1 **Osteopetrosis**
Case

Dr. Van D. Merkle DC, DABCI, DACBN, CCN, DCBCN, Vice President of CBCN

Dr. Andrew R. Dyer, DC

2 **Initial Contact – 11/3/05**

Lori,

I received an email today. I would normally delete any that I don't know. Anyway, I opened it and there was Kaleb's story.

I am located in Dayton, Ohio, and it may seem strange to get a response from a Nutritionist and Chiropractor, but I am an expert in Health and have been in practice for over 20 years. You can look at my website www.3000health.com for some cases that I did several years ago. I haven't had time to update it. I am usually scheduled 3-4 months in advance for people to see me for nutritional/health help. I have seen a few rare conditions and helped some.

There may be no 'cure' for Kaleb, but are there things that can be done to improve his health? That is what I may be able to provide. Maybe if his system can be optimized, his symptoms will stabilize. I offer no cure for Kaleb; just the possibility to get healthier.

I use laboratory testing to determine the course of nutritional therapy and nutrients and then retest to determine effectiveness.

I guarantee nothing, but I would be willing to do the laboratory testing that I need at my expense. I would also donate our time that would be necessary to implement what may be needed.

You may contact me by this email address. If you are not interested then no response is necessary.

I wish you well and will pray for you and Kaleb.

Sincerely,

Van D Merkle DC, CCN, DACBN, DABCI

3 **Initial Contact cont.**

Dr. Merkle-

Thank you so much for your email today. It actually made my day! Yes, we are very interested in working with you. After years of trying to help Kaleb and watching him suffer so much....we are willing to try this and see if it helps. The testimonials were very helpful on the site. And we completely understand there is no cure...but if we can help nutritionally, we'd be very pleased.

We will be out of town from Nov 8-11. We will be going to Shriners in St. Louis to see what there recommendations are for his hip.

Thank you again....even though that doesn't feel like near enough to say to you.

You definitely made a difference in a family's life today, and we appreciate it so much.

Please let me know what we need to do next.

Lori

■

4 **History of Osteopetrosis**

■ Albers-Schönberg Disease, or type II autosomal dominant osteopetrosis (ADO2), was described for

the first time in 1904 by the German radiologist, Heinrich Albers-Schönberg.

- ADO2 is the most common form of Osteopetrosis with an estimated prevalence of up to 5.5 per 100,000 inhabitants.
- Disease results from ineffective osteoclast-mediated bone resorption.

5 **How is ADO2 diagnosed?**

- Diagnosis is usually made from radiographs, which demonstrate widespread osteosclerosis and the presence of endobones (bone-within-a bone appearance), most commonly noted in the vertebrae (sandwich vertebrae), pelvis, and at the ends of the long bones.
- NBCE Pathology buzzwords = Rugger-jersey spine, Bone-in-Bone, Sandwich Vertebra, Marble Bone disease, Chalk Bone appearance, Albers-Schönberg disease, Erlenmeyer flask deformity.

6 **About Kaleb**

7 **Family History of Osteopetrosis**

- Mother's paternal uncle in his sixties, wheelchair bound...currently in a nursing home due to what they first believed was a broken neck. Now they are attributing the pain to Osteopetrosis.
- Maternal grandfather, 57. Underwent total hip replacement in April 2005. Still having problems because they didn't cut the 'tendon' or 'ligament' as much as they should have and they believe that is the source for the pain. He will be having a subsequent surgery soon.
- Maternal uncle, 37. Has had NUMEROUS broken bones, including the neck, back, arms, legs, ribs, jaw, shoulder, etc.
- Maternal cousin, 33. Has had a number of pins/plates, etc in her hips. Although it has been difficult, she lives a very active, productive life. She is a registered nurse and wheelchair bound.
- Patient's mother has positive radiological findings.
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8 **What is TRAP?**

- TRAP is an isoenzyme of the nonspecific acid phosphatases that is expressed by both erythrocytic and macrophagic cells. In bone, it is highly associated with the osteoclast. It is postulated that most of the serum activity of TRAP is derived from osteoclasts, and physiologic increases in serum levels are observed in children, presumably secondary to increased osteoclastic activity related to bone growth. Besides osteopetrosis, pathologically elevated TRAP levels are observed in the lysosomal storage disorder, Gaucher's disease, and conditions of increased bone resorption.

