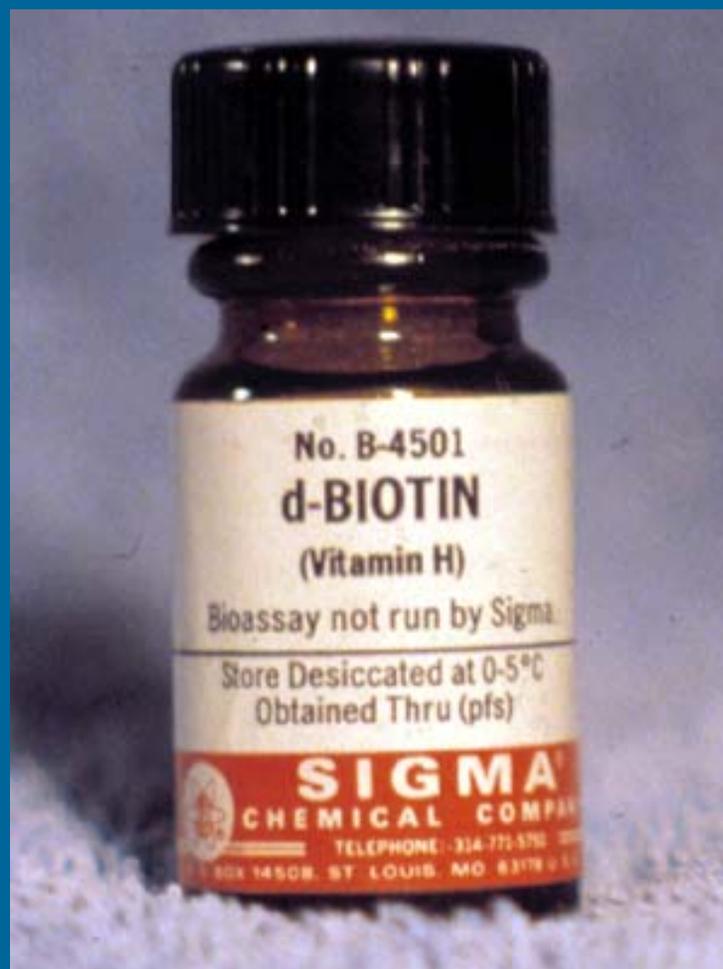


THE STORY OF BIOTINIDASE DEFICIENCY AND
ITS INTRODUCTION INTO NEWBORN
SCREENING:

THE ROLE OF SERENDIPITY

Barry Wolf, MD, PhD



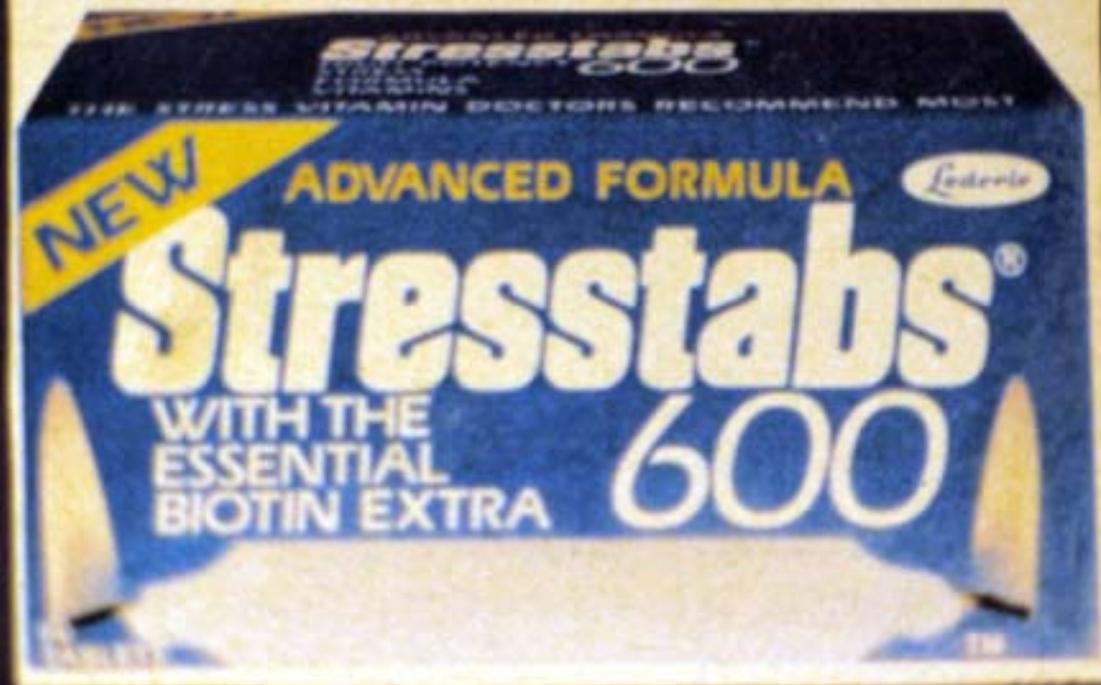
No. B-4501
d-BIOTIN
(Vitamin H)

Bioassay not run by Sigma

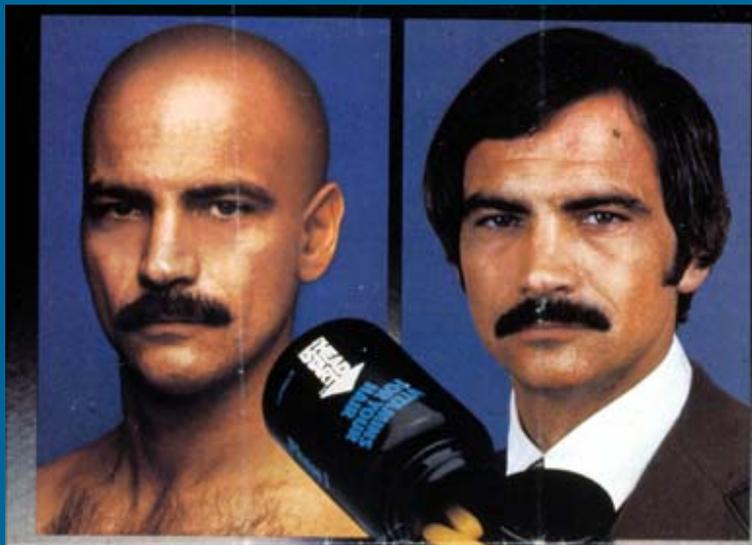
Store Desiccated at 0-5°C
Obtained Thru (pfs)

SIGMA
CHEMICAL COMPANY
TELEPHONE: 314-775-5700
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Advanced Formula STRESSTABS.[®]
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 it all off I thought I could finally rid myself of the problem. Vanity spurred me to retouch a photograph to see what I'd look like with nothing on top. After seeing the results my decision was made. As you can see from the photograph I am 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.

My crusade took me to dermatologists, specialists, and finally to nutritionists in search of an answer. I'd had enough of the magical and questionable remedies for baldness. Now I wanted substance and certainty.

As my studies progressed they began to point more and more to one area. Nutrition. Major nutrition experts backed my action and encouraged me to pursue my studies. They informed me that vitamins and minerals are absolutely essential for

keeping hair healthy and abundant. Long before it shows, hair begins to grow beneath the scalp. It is here and at this crucial time when the hair shaft requires proper nutrition. Hair cells reproduce seven times faster than other body cells. Even though your nutritional intake may be sufficient for the rest of your body, your hair may be starving.

An alternative began to be apparent. Hair may need a vitamin supplement for healthy growth. With the aid and advice of nutrition specialists I found such a supplement and alleviated my hair problems. It required 8 vitamins and 6 minerals in a specially combined form. Unfortunately this compound of precise ingredients required a bit more knowledge than elementary chemistry to be produced. This was its only drawback. Most people would lack the chemical know-how to mix and use the formula.

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

Now this product is available to you at every affordable price.

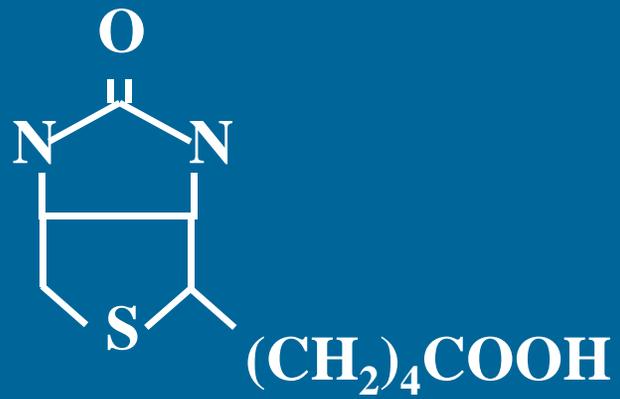
Though Head Start was developed for men with nutrient deficiencies, it has generated a positive response from women. More and more women are finding that Head Start conditions their hair like no ordinary chemical substitute can. Head Start builds hair shafts from the inside. No astringent or conditioner does this.

Brasium 321 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 nutrition researchers. Most recently we've added Brasium 321 to the Head Start formula. Studies indicate that certain elements are depleted with age. Brasium 321 supplements this natural loss, and is such an important nutrient discovery that I've placed my own name behind it.

So if you're like I am and look better with a healthy head of hair compared to a shave, send for Head Start today.

