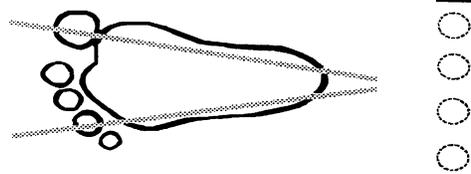


# NEWBORN SCREENING



April 2001

*Be Kind To Tiny Feet*

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*A newsletter of the Newborn Screening Program and the Newborn Screening Laboratory*

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## UTAH DEPARTMENT OF HEALTH ADDS HEMOGLOBINOPATHIES TO NEWBORN SCREENING PANEL

### **First Edition**

Presents a general over view of screening for Hemoglobinopathies and the Lab's role in newborn screening

Watch for the *Second Edition* on Hemoglobinopathies!  
For more detailed information about abnormal hemoglobins, follow up procedures, education, confirmation lab tests, and clinical treatment.



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Division of Community & Family Health Services, Newborn Screening Program: (801) 584-8256 fax: (801) 536-0966  
Division of Epidemiology & Laboratory Services, Newborn Screening Laboratory: (801) 584-8400 fax: (801) 584-8486

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## UTAH DEPARTMENT OF HEALTH ADDS NEWBORN SCREENING FOR HEMOGLOBINOPATHIES

On July 1, 2001, the Utah Department of Health, Division of Epidemiology and Laboratory Services, Newborn Screening Lab will begin testing all babies born in the state of Utah for hemoglobinopathies (hē"mō-glō"bī-nōp' ä-thēz). Hemoglobinopathies are an inherited (autosomal recessive) gene defect on the structure of hemoglobin found in red blood cells. Hemoglobin is the oxygen-carrying component of the red blood cells. Hemoglobin performs a vital function of delivering oxygen, from the lungs, to every cell in the body.

The primary purpose of newborn screening for hemoglobinopathies is the identification of infants with sickle cell disease (SCD); a group of genetic disorders characterized by the presence of sickle hemoglobin (HbS) in red blood cells. Four genotypes-HbSS (sickle cell anemia), HbSC (sickle hemoglobin C disease), Sβ<sup>+</sup>-thalassemia and Sβ<sup>0</sup>-thalassemia (the sickle Beta thalassemias)-account for most sickle cell disease in the United States. Nationwide, sickle cell disease is the most prevalent disorder identified by newborn screening. (1).

Newborn screening will help to, start to, identify the many hemoglobinopathy carriers (or hemoglobin *traits*). There are over 600 known structural hemoglobin variants. These variants are genetic defects in the hemoglobin-chain synthesis. Some variants cause serious health problems and others only a mild anemia. Watch for the second edition hemoglobinopathy newsletter that will

have more detail about hemoglobin variants.

Utah will join the other 47 states that screen for hemoglobinopathies. (1). A national Task Force on Newborn Screening was convened by the American Academy of Pediatrics (AAP), with funding from and at the request of the Maternal and Child Health Bureau (MCHB), Health Resources and Services Administration (HRSA), and the US Department of Health and Human Services (HHS). The AAP was asked to assemble the Task Force in recognition that pediatricians and other primary care health professional must take a lead in partnering with the public health organizations to examine the state newborn screening programs. The Task Force reported that changing demographics emphasize the importance of understanding cultural uniqueness and how culture affects healthcare. The advances in basic and clinical science and technology resulting from the Human Genome Project will offer unparalleled promise to improve abilities to promote health and prevent, diagnosis, and treat diseases in children. In the United States, technological advances have had, and will continue to have a significant impact on the sensitivity, specificity, and scope of newborn screening. (1).

Hemoglobinopathies are found in many ethnic groups. Listed in *Table 1* are the common hemoglobin variants and their geographic origins. Utah's population is growing more diverse and many of these geographic areas are now represented.

Nationally, there are approximately 50 infants who are identified as carriers of hemoglobin variants (or hemoglobin traits) for every one infant who is detected with SCD. (3). Some variants, especially the ones with unstable hemoglobin or those with altered oxygen affinity, will have clinical manifestations

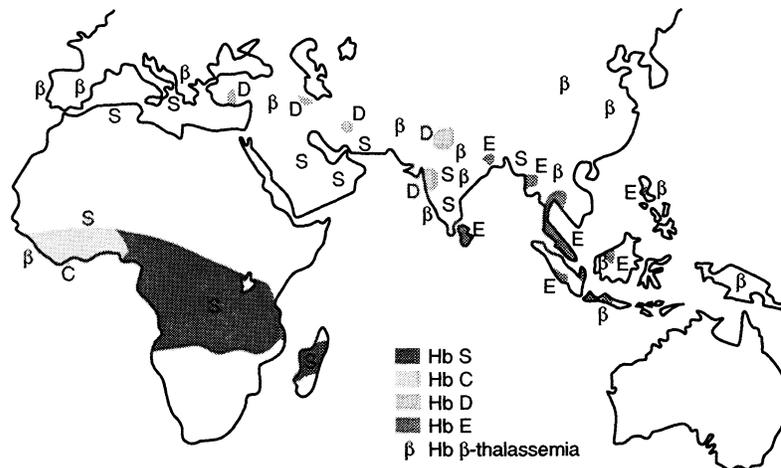
that need to be treated. Newborn screening for hemoglobinopathies will help to facilitate early treatment. Other variants can have no clinical consequences, but hold a future genetic potential to produce a child with SCD. (3).