--Journal of Clinical Endocrinology and Metabolism 2002

9 **What Do The Journals Say?**

- "In the pediatric group, TRAP is 100% sensitive and specific if a diagnostic cutoff of 35 U/L is used."

  --Journal of Clinical Endocrinology and Metabolism
- "The results indicated that in ADO2, serum TRAP reflects the number of osteoclasts and that the extremely high serum TRAP activity is a specific indicator of the disease. In the pediatric group, both total TRACP and TRACP 5b were 100% sensitive and specific for the diagnosis of ADO2 when the diagnostic cutoffs of 35 and 60 U/L were used."

  --Clinical Chemistry 2004
-

10 **REFERENCES**

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Creatine Kinase Accurately Diagnoses Type II Autosomal Dominant Osteopetrosis but Does Not Identify Gene Carriers. The Journal of Clinical Endocrinology and Metabolism 87(5) 2212-2217

- Alatalo et al. *Osteoclast-Derived Serum Tartrate-Resistant Acid Phosphatase 5b in Albers-Schönberg Disease (Type II Autosomal Dominant Osteopetrosis)* Clinical Chemistry 2004, 883-890

- www.Helpkaleb.com

- www.caringbridge.com/oh/kalebdavis/history.htm

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11 **Doctors around the World**

1 During the Davis family's search for the cause, they have spoken to doctors in the following areas:

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- Ohio (Columbus, Cleveland, Loudonville)

- Baltimore

- Boston

- South Carolina (Charleston and Columbia)

- Texas

- Illinois

2 - St. Louis, Missouri (Shriner's Hospital)

- Toronto, CANADA

- California (UCLA Med School)

- Utah

- Beijing, CHINA

- Dayton, OH
  Back to Health Center
  Dr. Van Merkle and Dr. Andrew Dyer

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12 **Kaleb and Lori (mom)**
Test Results

1 ■ KALEB's results from August, 2000.

- TRAP - 71.0 (4.3-21.2)
- CPK - 202 (50-180)
- CPK - BB 60% (0%)
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2 ■ LORI's results from August, 2000.

- TRAP - 41.4 (3.5-9.1)
- CPK - 138 (50-180)
- CPK-BB - 68% (0%)
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13 **CK: Creatine Kinase**

- Creatine Kinase is an enzyme found primarily in the heart and skeletal muscles, and to a lesser extent in the brain. Significant injury to any of these structures will lead to a measurable increase in CK levels.
- There are three Isoenzymes. Measuring them is of value in the presence of elevated levels of CK to determine the source of the elevation.
- Normal levels of CK/CPK are almost entirely MM, from skeletal muscle.

14 **Kaleb D. Past Medical History**

Medical History

- Birth to 1 year old, 1996
- Kaleb's medical history has been quite complex from the very beginning. He was never a "sick" baby, but he never had a good immune system. Everything got him down including the normal colds, ear infections, pneumonia, extended periods of diarrhea and other illnesses that don't normally knock babies for a loop.
- In June of 1996, we found out that his eyes were not aligned. Strabismus surgery was suggested, and he had a CT scan to rule out Osteopetrosis due to family history. This scan indicated no Osteopetrosis.

15 **1997-1998**

Kaleb underwent 4 strabismus surgeries to correct "lazy eye". This turned out to be a red flag as the pediatric ophthalmologist indicated that he had never done 4 strabismus surgeries on the same person.

An additional CT scan was ordered in August 1998, and the diagnosis of Osteopetrosis was made from that CT scan.