Biotin



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

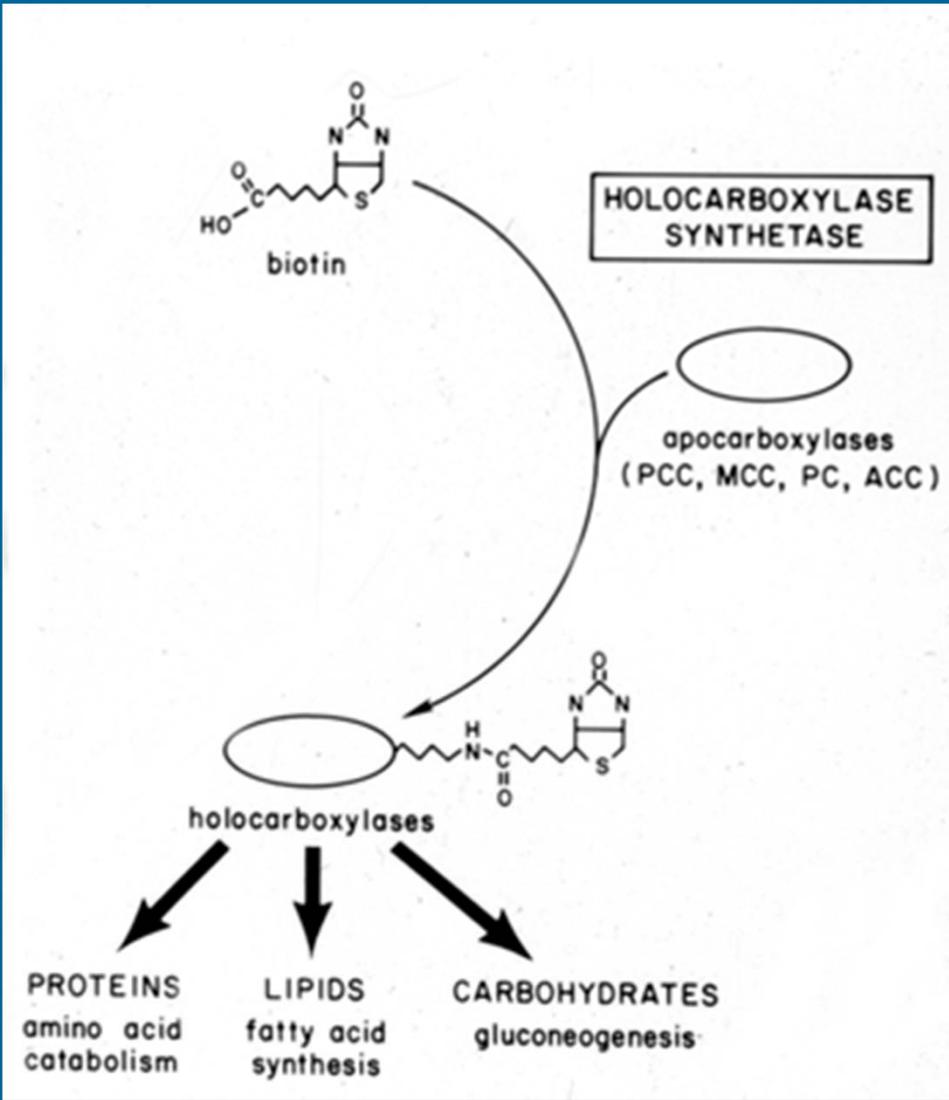
Catabolism of amino acids

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

Late-Onset MCD

Onset before 1 month

Onset after 1 month

Lethargy, seizures, ataxia, rash, hair loss, developmental delay

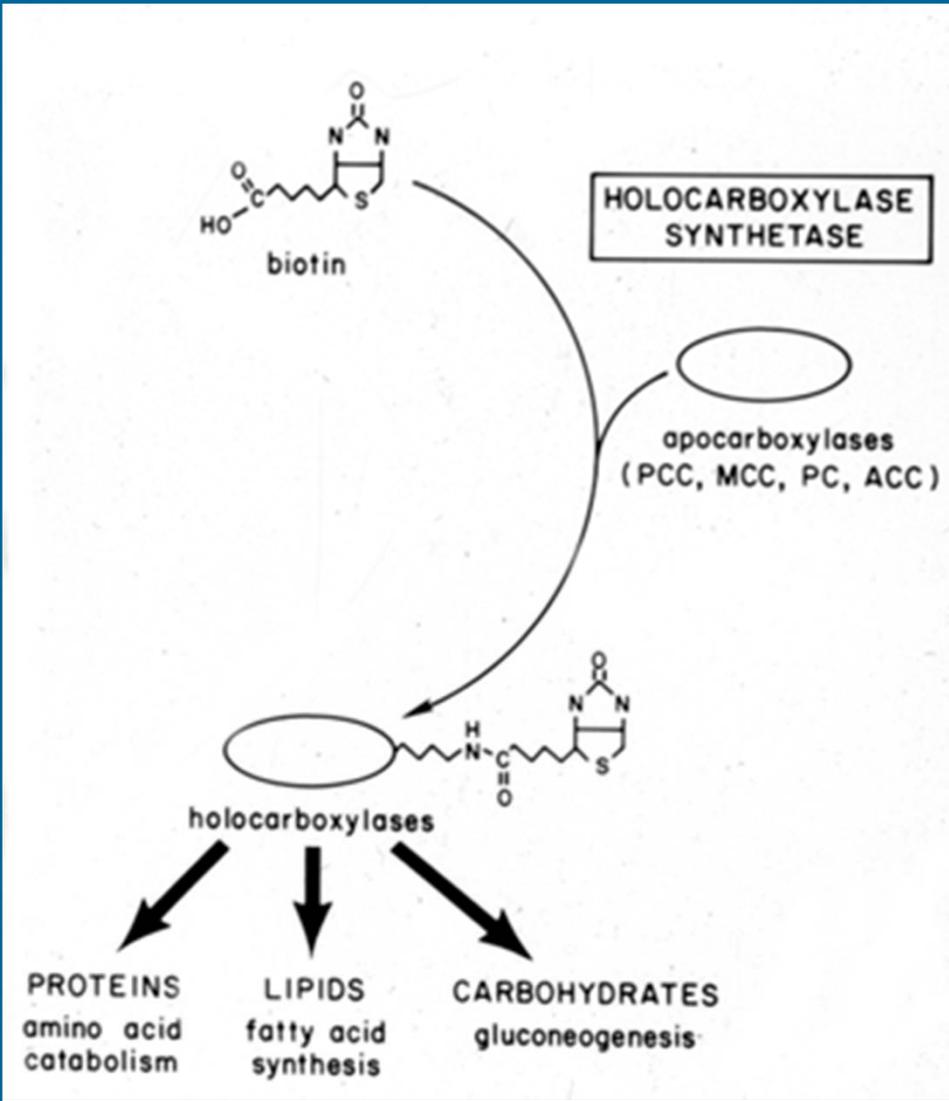
Ketolactic acidosis, organic aciduria, hyperammonemia

Biotin-Responsive

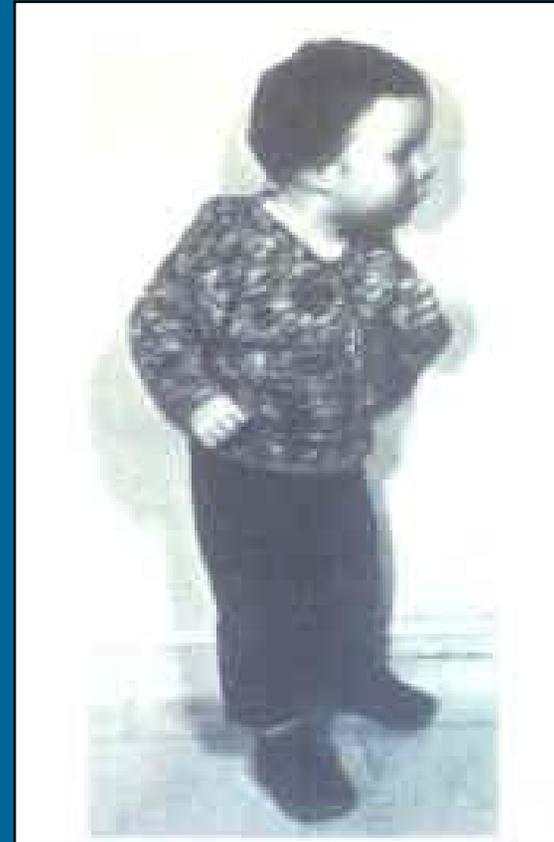
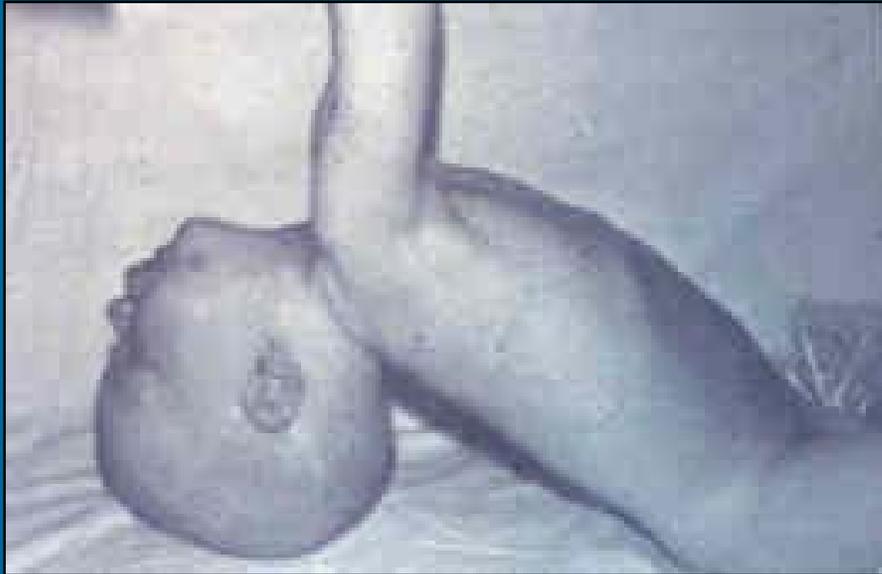
Normal plasma biotin