Table 1 (5)

HEMOGLOBIN (Hb) VARIANT	GEOGRAPHIC ORIGIN
HbS	Equatorial Africa, Greece, Sicily, Egypt, Turkey, India, & Iran
Alpha-thalassemia	Africa, Southeast Asia, China, Mediterranean, & Middle East
Beta-thalassemia	Africa, South Europe, Middle East, Southeast Asia
HbC	West & North Africa
HbD	India, Pakistan, Afghanistan, & Iran
HbE	Southeast Asia, India, Sri Lanka, & the Philippines



*Geographical Distribution of Hb S, C, D, E and  $\beta$ -thalassemias.*



THE UTAH DIVISION OF LABORATORY SERVICES  
THE LAB'S ROLE IN SCREENING FOR HEMOGLOBINOPATHIES  
Barbara Jepson, MT, ASCP  
Newborn Screening Lab Supervisor

In July 2001, the Newborn Screening Laboratory will begin screening all newborns, in the state of Utah, for hemoglobinopathies. This new screening test will be included with the panel of disorders that we currently screen for – congenital hypothyroidism (T4), phenylketonuria (PHE), and galactosemia (Galt). The Newborn Screening Lab accepts the responsibility of providing accurate, specific, and sensitive screening methods. Our mission is to provide rapid screening results to hospitals, physicians, and other health care professionals.

#### THE STRUCTURE OF HEMOGLOBIN

Hemoglobin is a protein, found in red blood cells, used in respiratory and circulatory functions. Hemoglobin transports oxygen from the lungs to the tissues and returns the carbon dioxide waste.

Proteins are made from chains of biological building blocks called amino acids. The hemoglobin molecule is made up of four groups of amino acid *globin* chains that are wrapped around four other chains of proteins known as *heme*. Letters of the Greek alphabet are used to differentiate the globin chains. In functional hemoglobin there are two amino acid **alpha** ( $\alpha$ ) globin chains and two other globin chains which can be either a **beta** ( $\beta$ ), **gamma** ( $\gamma$ ) or **delta** ( $\delta$ ) chain. The heme molecule plus the four globin chains make up the structure of hemoglobin. (3). (See pictures at the end of the article)

Genes that regulate the building of alpha, beta, gamma, or delta globins are located on a specific chromosome. A

defect in a globin gene will code for the wrong amino acid and change the structure of hemoglobin. This amino acid mutation causes the hemoglobin to not function properly. A mutation can cause an actual physical change in the shape of the protein. This change in structure is what causes the “sickle shape” of the red blood cells, in sickle cell anemia. Other hemoglobin disease states are caused by these mutations in a globin chain.

Each amino acid globin chain has one end that has a positive electrical charge (+) and one end that has a negative electrical charge (-). The different globins have different positive and negative charges. This electrical property is used in the laboratory method for separating and identifying the different kinds of hemoglobin. (4).

#### SAMPLE COLLECTION

The laboratory will be using the same dried blood spots samples that are currently collected by heelstick and mailed to the state lab. No additional blood samples will be needed. We will screen the first, required blood sample for hemoglobinopathies. The first specimen collection time will remain the same. It is very important that the sample be taken before any transfusions.

#### TESTING METHOD

Our laboratory will be using a method of hemoglobin screening called iso-electric focusing (IEF). Preparations of the punched, dried blood spot specimens are applied to *wells*, near the end of a *plate*. The plates are made out of a support medium such as *agarose* or *cellulose acetate* (think, clear, thick Jell-

mixed, in the plate, with different buffers (solutions that are at a stable pH). Potential of Hydrogen (pH) measures the degrees of acidity (vinegar is a weak acid, with a pH below 7) or alkalinity (bleach is alkaline, with a pH above 7) of a substance.