16 **Imaging**

- January 12th, 2006: We did a bilateral DEXA scan on Kaleb in our office.
- T-score on the R heel = -0.39

- T-score on the L heel = 0.00

17 **About Kaleb**

18 **Radiographic and Advanced Imaging for KD**

- Lumbar AP 1-12-2003
- Lateral 1-12-2003
- AP Pelvis 3-8-2005
- Lumbar Lateral 1-12-2006
- AP Pelvis 1-12-2006

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24 **Radiographic Studies for Lori Davis (Kaleb's mother)**

- Lateral Skull 12-31-2002
- Cervical Oblique 12-31-2002
- Cervical Lateral 12-31-2002
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28 **Disease Experts**

- The last 'Experts' on Osteopetrosis they saw in November of 2005 were from St. Louis and after several days of testing their final report to Kaleb and his family was that they will have to live with the fact that Kaleb will not get better and will be in a wheel chair the rest of his life.

29 **HEREDITY**

Does Kaleb have the ability to be as healthy as someone without the genetic predisposition??

Are there environmental factors that trigger or accelerate the Osteopetrosis?

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33 **Hair Test**

34 **Aluminum**

- Aluminum toxicity has been recognized in many settings where exposure is heavy or prolonged,

where renal function is limited, or where a previously accumulated bone burden is released in stress or illness.

- In aluminum-related bone disease, the predominant features are defective mineralization, aplastic bone disease (associated with painful spontaneous fractures, hypercalcemia, tumorous calcinosis), and osteomalacia that result from excessive deposits at the site of osteoid mineralization, where calcium would normally be placed.
  - Osteomalacia is a disease characterized by a gradual softening and bending of the bones with varying severity of pain; softening occurs because the bones contain osteoid tissue which has failed to calcify

- Becaria, A, Campbell, A, Bondy, SC: Aluminum as a toxicant. Toxicology and Industrial Health 2002; 18: 309-320.

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- Gilbert-Barness E, Barness LA, Wolff J: Aluminum toxicity. Arch Pediatr Adolesc Med 1998 May; 152(5): 511-2[Medline].

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35 **Lead**

Lead poisoning

- Manifestations may be highly varied, with multisystem involvement common.
  - Gastrointestinal - Colic, anorexia, nausea, vomiting, and constipation
  - Neurological - Headache, tremor, dizziness, malaise, extensor paralysis, mononeuritis, mental impairment, convulsions, and coma
  - Kidney - Fanconi syndrome, azotemia, isolated proximal tubular defects, rickets, or osteomalacia, delayed nephrotoxicity Hematological - Anemia
  - Miscellaneous - Muscle weakness
- Complications:
- Bone disease
  - Lead can interfere with bone development, leading to the formation of lead lines at bone metaphyses. These lines represent periods of growth arrest, not lead, per se.
  - Lead interferes with the conversion of 25-hydroxy vitamin D to 1,25-dihydroxy vitamin D and causes rickets or osteomalacia.

- MayoClinic.com, Lead Poisoning, March 15, 2005

36 **Lead cont.**

Additional Complications

- Nervous system and kidney damage
- Learning disabilities
- Speech, language and behavior problems
- Poor muscle coordination
- Decreased muscle and bone growth
- Hearing damage
- Memory and concentration problems
- Muscle and joint pain
- Damage to sperm-producing organs in men
- High blood pressure (hypertension)
- Infertility

Exposure to even low levels of lead can cause permanent damage. The greatest risk is to brain development, where irreversible damage may occur. High lead levels in children may cause seizures, unconsciousness and possibly death. Death by lead poisoning in children is rare, but it can happen.

