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Newborn Screening: Claiming Victory, Then and Now

BRADFORD THERRELL: If I can have your attention, we're still running a little bit behind and we need to move on, sorry about that. You'll have to debrief later. So I'm Bradford Therrell from the national newborn screening and genetic Resource Center in Texas. I have with me on stage beautiful young ladies to help me out. First on the far side Lanetta Jordan, the chief medical officer Sickle Cell Disease Association of America and the director of the sickle cell services memorial Health Care Center in Hollywood, Florida. Nearest to me is Jana Monaco, a parent and newborn screening advocate. A member of the secretary's advisory committee and she's the advocacy liaison for the organic as deem yeah association. Now both of these ladies have much longer resumes than that but you'll have to talk to them later to find out what those are. So here we go with a session on newborn screening, claiming the victory then and now. I'll go through some of the historical events of newborn screening and show you where HRSA has interacted to the benefit of this program. If I can get the slides to work. Which I'm not able to do. There we go. Still not working. If I could have the next slide. So the early days really start back in the early 1900s with a professor who originated the phrase inborn -- of metabolism. In the 1930s he identified PKU associated with mental retardation and developed the diaper test for PKU with ferric chloride. It was used as a screening test for a number of years while other people worked on ways to improve the system. Next slide. So if you look at this picture you'll see on the left side a young man who is 11 1/2 years old affected with PKU and on the right side his sibling who is two years old and was detected by screening and treated and was normal. This is the sort of thing we were seeking and was happening with urine screening. In the 1930s there was a urine screening and it took about 20 years until there was really a dietary treatment available for PKU. And so in 1953 a professor from Germany who was in England came up with the dietary treatment and published it and a few years later Bob Guthrie began working on a blood procedure to detect PKU. In 1959 he first reported this in papers at a meeting.

It wasn't his final publication, however, which he had trouble getting done at the time because people didn't want to publish this material. I'll talk more about that later. I had the privilege of knowing both of these gentlemen. This is a picture of me at a very earlier age with both of them. Professor BICKLE couldn't remember my name so he used to call me the kid from Austin. I'm not such a kid anymore. About 1962 the children's bureau got involved in newborn screening for PKU and funded a study on efficacy of newborn screening and also at that point in time there was funding given to the Massachusetts Department of Health to begin a voluntary newborn screening program as a pilot to see how it would work in a public health setting. 1963 Guthrie's paper came out on PKU and he being an advocate and working with the retarded citizens group actually began to push the concept of PKU screening in the public health environment and was successful. Also about 1962 you'll see that President Kennedy gave the first Joseph P. Kennedy international award in mental retardation and professor FELIG was one of those recipients. This is a picture at the presentation. In 1960s, people were beginning to do this blood screening for PKU and it was getting such widespread press that there needed to be some consensus conference held internationally to talk about where this was going and what the rules should be with respect to screening and so 1966 there was a conference first international conference in Yugoslavia sponsored by the children's bureau and there were 13 different countries attending that meeting. 1969 a second conference was held in Tel Aviv also sponsored by the children's bureau. The person who was really responsible for this is shown in this slide Rudy, who worked at the children's bureau and then HRSA for many, many years and we presented him with a plaque in 1994 shortly before his retirement and he passed away in the year 2000. Rudy was the one who was at these meetings, at the table thinking forward about what we could do with PKU and how the monies that were available could be spent to help these programs not only in the U.S. but in other countries of the world. So then in the 60s then we started PKU screening. It got to the point where we needed some international involvement and actually the first Asian program became organized in 1966. So in the late 60s this person on the left, Bob Phillips, who was an inventor, actually developed an automated procedure for punching the blood spots. So whereas in the past we had been punching manually with hand punches like you punch notebook paper his allowed to you do four tests with the same energy that you could do one in terms of preparation so we began to think about automation of newborn screening. Today it punches six specimens at the same time and looks like this. So in the 70s, with the advent of this automated procedures for punching discs people got interested in other types of procedures. A man from Quebec published his work on thyroid that he had done in California as a fellow under Dale fisher. 1973 Mike working with Bob Guthrie in buffalo published his procedure on sickle cell from blood spot. In 1977 Sonia pang who moved to Cornell. People looked at what else you could do from dry blood spot. 1975 national academy of sciences reported on current practices looking at problems and giving guidance for maximum effectiveness of