↓ or low nl plasma biotin

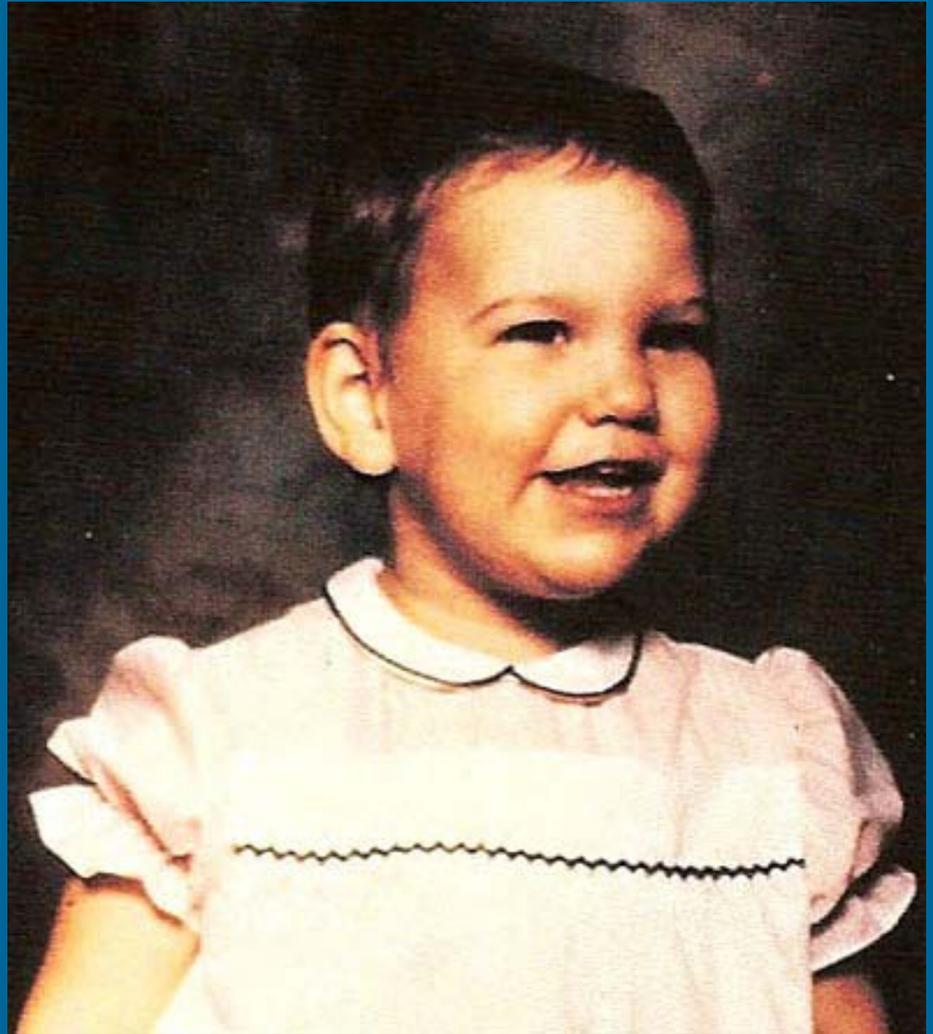
HCS deficiency

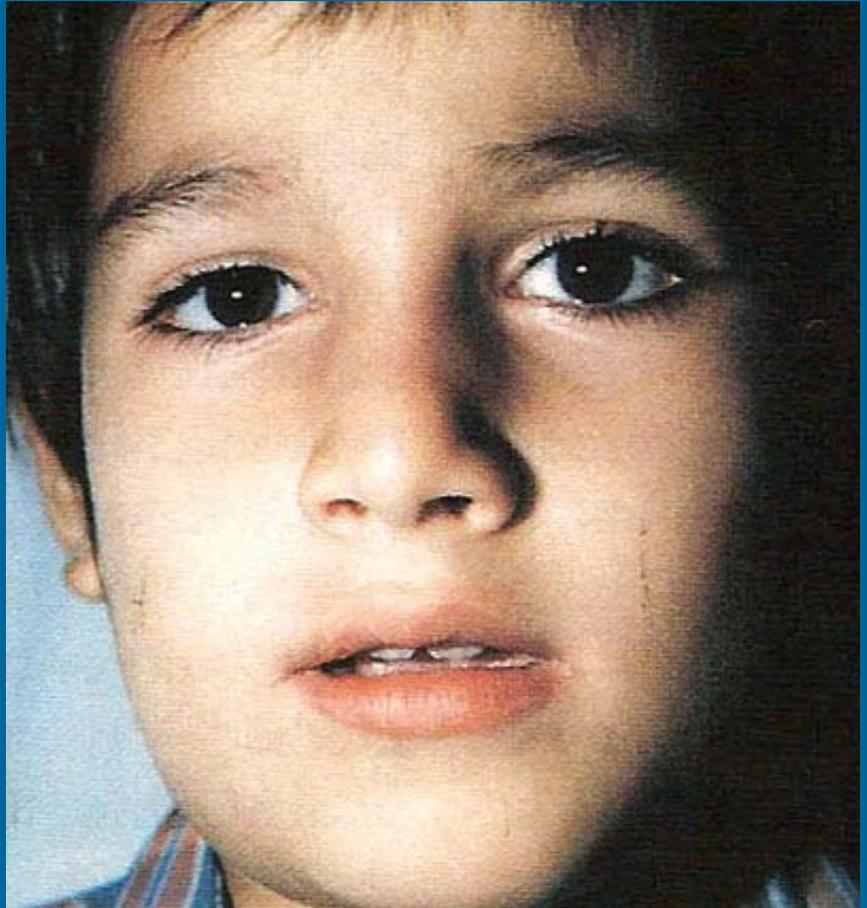




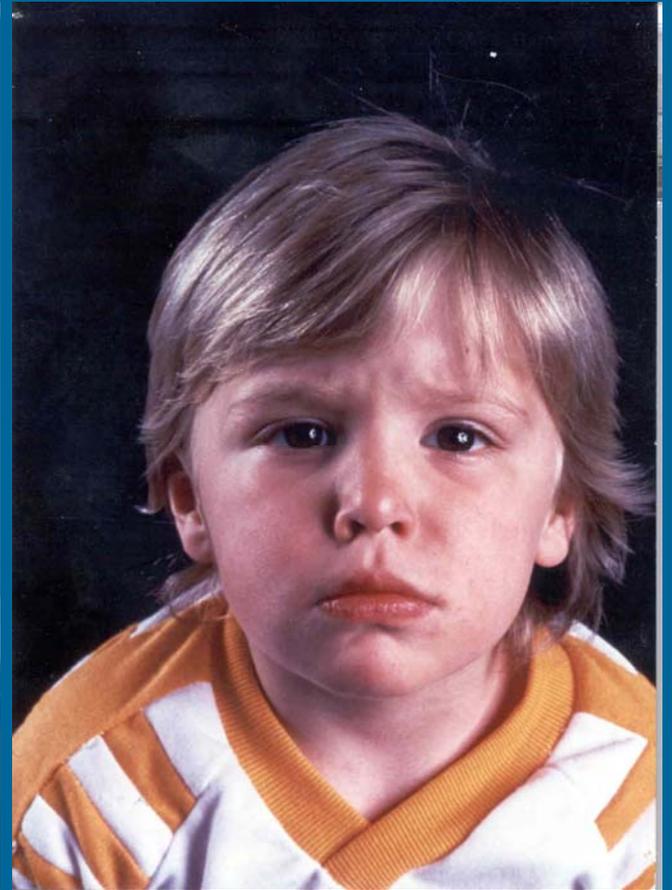
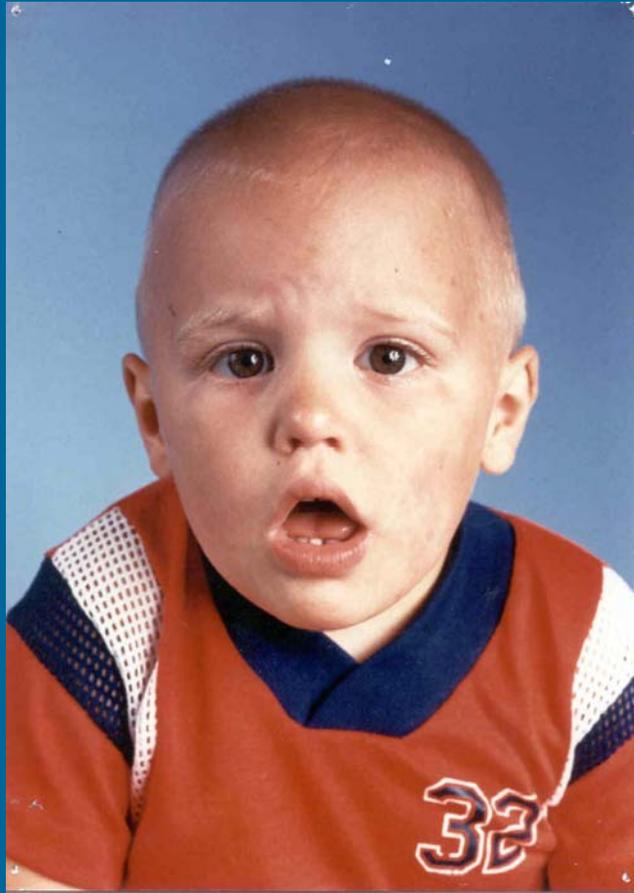