Centers for Disease Control and Prevention: Blood lead levels in young children--United States and selected states, 1996

1999. Morb Mortal Wkly Rep 2000 Dec 22; 49(50): 1133-7.

Centers for Disease Control and Prevention: Update: blood lead levels--United States, 1991-1994. Morb Mortal Wkly Rep

1997 Feb 21; 46(7): 141-6.

Centers for Disease Control and Prevention: Blood lead levels in young children--United States and selected states, 1996-

1999. Morb Mortal Wkly Rep 2000 Dec 22; 49(50

Hu H, Aro A, Payton M, et al: The relationship of bone and blood lead to hypertension. The Normative Aging Study. JAMA

1996 Apr 17; 275(15): 1171-6.

Landrigan PJ, Todd AC: Lead poisoning. West J Med 1994 Aug; 161(2): 153-9.

37 ☐ **Mercury**

One disease symptom of Mercury poisoning: Osteomyelitis

- What Is Osteomyelitis?
  Osteomyelitis (pronounced: os-tee-oh-my-uh-lie-tus) is a bone infection often caused by a bacteria called Staphylococcus aureus (pronounced: sta-fuh-low-kah-kus are-ee-us). Depending on how the bone becomes infected and the age of the person, other types of bacteria can cause it, too. In kids and teens, osteomyelitis usually affects the long bones of the arms and legs.
- Bacteria can infect bones in a number of ways. Bacteria can travel into the bone through the bloodstream from other infected areas in the body. This is called hematogenous (pronounced: heh-meh-tah-gen-us) (hema refers to the blood) osteomyelitis, and is the most common way that people get bone infections.
- Another way is by direct infection, when bacteria enter the body's tissues through a wound and travel to the bone (like after an injury or trauma). Open fractures - breaks in the bone with the skin also open - are the injuries that most often develop osteomyelitis.
- Mercury poisoning has a long list of mild to extremely severe symptoms. For more information, please visit the following websites:
  - Sam Queen and Betty A. Queen, Chronic Mercury Toxicity, New Hope Against an Endemic

Disease, 1996.
- Stock, "Die Defaehrlichket des Quecksilberdampfes"; F. Gasser, "Quecksilberbelastung im Menschlichen Korper durch Amalgam," *Med.-Biol. Arbeits und Forschungsgemeinsch* (Baden-Baden, Germany: Dtsch. Zahnarzt., 1976): K. D. Jorgensen, "The Mechanism of Marginal Fracture of Amalgam fillings," *Acta Odont. Scan.* 23 (1965): 347.

38 **Cadmium**

- Cadmium is a toxic heavy metal with no positive metabolic function in the body, and is relatively rare but more toxic than Lead. Hair cadmium levels provide an excellent indication of body burden. Moderately high cadmium levels are consistent with hypertension, while very severe cadmium toxicity can cause hypotension. Cadmium affects the Kidneys, lungs, testes, arterial walls, bone and interferes with many enzymatic systems and depletes glutathione, leads to anemia, proteinuria, glucosurea, depletes calcium, phosphorus and zinc. Cadmium absorption is reduced by zinc, calcium and selenium. Alkaline Phosphatase is commonly elevated with Cadmium toxicity.

39 **Copper**

Copper could be called a nutritive paradox, since its merit also forms the basis of its detriment. When it comes to helping or hindering health, the metal's equivocal nature lies in the fact that copper is a pro-oxidant. That means that its good reputation for doing good deeds—aiding the transport of iron, preventing the transformation of good fat into bad fat (lipid peroxidation), helping wounds to heal—is sullied by its association with spurring on free radical activity and its subsequent oxidative damage at the cellular, tissue and organ levels.(1) Oxidative damage has been implicated in aging, as well as the development of cancer, heart disease and many other diseases. Some evidence points to patients with Wilson's disease (an inherited genetic defect that causes a buildup of copper and the inability to release the metal), have signs of lipid peroxidation in their livers. Wilson's disease can result in damage to the liver, kidneys, brain and eyes, as well as anemia (due to compromised iron absorption), jaundice and softening of the bones. Some patients have also been known to develop cirrhosis of the liver as a result of the copper-mediated oxidative damage. Myocardial infarction (MI) patients have been found to have high levels of plasma copper too.(2) It seems that copper may heighten the inflammatory response through oxidation that may lead to atherosclerosis. Meanwhile, other evidence, such as a study from the University of Heidelberg, Germany, suggests that copper-induced oxidation may play a role in the development of Alzheimer's disease. That's because copper-mediated oxidative damage has been implicated in promoting the toxicity of beta A4 (A beta) and the metabolization of amyloid precursor protein (APP), two contributing factors to the neurodegenerative pathology.(3)