newborn screening program. It was important for a number of reasons but most particularly because this publication pointed to the fact that we needed better quality tools in laboratories and noted that a single laboratory within CDC, for instance, should be responsible for maintaining the proficiency of regional screening laboratories. Unfortunately CDC didn't have any money to do this and so to their benefit HRSA came to the rescue in 1979 and a memo of understanding was signed between doctors at CDC and HRSA. Granting them some funds to get the quality control program going at CDC. So that program flourished with those funds until about 2000, I think. And they just celebrated their 30th anniversary a few years ago and now they serve over 475 laboratories and over 75 countries with more than 50 an light. It was essential back in the early days of this that HRSA be forward thinking and put their money to help CDC. This is the letter from Bob Guthrie that was sent to CDC at that time saying that he was delighted to receive the call that CDC was going to begin their laboratory testing and he would help in any way he could. He was really concerned they would work on thyroid and not work on PKU and so he took some pains to make sure that metabolic disorders were included in their screening procedures. Also in the late 1970s, we began to look at hypothyroidism seriously and had our first national meeting focusing on the newborn screening in 1979. We came to the 80s and we've been spending so much time on expansion in the 70s we sort of sat back and thought about how to better track these patients. Microcomputers were just coming onto the scene and programs like our program in Texas where I was a laboratory director and programs in New York which were the larger programs in the country needed computerization if they were going to move forward. A lot of work went on with microcomputers in the 80s. We had continuing newborn screening meetings on a national level. We were able to actually have our first international meetings on thyroid and PKU in Japan and then we were able to host the first North American meeting in Texas in the late 1980s and it's at that meeting where we began to talk about international quality assurance which led to a meeting in Japan the following year and that led to the development of international society for newborn screening. The 1980s was spent basically cleaning up our act and getting automated. Late 1980s, Ed McCADE started working on extraction of DNA from blood spots and Ferrell looking at it for cystic fibrosis in the early 1990s. 1990 also Dave Millington started talking about -- Don chase and others both worked on better procedures for newborn screening and so during the 1990s, a lot of emphasis went into the research on better methodologies which as you know now has led to expansion sort of beyond belief. So we went from a -- we started with a paradigm shift in the 1990s. We actually went from thinking about one test for one disorder to looking at multiplex assays where from one test we get many disorders. Particularly this was important in hemoglobin in and metabolic conditions with --

LANETTA JORDAN: Good afternoon. I send you greetings from the sickle Sickle Cell Disease Association of America who has had a longstanding relationship with Maternal and Child Health and child health and we're very excited to be part of the program today and I want to thank Dr. Michele for inviting me to give a brief presentation. Sickle cell disease is quite exciting in this day and time. Exciting in that this year actually marks the 100th year anniversary of the celebration of sickle cell disease in the first identification of the clinical findings of sickle cell disease in America. Sickle cell disease is a transformation from a disease of slaves to an immigrant disease to an American public health challenge. It most definitely is a public health challenge today. Dr. James Herrick back in 1910 reports the first clinical findings on sickle cell disease and describes the findings as such. Unusual blood findings none of which I've seen described. Whether the blood picture represents -- if it's a peek -- area condition of the blood or characteristic of some particular disease I cannot at present answer. So this is in 1910. In 1915 there was another description. The unusual character of the blood findings in the case here recorded is alone sufficient to justify its work. When we compare these findings as well as the clinical history with two similar cases previously reported, one by James Herrick and the other by R.E. Washburn we're forced to the conclusion that we have indeed three cases, a group which belongs quite apart from anything here to foredescribed. These three cases have points of resemblance so characteristic and constant that they can't be explained as accidental. When we talk about the identity of sickle cell disease, the -- in 1947, almost 30 years after those reports, the journal of American Medical Association reported that sickle cell -- the most significant feature of sickle cell anemia is not is definition of a right row sites but it's the only known disease completely confined to a single race. And we certainly know that it's not the case. HRSA certainly knew this was not the case. It is a multi-centric origin. Certainly originating from Africa and those other areas where malaria was endemic. Where as the saying goes, wherever you go your genes go with you. This is why we have sickle cell disease and other hemoglobin disorders in the United States. Hemoglobin -- because of newborn screening and the identification of newborn screening and the data collected on infants and prevalence sickle cell disease is the most common newborn screening finding to date. I understand this may change but as of today sickle cell disease is the most common of that found in newborn screenings. The life expectancy of individuals born with sickle cell disease has certainly improved. In the 70s we saw a life expectancy of about 14 years of age. Today we're looking at the fourth, fifth, even, sixth, seventh and one division in her 80s stage of life. What we primarily use today, the last note is the one that really took us from age 14 to these higher decades that we see today. In terms of treatment, we have hydroxyl Rhea and I will highlight this is the only FDA approved drug for sickle cell disease and it is the only drug after 100 years of clinical description. We certainly can do better than that, I think. We also have transfusions either acute, chronic or ep -- episode -- the reason we're here in celebration of today is because of universal newborn screening and