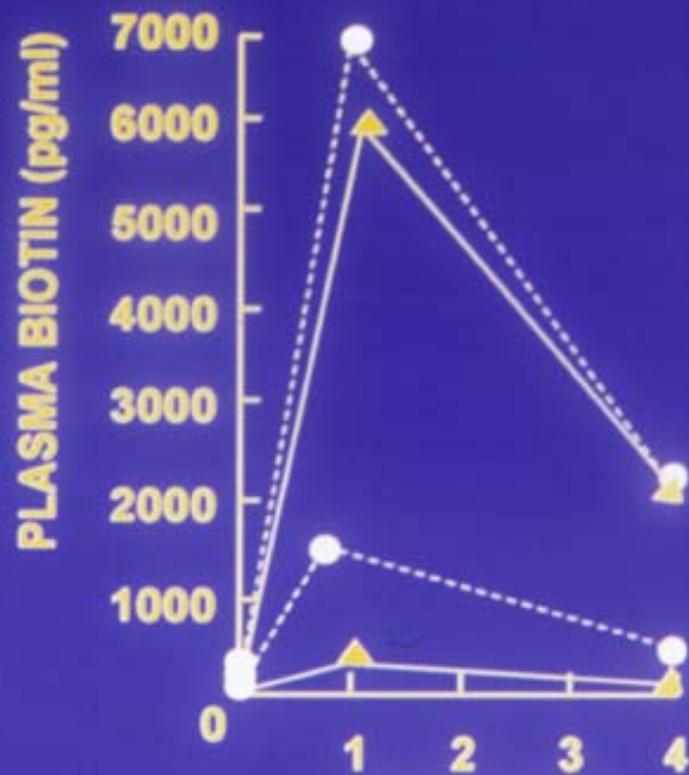


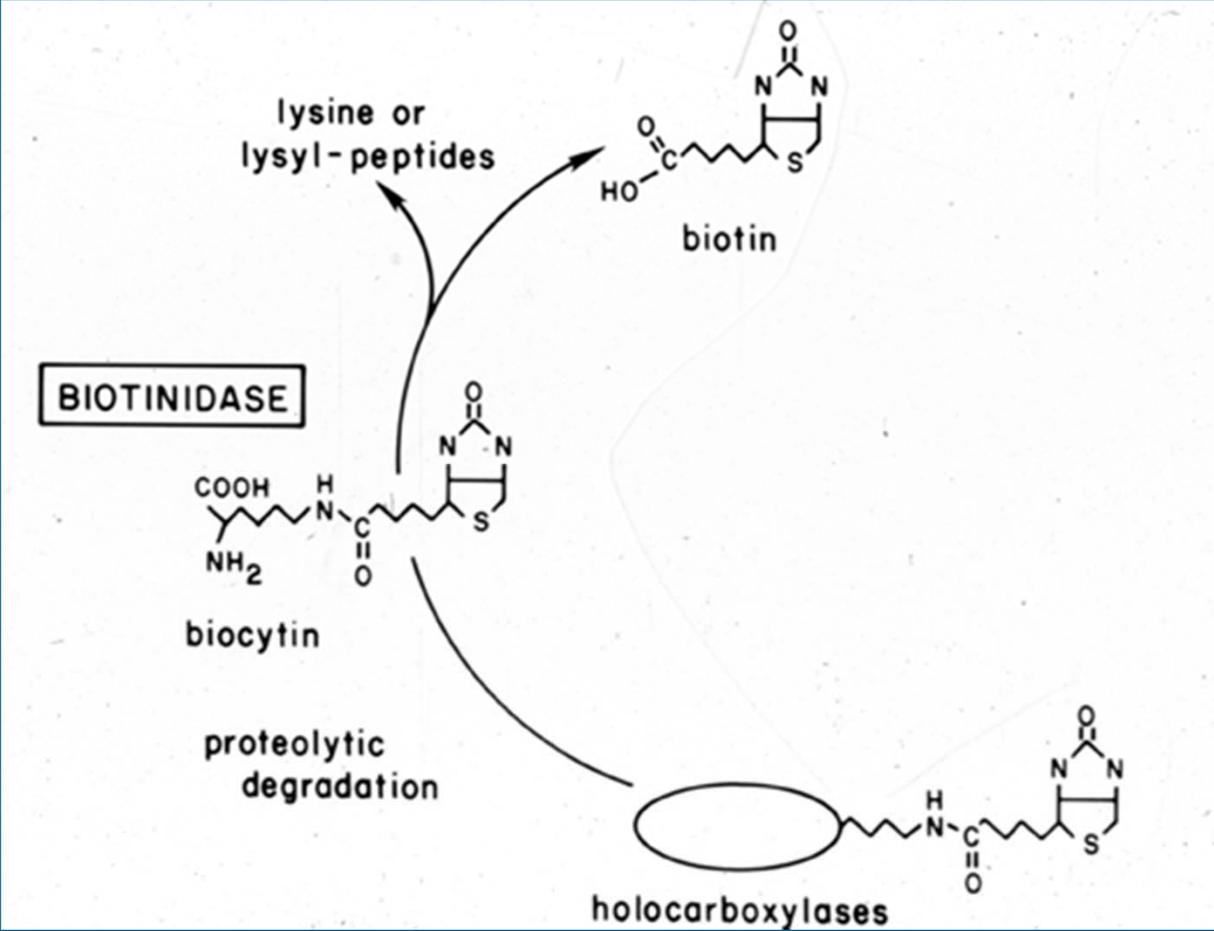


Hair growth with biotin treatment



Relation between the Biotin Dose and Plasma Biotin Concentration in the Patient (▲) and in a Normal Control (●)



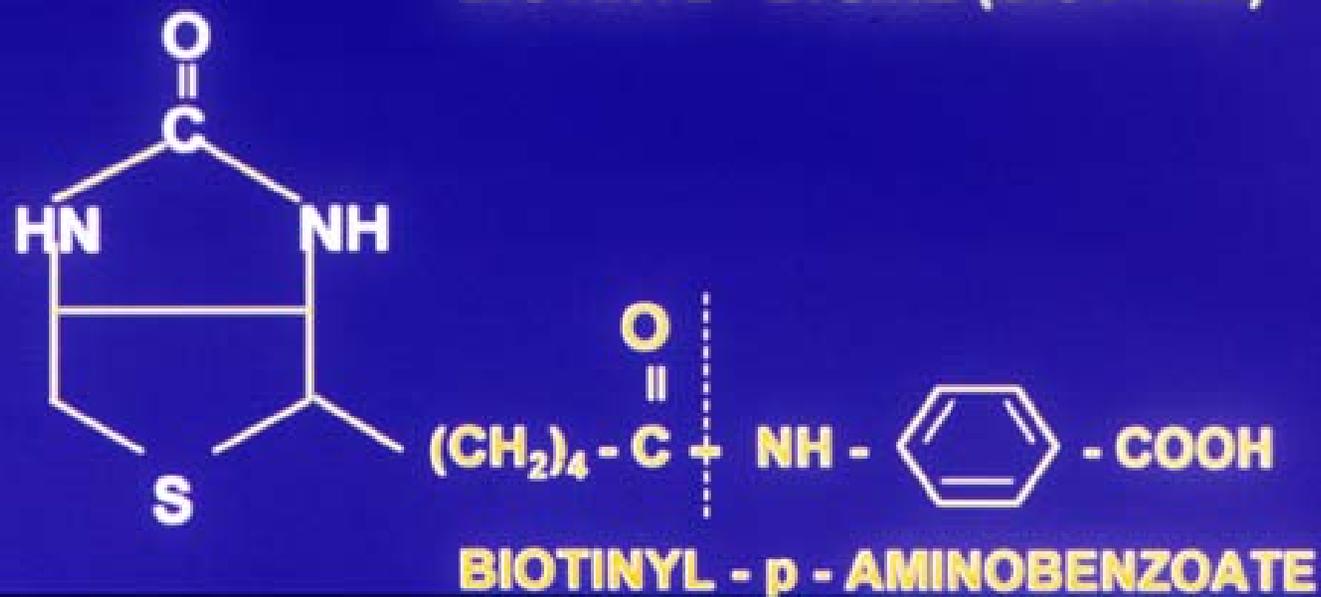
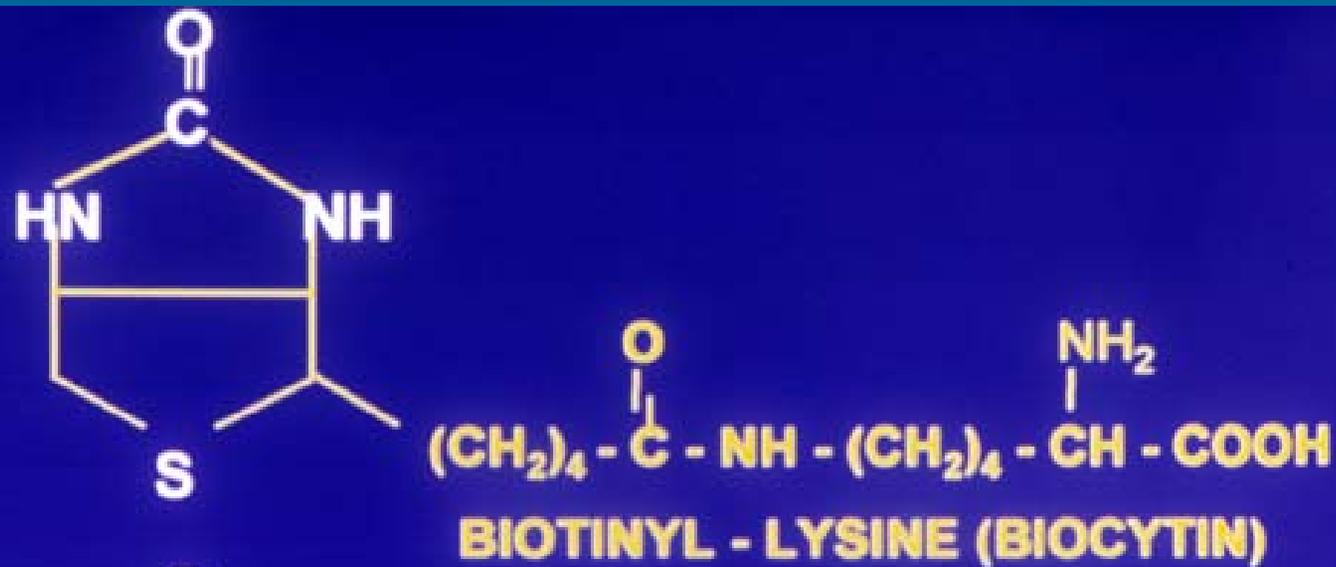