1. Dameron CT, et al. Mechanisms for protection against copper toxicity. Am J Clin Nutr 1998 May;67(5 Suppl):1091S-1097S.
2. Trace elements in prognosis of myocardial infarction and sudden coronary death. Journal of Trace Elements in Experimental Medicine (USA), 1996, 9/2(57-62).
3. Multhaup G. Amyloid precursor protein, copper and Alzheimer's disease. Biomed Pharmacother 1997;51(3):105-11.

40 **Copper Toxicity**

Copper Toxicity: excessive copper levels that have been associated with physical and mental fatigue, anxiety, depression and other mental problems, schizophrenia, learning disabilities,

hyperactivity/ADD, moodswings (sometimes violent, criminal or psychotic behavior) and general behavioral problems, memory and concentration problems, postpartum depression, spinal and vascular degeneration, headaches, increased risk of infections, insomnia and other sleep disorders, arthritis, spinal/muscle/joint aches and pains, seizure, delirium, stuttering, hyperactivity, arthralgias, myalgias, hypertension, gingivitis, dermatitis, discoloration of skin/hair, preeclampsia, weight gain, hemangiomas and several cancers.

Toxicity is not the only concern; Just having an improper balance of copper, iron and zinc can result in poor copper status, which over time may lead to heart and circulatory problems, bone abnormalities and complications in the immune system.

- Jensen LS. Precipitation of a selenium deficiency by high dietary levels of copper and zinc. Proc Soc Exp Biol Med 1975;149(1):113-116.

- Avery SV, Howlett NG, Radice S. Copper toxicity towards Saccharomyces cerevisiae: dependence on plasma membrane fatty acid composition. Appl Environ Microbiol 1996;62 (11) :3960-3966.

- "Copper and Human Health and Safety," George A Cypher, International Copper Association Limited, 260 Madison Avenue, New York, NY 10016, USA.

- "Copper in Human Health," Technical Note TN 34, Copper Development Association, Orchard House, Mutton Lane, Potters Bar, Herts EN6 3AP, UK.

- "Copper in Plant, Animal and Human Nutrition," Technical Note TN 35, Copper Development Association, Orchard House, Mutton Lane, Potters Bar, Herts EN6 3AP, UK.

- "Copper, The Directory of Nutritional Supplements," The Vitamin Connection, January/February 1992

- "Dietary Reference Values for Food Energy and Nutrients for the United Kingdom – Report on Health and Social Subjects 41," Department of Health, HMSO, London 1991.

41 **Copper – Ceruloplasmin**

- Ceruloplasmin is a test that measures the amount of ceruloplasmin (a copper-containing protein) in blood serum.
- Test Results:
  - Copper values are low in cases of Wilson's disease, Menke's kinky hair syndrome, malabsorption, cystic fibrosis and malnutrition.
  - Elevated values are associated with infections, pregnancy, estrogen or anti-seizure drug use, inflammation, tissue necrosis, trauma, cancer, anemias, excessive dietary intake, and with systemic lupus erythematosus. The majority of serum copper is bound to ceruloplamsin and the remaining copper is bound to albumin, metallothionein or other proteins.
- Copper excess lowers serum ceruloplasmin (CP) oxidase activity, which results in compromised free radical scavenging capacity and potentially an increase in oxidative damage.(19)
  - Medline Plus, Ceruloplasmin, Feb 9, 2005.

