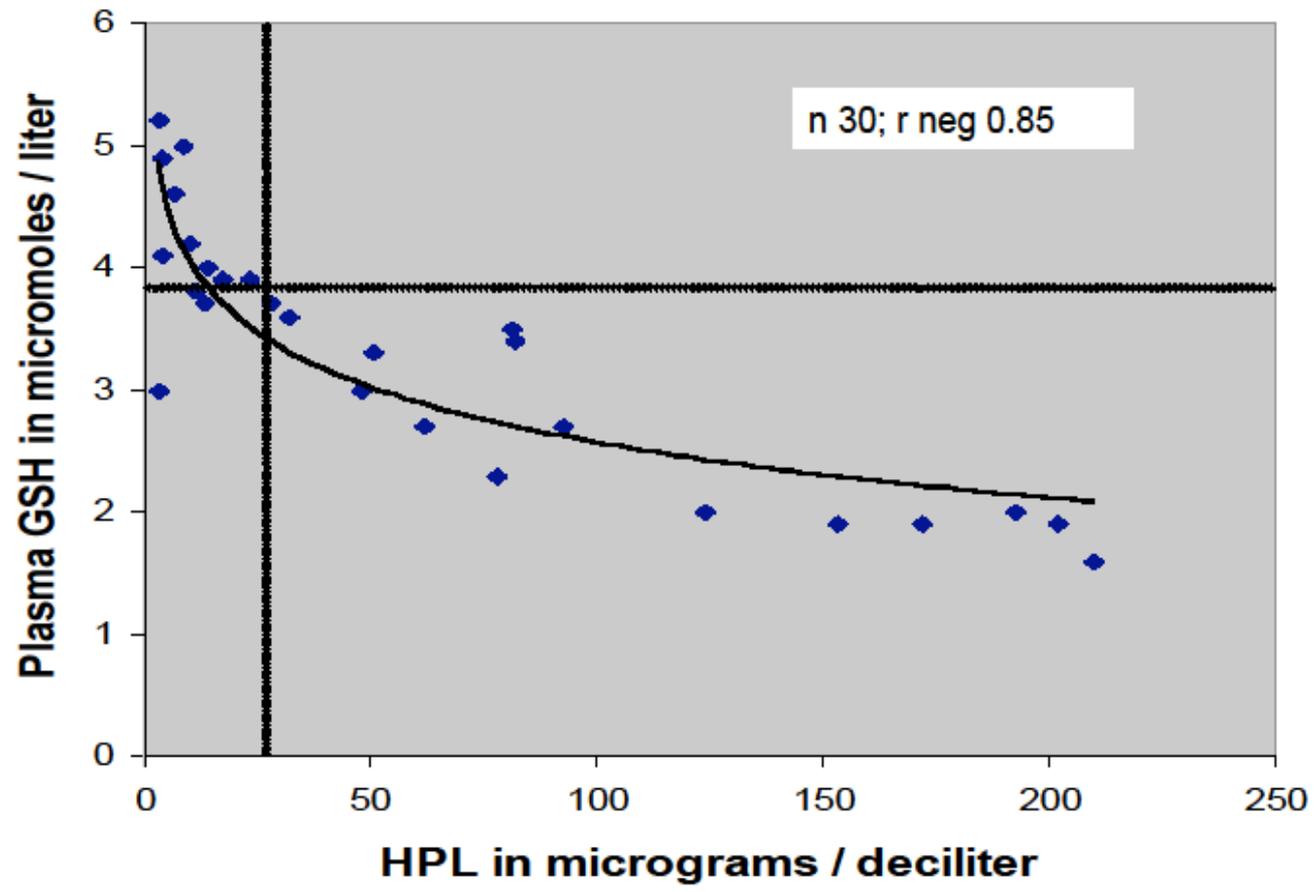


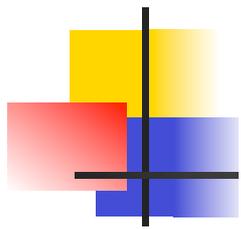
## HPL and Plasma Biotin



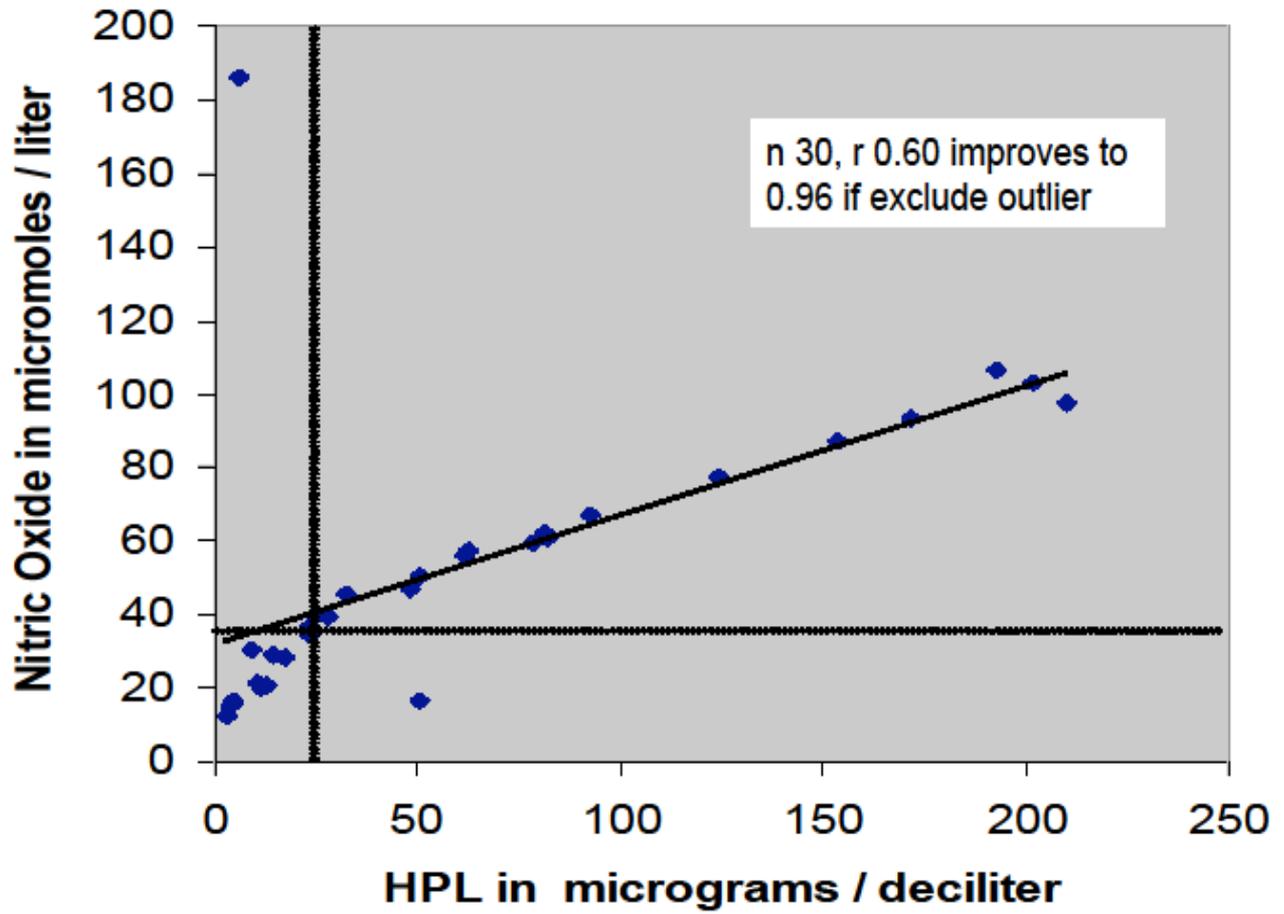


# HPL and Plasma Reduced Glutathione

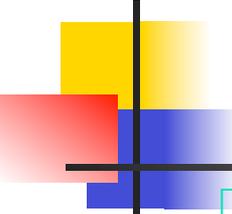




## HPL and Plasma Nitric Oxide







# Diagnosis

When to suspect HPU: diagnosis of Autism and other disorders on the spectrum (i.e. Rett, Asperger), mold illness, Lyme disease, CFIDS, FMS, heavy metal toxicity