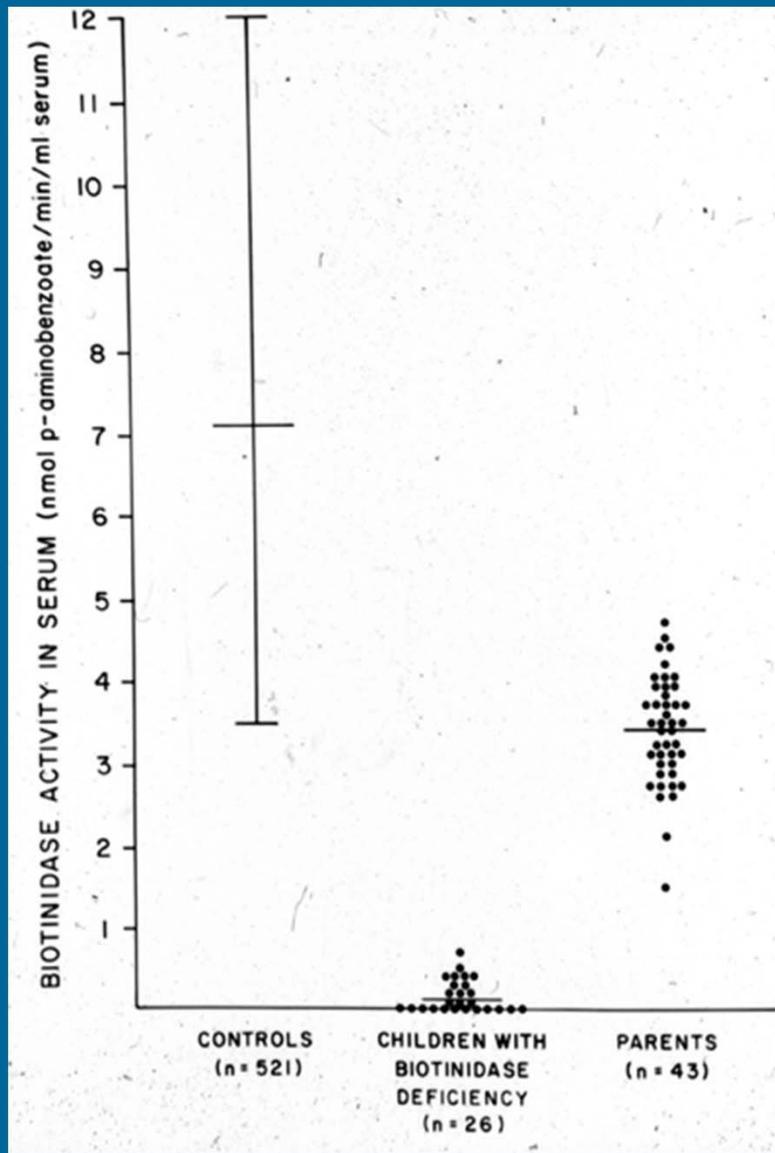
To Dr Barry Wolf
with compliments
Author

