THE STORY OF BIOTINIDASE DEFICIENCY AND ITS INTRODUCTION INTO NEWBORN SCREENING:

THE ROLE OF SERENDIPITY

Barry Wolf, MD, PhD
d-BIOTIN
(Vitamin H)

Bioassay not run by Sigma.

Store Desiccated at 0-5°C

 Obtained Thru (pfs)
Advanced Formula STRESSSTABS. No other stress formula vitamin can hold a candle to it.
I wasn’t getting ENOUGH VITAMINS FOR MY HAIR.

I wasn’t. There was a time when my hair caused me problems. In fact, I tried doing anything and everything that made sense and even a few things that made no sense. I even considered shaving my head. By taking all of it, I thought I could finally rid myself of the problem.

Many people would have taken a pill and looked like nothing on top. After seeing the results my decision was made. As you can see from the photograph, I was considerably more handsome with lots of healthy hair. There had to be a way of improving my hair.

In 1971 I discovered Head Start Vitamins for My Hair.

It surprised me to discover that vitamins, minerals, and minerals could work. I had never had enough of the magical unsubstantiated remedies for baldness. Now I wanted substance and certainty.

As my studies progressed they began to point more and more to the area of nutrition. Major nutrition experts backed my actions and experiments, and it was thus confirmed that vitamins and minerals are absolutely essential for

Keeping hair health is not complete. Long before we know, hair begins to grow beneath the skin. If this crucial time when the hair shaft requires proper vitamins and minerals is missed, then other body cells, which depend on your nutritional integrity are sufficient for the normal function of your hair.

An alternative began to be apparent. Hair requires vitamins in increased amounts for healthy growth. With the aid of a nutritional specialist, I discovered a supplement that solved my problem. It required 12 vitamins and minerals in a specially compounded form. Unfortunately, this compound of precious ingredients required that more knowledge be produced. This was the only drawback. Most people would lack the chemical knowledge to mix and use the formula.

After six months of careful and encouraging experimentation of effective and affordable solutions was found. I was able to combine the necessary vitamins and minerals in exact amounts needed to maintain healthy and manageable hair.

Braun 31 improves Head Start in 1977.

Now, Head Start is not a magical baldness remedy. It is an advanced formula for valuable hair care. Over the years we’ve added other essential minerals and vitamins upon recommendation from nutritional specialists. Most recently we’ve added Braun 31 to the Head Start vitamin solution. Certain elements are deposited with age. Braun 31 supplements the natural loss, and is an important nutrient discovery that’s replaced my own need for it.

So if you’re like I am and look better with a healthy head of hair, come to a hair salon, buy Head Start today.
Biotin

• B-Complex vitamin
• Coenzyme for 4 carboxylases in man
• Present in the unbound form in plants and fruits
• Present in protein-bound form in animal tissues
• Biotin deficiency is difficult to induce in mammals - fed raw eggs or avidin
• Biotin deficiency results in neurological and cutaneous problems
Biotin-Dependent Carboxylases

Propionyl-CoA carboxylase  Catabolism of amino acids
Beta-methylcrotonyl-CoA carboxylase  Catabolism of amino acids
Pyruvate carboxylase  First step of glucose synthesis
Acetyl-CoA carboxylase  First step of fatty acid synthesis
TWO FORMS OF MULTIPLE CARBOXYLASE DEFICIENCY

**Early-Onset MCD**
- Onset before 1 month
- Lethargy, seizures, ataxia, rash, hair loss, developmental delay
- Ketolactic acidosis, organic aciduria, hyperammonemia
- Biotin-Responsive
  - Normal plasma biotin

**late-Onset MCD**
- Onset after 1 month
- or low nl plasma biotin
- HCS deficiency
HOLOCARBOXYLASE SYNTHETASE

Biotin

Apocarboxylases (PCC, MCC, PC, ACC)

Holocarboxylases

Proteins
- Amino acid catabolism

Lipids
- Fatty acid synthesis

Carbohydrates
- Gluconeogenesis
Hair growth with biotin treatment
Relation between the Biotin Dose and Plasma Biotin Concentration in the Patient (▲) and in a Normal Control (●)
ANIMAL BIOTINIDASE