- 24-hr urine test for KPU (Biolab(?), [www.KEAC.com](http://www.KEAC.com)).
  - 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 or with breakfast:

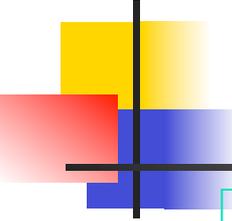
- **Zinc** up to 600 mg/day ( =100 mg elemental zinc) for 3-4 months (as z-carnosine, picolinate, gluconate, citrate or sulfate) Later in the treatment less zinc is needed for maintainance
- Manganese 5-25 mg/day
- MicroMinerals 1 tbsp (BioPure)
- **Biotin** 10 mg

after breakfast

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

p.m. before bedtime:

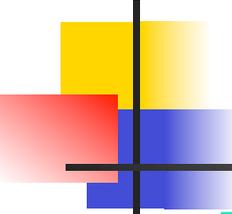
- **P-5-P** 50 mg, **B-6** 25 mg (up to 800 mg B6)
- Magnesium glycinate 600 mg (up to 1600 mg)
- Detox protocol
- Psychiatric symptoms: **Niacin** 500 -1000 mg tid
- To improve bile quality/neurotoxin elimination/normalizing brain rhythms: **Taurine** 500 mg tid.
- Ideal syergistic combination of ingredients: "**Core**" from BioPure. Maintainance dose: 4/day most patients prefer to take Core in divided doses throughout the day)



## other considerations

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- Contraindication to zinc: high levels of MMP-9. Zinc dependent inflammatory enzyme, causing connective tissue demolition. In this case HPU may be adaptive (=protective). Resolve inflammation/MMP-9 first (high dose chlorella vulg, etc.)
- 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 ART or red cell mineral test and replace if indicated (3-6 mg/day)
- Food allergies: most HPU patients are chromium deficient
- Brain allergies/sulfur handling problems: use Molybdenum
- Always have metal- detox agents on board (see next page) – zinc mobilizes lead and cadmium
- 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
- Contraindications: zinc allergies are common and must be resolved. Most common cause: psycho-emotional (operant conditioning – zinc-frequency tied to unpleasant/traumatic memory). Use PK/MFT to uncouple



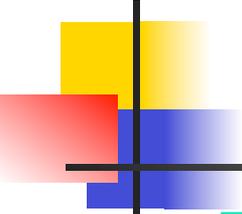
# garlic

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- Garlic is the holy grail of Lyme treatment
- Organic high alliin freeze dried garlic releases 13 mg of allicin when it is dissolved (unmatched by any other product)
- Even 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 ( which are common on f.d.garlic)

# Metal detox (while on KPU treatment)

- 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. chlorella: chloenergy from BioPure.eu – 5-10tbl t.i.d
  - c. Valkion singlet oxygen energy: water and inhalation
  
- To mobilize metals from their binding sites
  - a. Homeo K Clear – 5drops twice daily
  - b. energized cilantro tincture 15 drops t.i.d
  
- To shuttle metals from intracellular environment to the liver: branched chain amino acids, NAC, DMPS, DMSA, Taurine, Glycine. Enhances absorption of all nutrients given at same time
  
- Matrix transport of mobilized metals and facilitated kidney excretion:
  - a. Matrix electrolyte 2 tbsp in daily water (BioPure) and M-water
  - b. substitute KPU related chronic trace mineral losses with mono- atomic elements: MicroMinerals (BioPure): 2 tbsp in daily water