Known hemoglobin controls are applied to each plate along with the dried blood spot specimen preparations. Each sample has its own well on the plate. An electric current is applied across the plate so the charge runs through the support medium. The plate has a positive side and a negative side (just like the globins). The different pH buffers, in the support medium, are affected by the charge and separate out into zones. These pH zones sharpen the separation of the globin bands. The charges cause the globins also to separate. The globins with a positive charge will move toward the negative end of the plate and the negative charges move towards the positive end. During the separation, bands are created. Each hemoglobin has its own band. The current is stopped. The bands are made visible by developing the plate with a dye. Each known hemoglobin sample and unknown hemoglobin sample will show a picture of bands, separated out, along the path, from its well. (see picture)

The unknown samples are compared to the known samples of hemoglobin bands. The bands are read by lining up the bands that moved to the same place, on the medium, as the control band or known bands. The relative amounts of hemoglobin, in the bands, can be determined, visually, by noting the darkness or lightness of the dyed bands.

The banded medium is dried onto the plate. Our laboratory will scan these

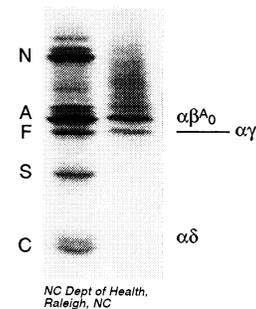
“picture-like” plates into a computer for storage of the screening result. (6).

#### REPORTING HEMOGLOBIN RESULTS

Each banded picture will be read by trained laboratory personnel and reviewed by the supervisory scientist. All samples that show “typical bands” for newborn hemoglobin will be reported out as normal hemoglobin. Hemoglobin results will be added to and reported on the first screen mailed to the hospitals.

#### Newborn

*Hb AF*



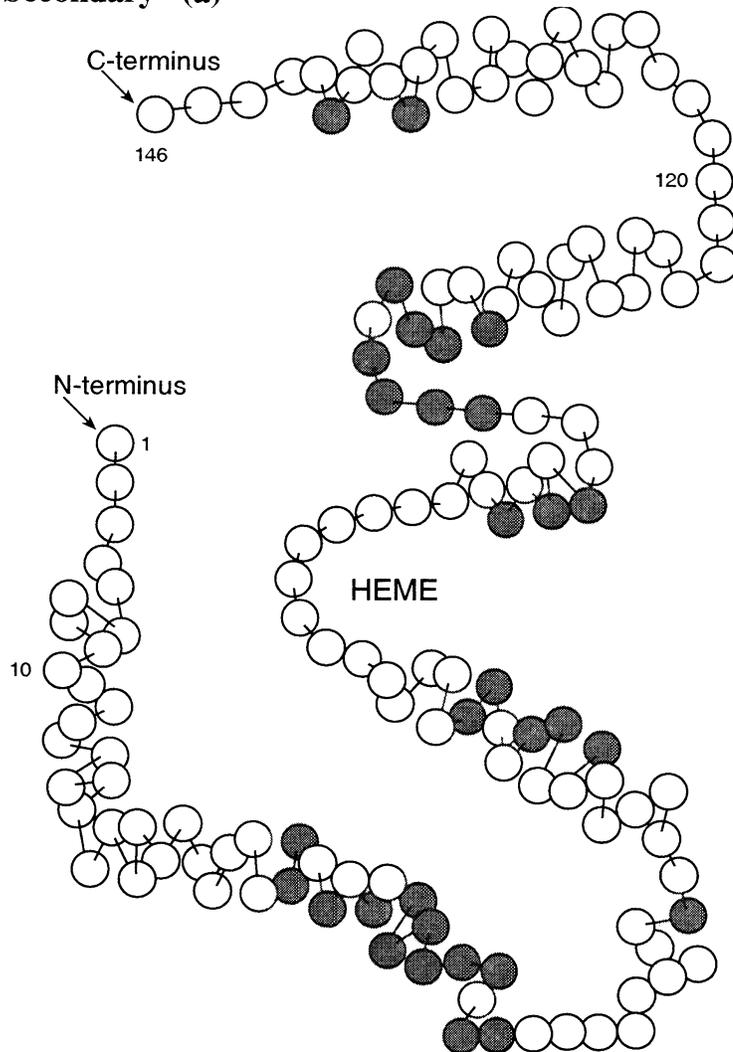
Any samples showing bands suggestive of abnormal hemoglobin or atypical banding patterns, will be retested, using the same dried blood specimen. IEF methodology is only a screening test. The report will reflect the “suspected” bands of hemoglobin type and relative quantity. Follow-up confirmatory testing will need to be done to determine the actual “type” of hemoglobin. Suspected abnormalities in the hemoglobin-screening test will be given to the Newborn Screening Program’s follow-up nurses. The nurses will coordinate the confirmatory testing and follow-up with the primary care physicians, families, labs, counselors, specialists, or other healthcare providers. (The second edition on hemoglobinopathies will have more information about follow up procedures).