BY

JAAKKO PISPA

HELSINKI
BIOTINYL - LYSINE (BIOCYTIN)

BIOTINYL - p - AMINOBENZOATE
Biotin Cycle

- Biotinidase
- Biocytin
- Protease Degradation
- Free Biotin
- Apocarboxylases
- Holocarboxylase Synthetase
- Holocarboxylases
- Amino Acid Catabolism
- Fatty Acid Synthesis
- Gluconeogenesis
Biotin Cycle

- Biotinidase
- Biocytin
- Protease Degradation
- Free Biotin
- Lysine
- Holocarboxylase Synthetase
- Apocarboxylases
- Holocarboxylases
- Amino Acid Catabolism
- Fatty Acid Synthesis
- Gluconeogenesis
Clinical Features Biotinidase Deficiency

- Seizures
- Lethargy
- Hypotonia
- Ataxia
- Cutaneous abnormalities, such as rash, alopecia and conjunctivitis
- Abnormal organic acids
- Hyperammonemia
- Sensorineural hearing loss
- Optic atrophy
- Cellular immunity abnormalities
- Developmental delay
Structure of the Human Biotinidase Gene

Exons 1a+1b: 169 bp
Exon 1c: 301 bp
Exon 2: 265 bp
Exon 3: 150 bp
Exon 4: 1502 bp

Intron 1a: 113 bp
Intron 1b: 33.6 kb
Intron 2: 6.22 kb
Intron 3: 712 bp
Reasons for Newborn Screening for Biotinidase Deficiency

• The disorder can result in irreversible neurological abnormalities.

• Children with the disorder do not exhibit symptoms immediately after birth; symptoms usually occur at several months of age or later.

• The disorder can be effectively treated with a simple, inexpensive form of therapy, oral biotin. There is no known toxicity of the vitamin.
• Symptoms can effectively be prevented from occurring with treatment.

• Primary care physicians and other health professionals usually are not familiar with the disorder and routinely do not include it in their differential diagnoses.

• The method of screening is inexpensive compared to other newborn screening tests.
Accession # 103257
Infant Name/Sex HARRY LESS
Mother's Name HOP LESS
Date of Birth 5/19/02

AFFIX BARCODE LABEL ABOVE OR PRINT PATIENT INFORMATION

ALL SAMPLES:
COMPLETE THE FOLLOWING
DATE OF COLLECTION 5 24 02
TIME OF COLLECTION 11:00
COLLECTOR INITIALS BLW
INFANT TRANSFUSED? Y [ ] N [X]

SECOND BLOOD ONLY:
PRINT NAME OF PRIMARY CARE PROVIDER
DR. WOLF

STATE OF CONNECTICUT • DEPT. OF PUBLIC HEALTH
DIVISION OF LABORATORY SERVICES
P.O. BOX 1880 • HARTFORD, CT 06142
(800) 529-6565
<table>
<thead>
<tr>
<th>Sister</th>
<th>Brother</th>
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<tbody>
<tr>
<td>• Skin rash</td>
<td>• Skin rash</td>
</tr>
<tr>
<td>• Blurred speech</td>
<td>• Poor vocabulary</td>
</tr>
<tr>
<td>• Poor articulation</td>
<td>• Poor articulation</td>
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<tr>
<td>• Hypotonia</td>
<td>• Hypotonia</td>
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<td>• Delayed motor function</td>
<td>• Delayed motor function</td>
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<td>• Intention tremor</td>
<td>• Hand tremor</td>
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<tr>
<td>• Clumsiness</td>
<td>• Wide-based gait</td>
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<tr>
<td>• Low normal development</td>
<td>• Borderline normal development</td>
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• Newborn screening for biotinidase deficiency is now performed in all the states in the U.S. and in over 30 countries in the world.
• Today, around the world, literally hundreds, if not thousands, of newborns have been identified as having biotinidase deficiency and have been treated since birth with biotin.
• Evidence supports that these children are doing well and we have all the expectations that they will have a normal life as long as they continue their daily vitamin supplement.
EPILOGUE

“If you have to have an inherited metabolic disease. . . . biotinidase deficiency is the one to have.”