ANIMAL BIOTINIDASE

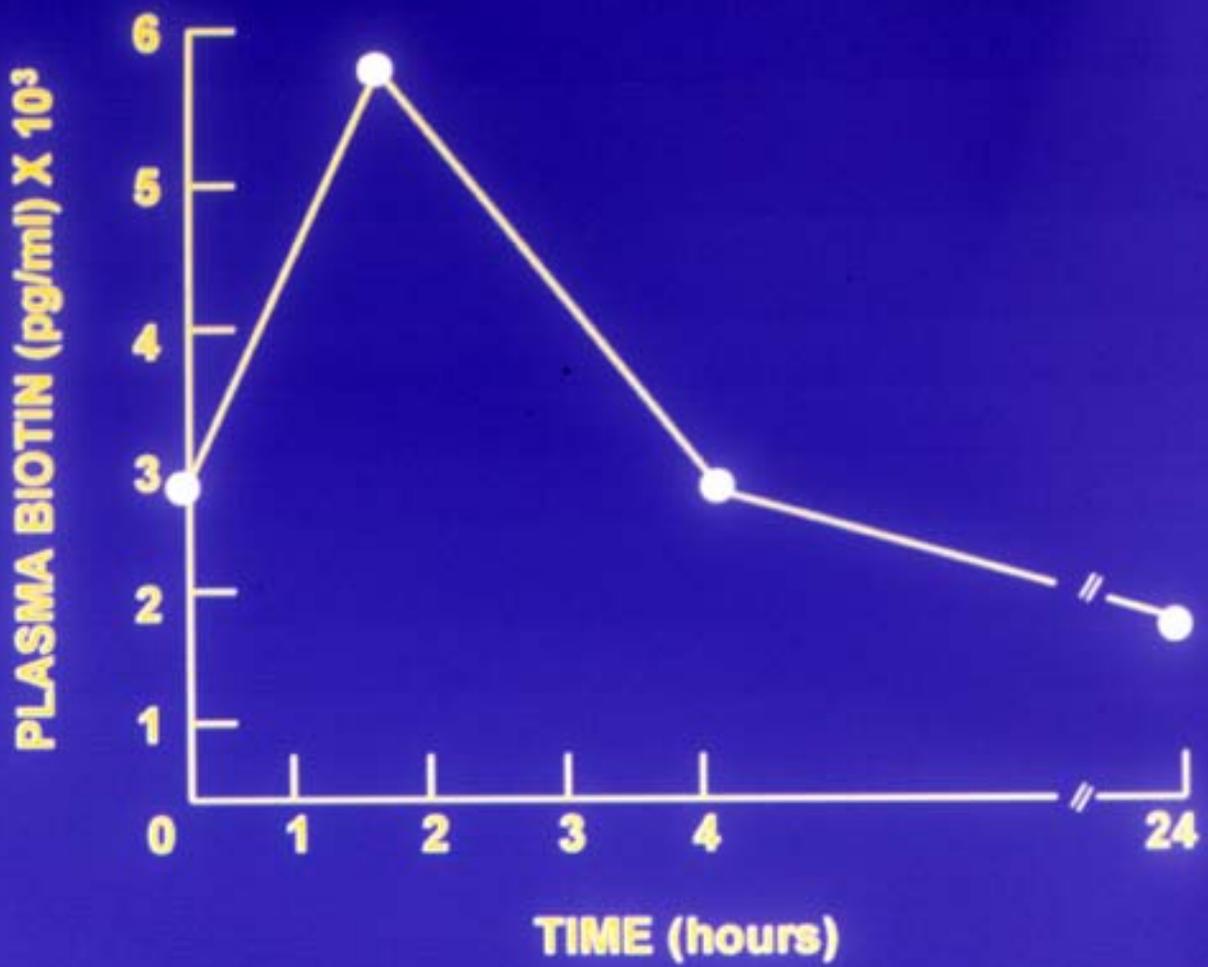
BY
JAAKKO PISPA

HELSINKI

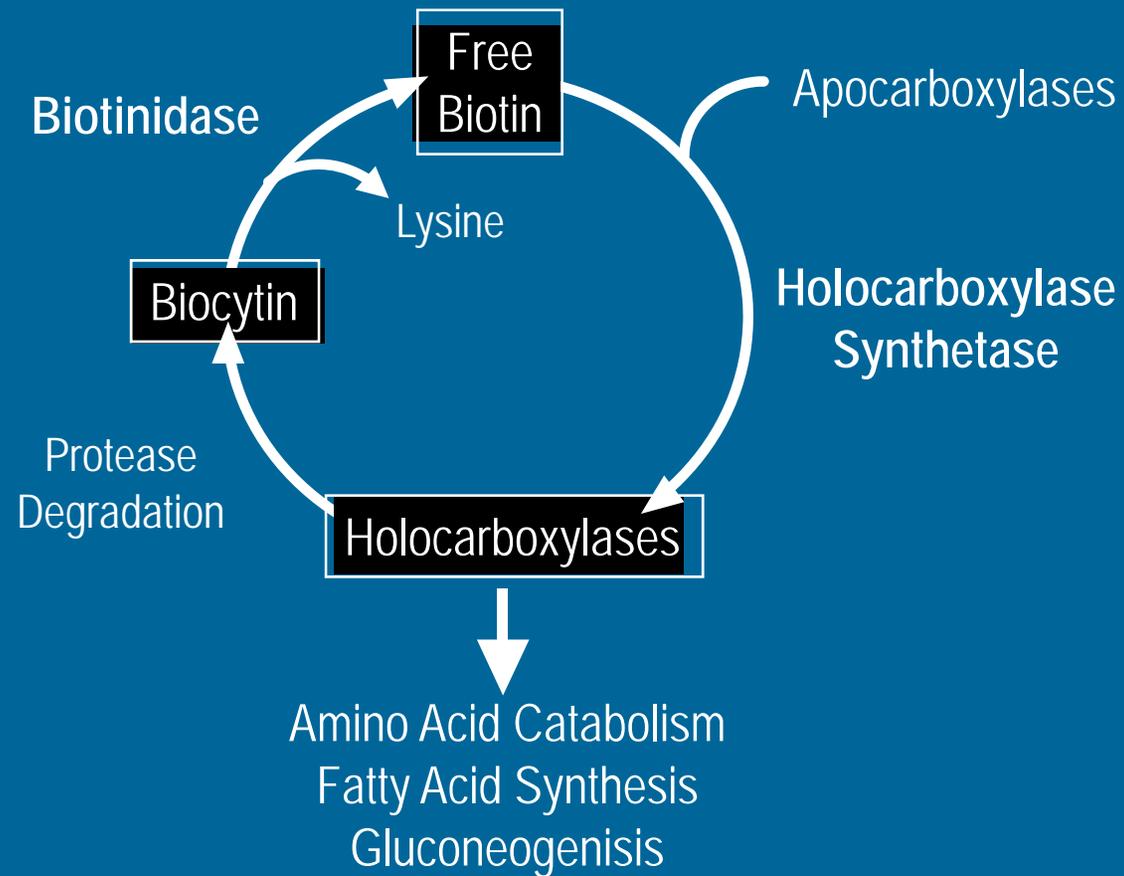




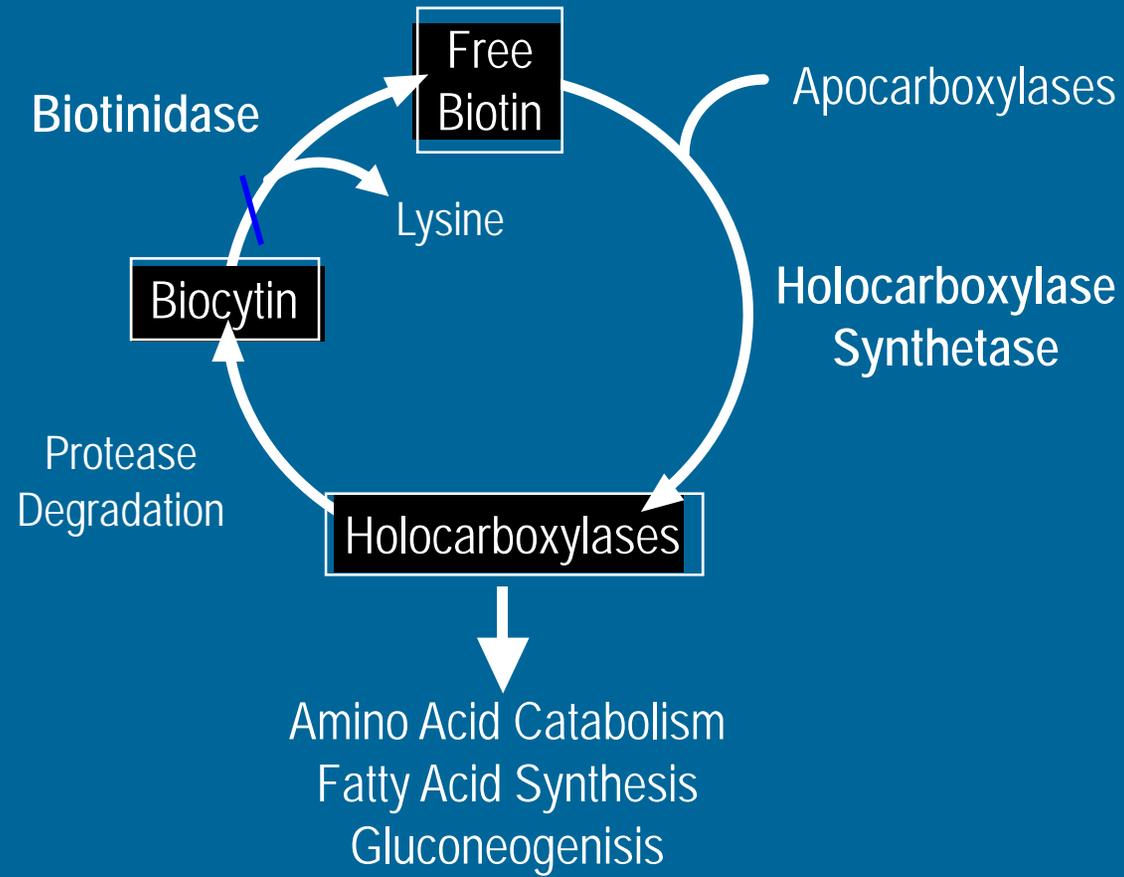




Biotin Cycle



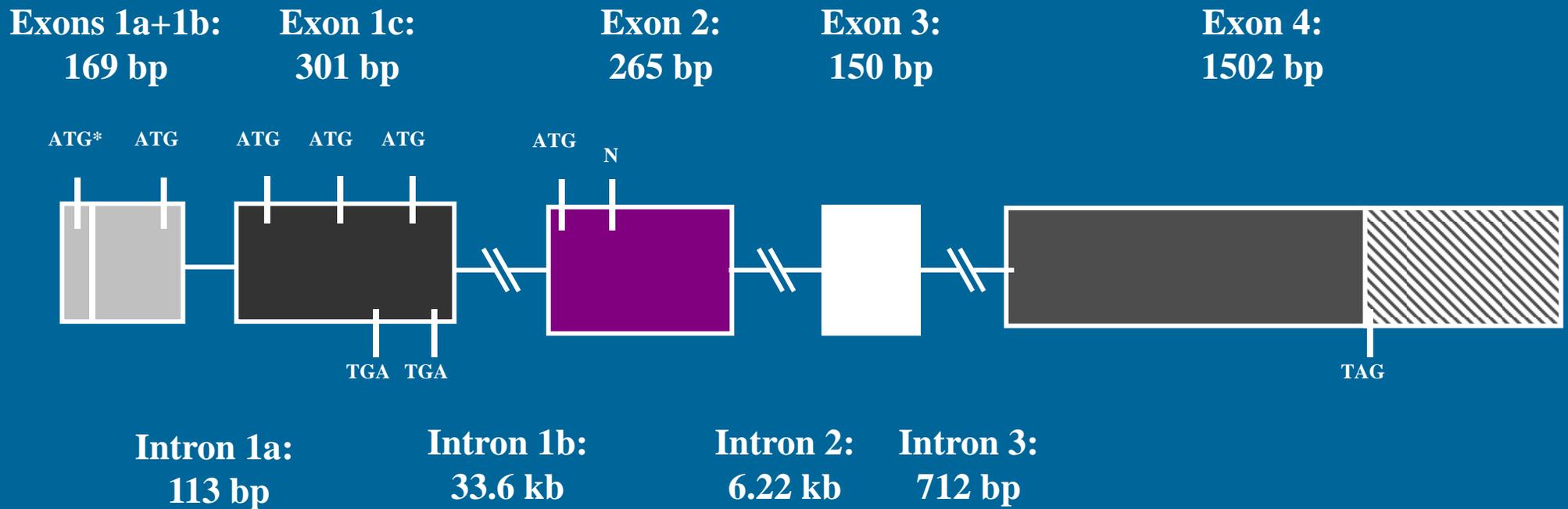
Biotin Cycle



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





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.



S&S[®] 903[™] LOT # W-011
SATURATE ALL CIRCLES COMPLETELY

Accession # 103257
Infant Name/Sex HARRY LESS M
Mother's Name HOPE 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
Mo. Day Yr.

TIME OF COLLECTION 11:00

COLLECTOR INITIALS BW

INFANT TRANSFUSED? Y [] N [X]

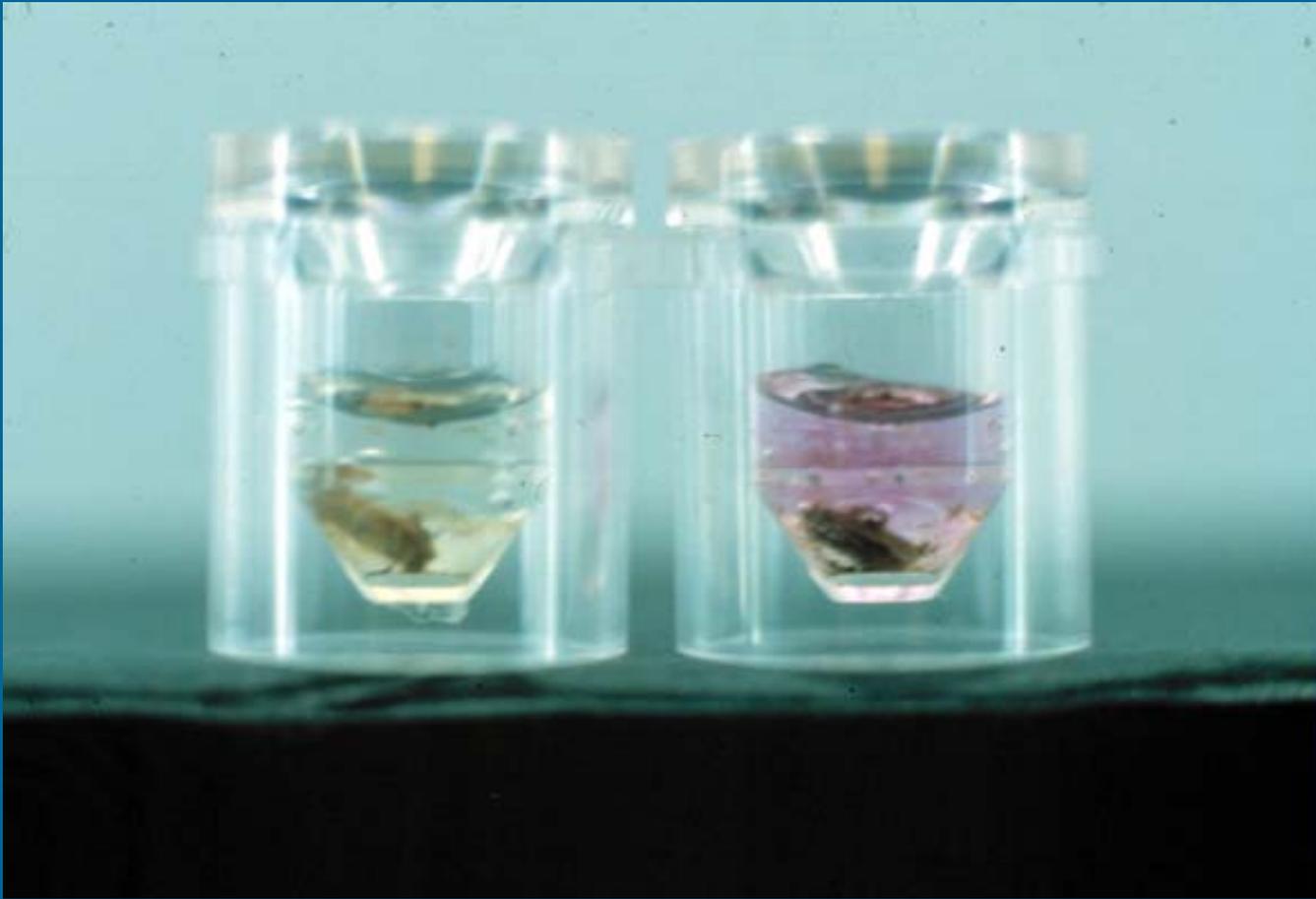
SECOND BLOOD ONLY:

PRINT NAME OF PRIMARY CARE PROVIDER

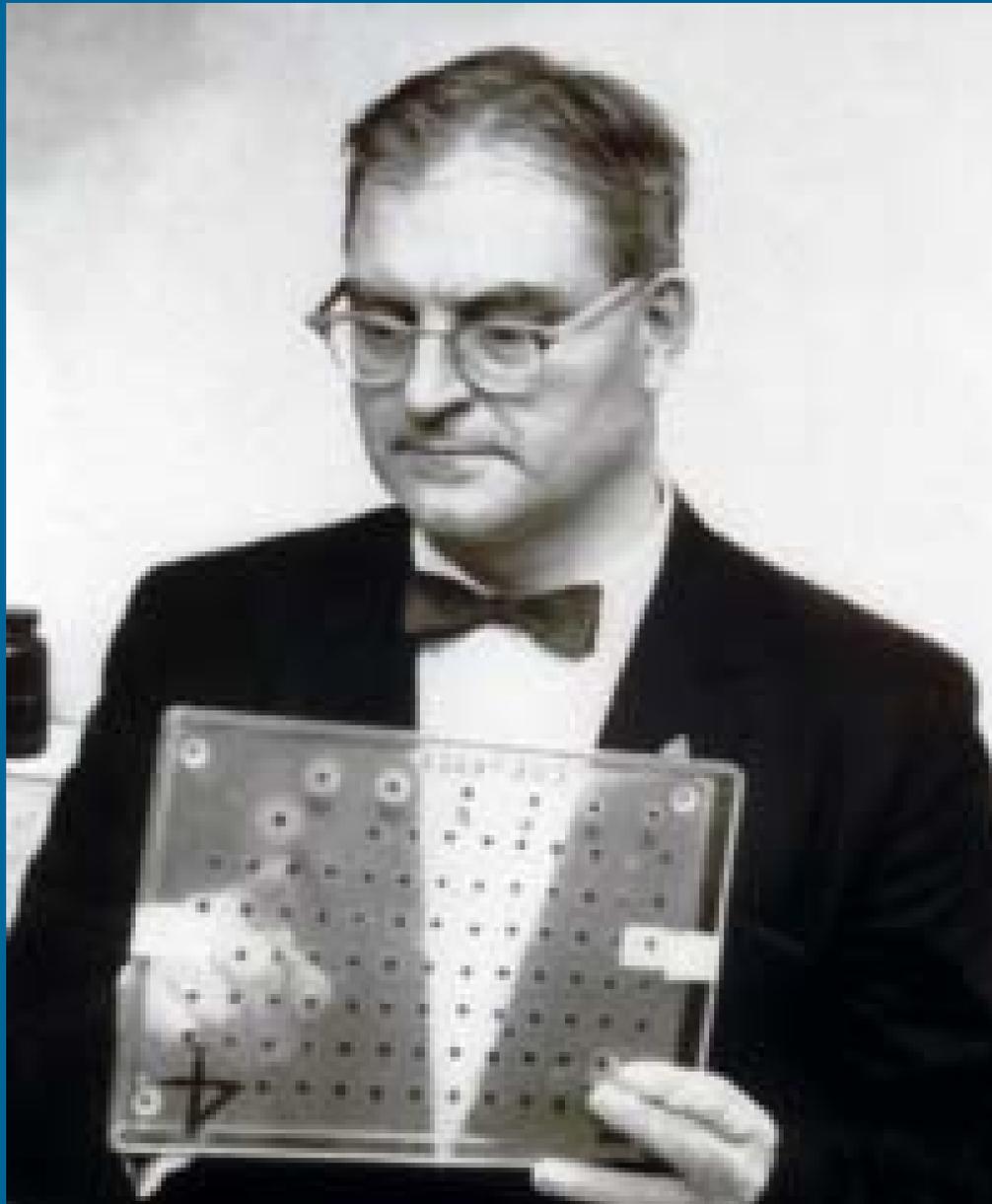
DR. WOLF

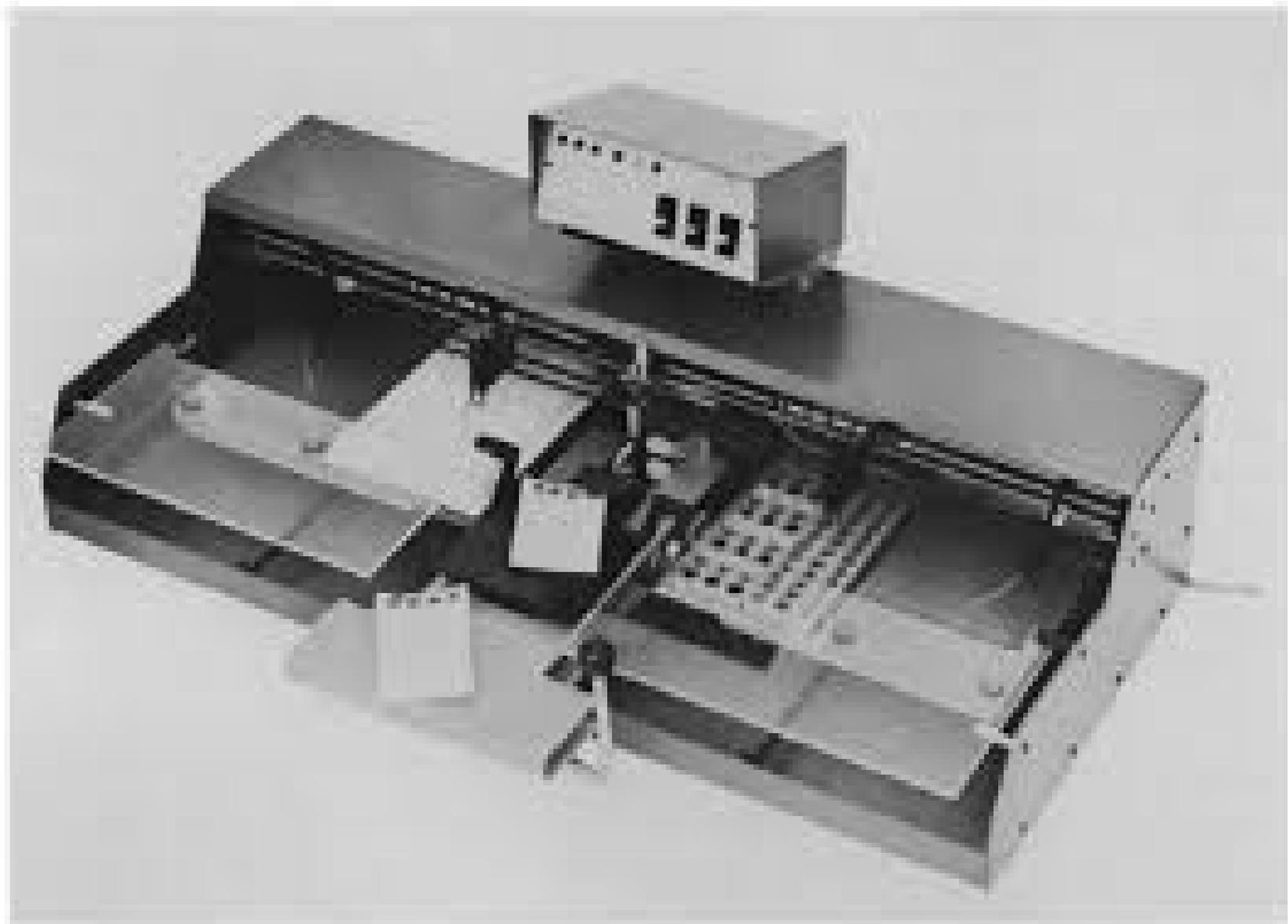
STATE OF CONNECTICUT • DEPT. OF PUBLIC HEALTH
DIVISION OF LABORATORY SERVICES
P.O. BOX 1689 • HARTFORD, CT 06144
(860) 509-8566