# The healing crisis

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- Watch out for the detox crisis 2-6 weeks into the treatment, and then other waves of it months into it (high dose zinc mobilizes high amounts of lead, cadmium and other toxic elements)
- 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
- DMPS (3-6 mg/kg) injected into subcutaneous fat- even daily for a few days, then once/2 weeks. Alternative: drink!
- 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 (40 tbl tid) and/or MicroSilica 100 mg tid - qid)
- 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

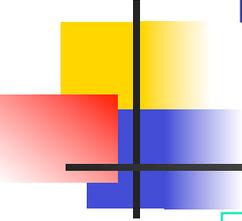
## Mercury

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 .



## KPU is a frequent co-factor in patients with:

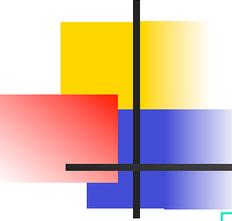
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1. heavy metal toxicity (detox pathways are overwhelmed and ineffective, lack of glutathione)
2. Mold illness and Lyme disease (microbes induce KPU enzymes to deplete white cells of zinc and weaken their fighting abilities)
3. Many -if not most - neurological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

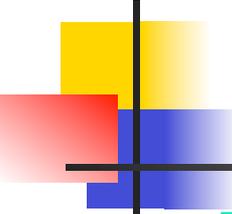
- Many KPU patients are copper intolerant, but also copper deficient in various body compartments (wbc, cranial nerves, frontal lobe/dopamine, etc.): use homeopathic copper (cuprum met, cuprum sulf.) and Acai to improve copper regulation
- Zinc may have a synergistic effect with mercury and may temporarily increase toxic symptoms
- Zinc is a sulfhydryl affinitive metal and binds to the same metal complexing agents as mercury (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 (MicroSilica, 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 KPU protocol improves hormonal status. Patient may become symptomatic (hyperthyroid, no more need for thyroid, progesterone etc.)
- The kidneys often need support with drainage remedies (Matrix electrolyte, Matrix Minerals, M-Water)



## Recent Literature

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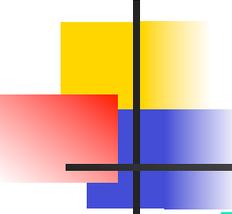
- Graham 1979: HPL acutely depresses hepatic microsomal heme and p450 levels
- Ames 2002: Experimental heme depression lowers intracellular zinc, induces NOS and increases oxidative stress
- Audhya T et al: Discerning the Mauve Factor, Part I. *Altern Ther Health Med.* 2008 Mar-Apr;14(2):40-50.
- Part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



# cases

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- 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: KPU pos. (32) – after poor collection
- Treatment: KPU 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 1<sup>st</sup> 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

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- 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).

# Klinghardt H-7 Method

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

How to make an auto-nosode (works for any condition that involves derailed immune responses):

- Collect specimen, best is tongue scrapings. Stretch with just enough clean water so it's a liquid. This is your H0 ( H-zero) mother tincture.
- Dilute with 5 parts water (5:1) and secuss 50 times. This is your H1 ( H-one).
- Empty bottle to 1/6<sup>th</sup> of previous content, fill with water. Secuss 50 times. This is your H2
- Continue until H-5. Use Matrix Elektrolyte for next step -instead of water – this sterilizes the content osmotically. This is your H6. Next step with water again. This is your H7, 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
- To ease into the treatment, take a small amount of H-7 into a second small tincture bottle, add 5 parts water and secuss. Give 4 drops 6 times per day under the tongue. After 1 week – if there is no Herx, discard and use the H7 bottle. Redo this process every 6 weeks. Stay with H7, unless you use ART to fine tune the final dilution. After 6 weeks use H6, then H5, Stay on H5 for long time.
- To make effective regulation remedies for dietary supplements: use H5 and/or H6 dilution