QUALITY ASSURANCE

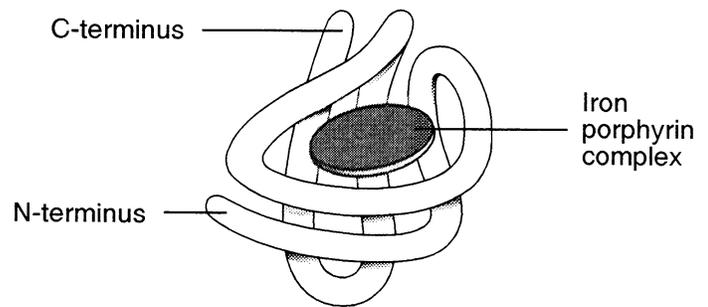
The Newborn Screening Lab has met the requirements and is licensed under the Clinical Laboratory Improvement Act of 1988 (CLIA 88). The lab participates in regular proficiency testing. The proficiency testing is given by an outside agency. Our lab just passed a CLIA inspection on 03/07/01. Our laboratory holds a high commitment for quality screening of each newborn in Utah. We invite any questions or comments from the community. Your feedback will help us to improve our screening procedures.

## Structure of Hemoglobin

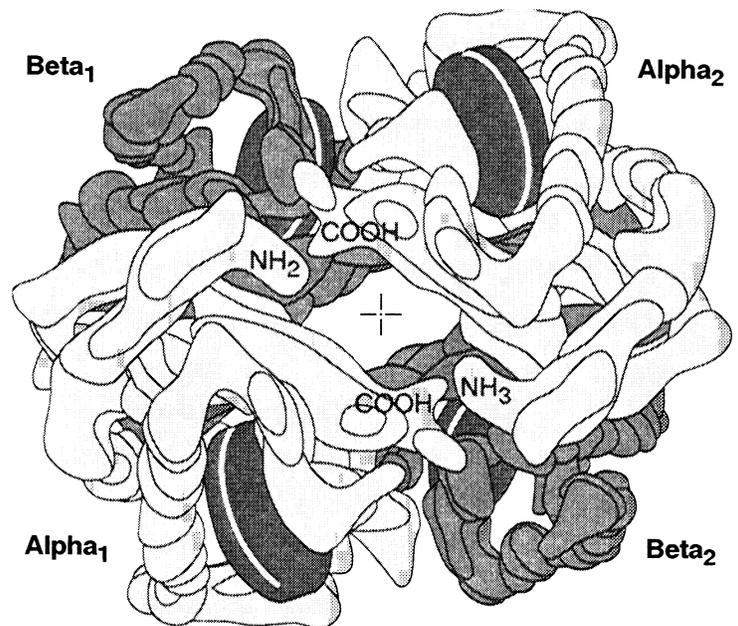
Secondary\* (a)



Tertiary (b)



Quaternary\* (c)



\* Adapted from Huisman, THJ. *The Hemoglobinopathies*, D.R. Higgs and Weatherall Eds.

## **EDITORS CORNER (Page)**

We would like to say Goodbye to Dan Andrews. Dan was the Newborn Screening Lab supervisor for 5 years. We all wish you success in your new position.

Welcome to Barbara Jepsen! Read her article about the lab's role in screening for hemoglobinopathies. Barbara has two years experience with isoelectric focusing (IEF) and 26 years experience with other laboratory methods.

Carroll Hobbs joined the lab in August of 2000 and Robert Bigelow joined us in October of 2000. They are both Lab Technicians in the newborn-screening lab. I apologize for the late acknowledgement of your arrival! Welcome and we are glad that you are a part of our team.

We are excited about our new affiliation with the University of Utah, Division of Pediatric Hematology at Primary Children's Medical Center. Hematology will consult for the Department of Health about hemoglobinopathy newborn screening and play a vital role in developing the follow up protocols. **JAN BAGLEY, RN**

## References

1. A Report From the Newborn Screening Task Force Convened in Washington DC, May, 1999. Pediatrics Supplement August 2000, Volume 106, Number 2: 392.
2. Mountain States Regional Genetics Service Network. Newborn Screening Practitioner's Manual. (2nd ed.). 1996.
3. Huntsman, R.G. (1987). Sickle-cell anemia and thalassemia. Published by the Canadian sickle cell society. Ohio: Isolab, Inc.
4. United States Department of Health and Human Services. Sickle cell disease; comprehensive screening and management in newborns and infants. Clinical practice guidelines #6. April 1993.
5. Vermont Newborn Screening Program. <http://www.vtmednet.org> April 1, 2001.
6. Hocking, D.R. (1997). The separation and Identification of Hemoglobin Variants by Isoelectric Focusing Electrophoresis: An Interpretive Guide. (Perkin Elmer-Wallac) Ohio: Isolab, Inc.

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Utah Department of Health  
Division of Community and Family  
Health Services  
Newborn Screening Program  
Box 144710  
Salt Lake City, Utah 84114-4710

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