* It is important to note that these toxic elements carry a wide range of mild to severe side effects and complications that are not bone-related.

42 **Ceruloplasmin**

Ceruloplasmin testing was performed on Kaleb to rule out the possibility of error in the initial findings of copper toxicity in his hair test and urinary analysis due to external contamination or lab error. The ceruloplasmin test confirms that excess copper is present within the blood serum.

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44 **DMSA post-test results for Kaleb Davis (Dec. 2005)**

45 **Well Sample**

46 **First Draw Sample (Pipes)**

47 **The Take-Home Message**

- This case is in the early stages, but in just three weeks we saw results/progress in fact he was able to stop all pain medication.
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50 **TRAP Results for Kaleb Davis**

- TRAP = 71 August of 2000
-
- TRAP = 37.6 (4.3-21.2) February 17, 2006
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- TRAP = 32.1 U/L on 3-13-2006.
-
- TRAP = 24.6 U/L on 5-23-2006

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51 **Excerpts from Lori Davis's Website**

- Thought it was time to give another update. We went to Dayton yesterday to see the nutritionist and chiropractor. This man and his staff have been wonderful to our family and we feel very blessed that they "found" us! Amazing story.

- We have completely changed the majority of our eating habits lately. The blood/hair/urine/stool samples that we took in December indicating heavy metal toxicity. We are trying to eliminate these metals from Kaleb's system so we are changing our diet as well as many other things in his environment (including type of shampoo, etc). This is a huge change for us but it's something we should have been conscious of all along, now it's catching up with us. So, lots and lots of changes.

- On a down note, the X-rays definitely showed scoliosis which is very concerning. Right now we are doing exercises to try to reverse the curve and we are continuing total non-weight bearing on the hip. The other down note was the X-ray showed possible fractures of the hip which is not something we want to hear. And, the amount of cartilage and joint space is very, very small in the hip area. This is very concerning. The doctor said "Miracles do happen". We're praying for that miracle.
-

http://www.caringbridge.com/oh/kalebdavis/history.htm

52 **Web Update from Lori 2/3/2006**

- On Thursday, we went to Dayton to see Dr. Merkle. Can I say one more time Thank You God for bringing this man into our lives? Do I think that he will cure Kaleb....no. That is NOT my

expectation. But I do believe that if we can get the metals out of his body, continue with the organic foods/soaps/etc...and get his body in the best shape possible, that this will definitely NOT be detrimental to him. I am just so very thankful we have this man working with us. I am still amazed.

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- http://www.caringbridge.com/oh/kalebdavis/history.htm

53 **1-7-2007 update**

- Ceruloplasmin and serum copper were chronically elevated.
  - How can these be lowered?
    - Copper chelation with tetrathiomolybdate, penicillamine and triethylene tetramine dihydrochloride

54 **The Slippery Slope of Genetic Testing**

- Ethics: Pregnancy-fetal traits, abortion Jobs, Insurance, Schools
  - Abortion of less than perfect genetic traits
    - Dwarfs, too short, not enough hair, not smart enough, not athletic enough
- Medical Mentality
  - No need to look further
  - Not the patients fault- relieved of responsibility
  - Patient options- Surgery, drugs, futility
- Natural/alternative
  - Genes load the gun...environment pulls the trigger.
  - Are there now environmental exposures that are allowing or causing these genes to be activated?
  - If it is a dominant gene, why didn't it die out already?
  - We can improve health- can we get patient as healthy as they were before the genetic disease started?
  -

55 **Just Two Possibilities With My Care**

1. The patient gets better
2. The patient doesn't get better, they won't/can't get worse.

NOTHING TO LOSE TAKING CARE OF THIS TYPE OF PATIENT.

56 **The Challenge**

- Are you willing to reach out?
- Are you willing to be the 'One'?
-