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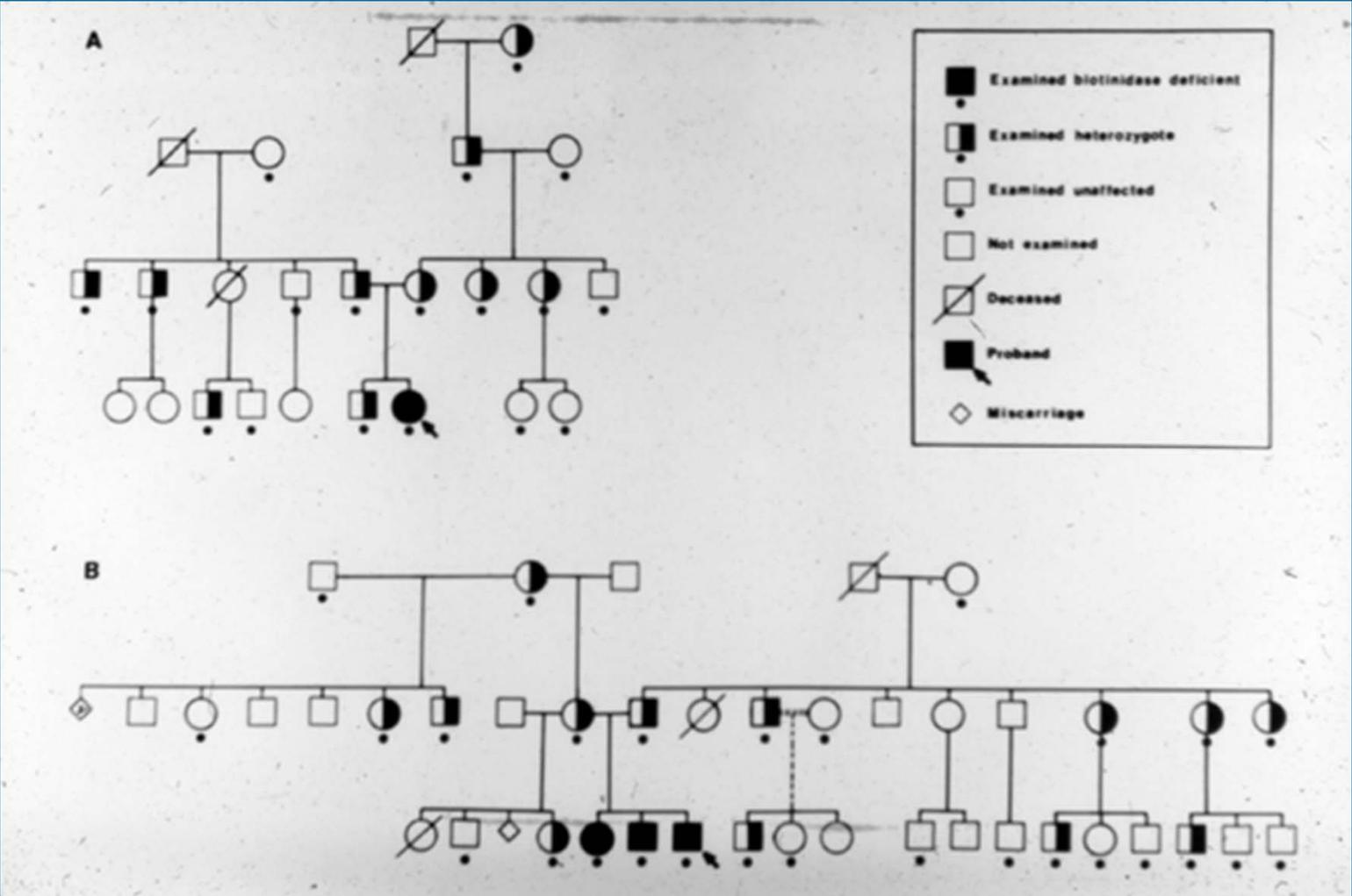


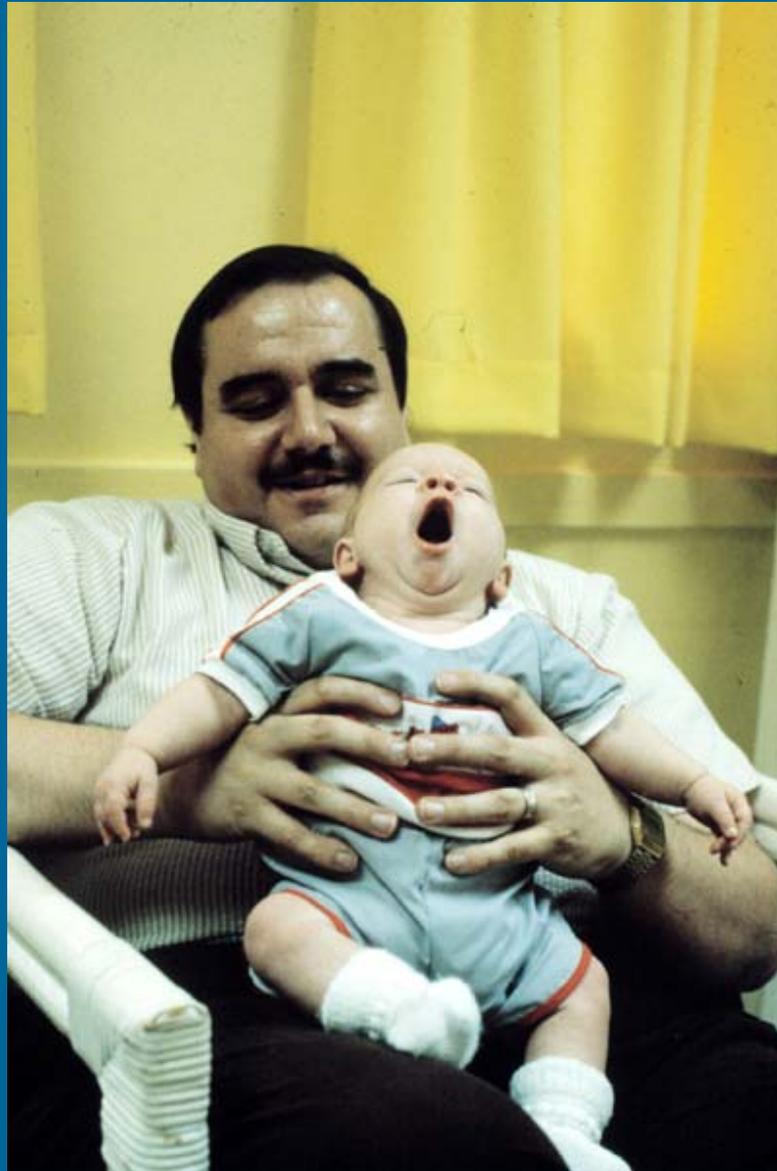


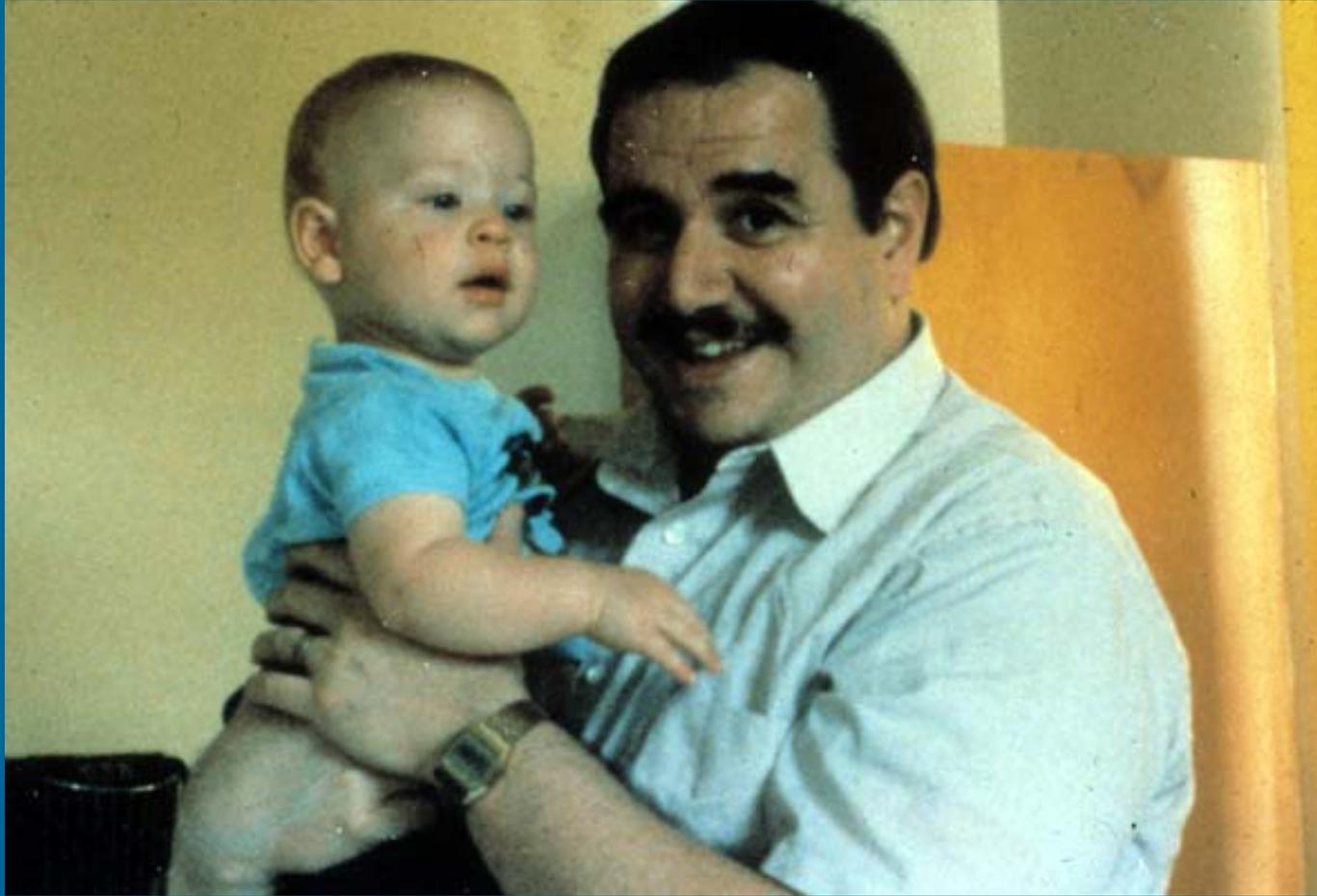














Sister

- Skin rash
- Blurred speech
- Poor articulation
- Hypotonia
- Delayed motor function
- Intention tremor
- Clumsiness
- Low normal development

Brother

- Skin rash
- Poor vocabulary
- Poor articulation
- Hypotonia
- Delayed motor function
- Hand tremor
- Wide-based gait
- Borderline normal development







- 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.”