prophylaxis. Because of that, the childhood mortality rate has decreased 42% when Penicillin was implemented. This was certainly very celebratory for HRSA and the national institutes of health who collaborated during this time so we could certainly realize where we are today in terms of improved mortality. Advances in identification and treatment, newborn screenings, modern pain management, pain is certainly the characteristic feature of sickle cell disease. Many challenges with pain management. Stroke prevention strategies, transcranial MRI. Red blood cell transfusion, other therapy which is approved for adults but there are clinical trials to which it's used in children. Neuropsychological dysfunction there is an active clinical trial involved in that area now. Stem cell transplantation, there have been translation there. Pre-marital and pre-pregnancy and other counseling related to sickle cell disease. The first identified genetic disease. It is the impetus for the human genome project. There are many complications now that individuals are living with sickle cell disease so these complications are very serious but it is now a chronic disease and we certainly feel that it's a chronic disease that can be managed. But a quick look at all of these disorders and complications that occur with sickle cell disease. They don't always occur. Some individuals who never have any of the complications but they can occur and we certainly need to have a system of care in place to care for individuals as they age. We have a national sickle cell disease advocacy association. It was founded by Dr. Charles WHITTEN, a pediatrician. The goal of the Sickle Cell Disease Association of America is to advocate for and enhance the membership. We have community-based organizations so we want to enhance the membership of their ability to improve the quality of health, life and services for individuals and families in communities affected by sickle cell disease. It is a disease that involves the entire family and involves the entire community. The public advocacy is one of the -- is a major focus of the national organization and it is the highest level of awareness where we can bring issues to the community. We have 50 member organizations in 28 states. They provide social support, community awareness, genetic counseling and screening. We have other advocacy initiatives. We did have great excitement in the 70s related to sickle cell disease. There was a sickle cell control act passed by the Nixon administration. Bill Cosby and Sidney PORTIA had movies that talk about sickle cell disease. We don't have that type of leadership in advocacy but we're striving to bring that awareness back nationally. We have national sickle cell awareness day and we're looking at very long term advocacy strategies and look forward to participating with HRSA in advancing the national agenda for sickle cell disease. Thank you. [Applause]

BRADFORD THERRELL: So where has advocacy gotten us? First newborn screening program for sickle cell was in New York in 1975. If you look a few years later in 1987, the map looked something like this. The darker states are the ones that were doing mandated screening on all populations. It was about that time that also we got into -- we got the results of Penicillin prophylaxis random trials talking

about how effective it could be. This led to an NIH consensus conference in 1987 which basically said that all states should be screening for all babies for sickle cell anemia. HRSA made funds available in 1987 to get things kick things off to get it started. This is the map in 1987. This is a map a few years later. It keeps moving on and moving on until finally, with the help of HRSA funds to the American Academy of Pediatrics to educate these last two states finally in 2006 there was finally 100% of the states mandating newborn screening for it. It took us from 1987 to 2006 for that to happen. It wouldn't have happened without HRSA's involvement, by the way. Here we are into the 2000s and we're looking at more and more national meetings on newborn screening. We're looking at newborn hearing screening coming forward. Public pressure to expand. Looking at integration of data, one-stop shopping. American College of medical genetics report came out recommending a core panel tests with HRSA funding and HRSA funding has supported many of these programs including now save the babies act from the Federal government. This is what's going on in the 2000s. And HRSA has continued to put these funds forward to help support these programs. Now I want to switch to Jana Monaco and she'll talk about the importance of expanded newborn screening in her life.

JANA MONACO Hi, it is so great to be here to celebrate this special event and it is my passion with newborn screening but I do wear a hat with the DC LEND program as a family faculty member which I'm also very proud of. Many of you know my children and know the role that they played with newborn screening. Here they are. This is a past photo of my son, Stephen, the third of four children along with my daughter Carolyn. Nine years ago I was told by a neuropsychologist that my son east rehab from a traumatic brain injury was a marathon, not a Sprint. You can see how far we've come as a nation with newborn screening and what still needs to be accomplished. It has been a marathon with hurdles along the way and we've certainly claimed victories. Behind the language, numbers and data are the true achievements and successes. They're the many -- like Caroline who is eight years old. Diagnosed before she was born and screened at birth. With early intervention of lifelong diet management, medication, specialized care from her geneticist here she's a typical second grader. Like any good race victories are preceded by many defeats which has motivated and encouraged the world of science and medicine to continue the race of achieving newborn screening. Those defeats are the lives of babies and children lost far too young to lack of comprehensive newborn screening for children like my son, Stephen, who will turn 13 next week, a great milestone. His life was drastically altered at age 3 1/2 due to a late diagnosis of as deem yeah resulting in a metabolic encephalopathy. The little boy in the picture with the smile sitting so proudly eating a piece of pizza is a distant memory for my family and me. One of many that we cherish. That photo and the one before you are constant reminders of what we have had and what we tragically lost and they are what continue to inspire me to advocate for this important program. Done

differently 13 years ago could have made a significant effect on Stephen's life. Today he's nine years into his long marathon. Slowly making strides and milestones despite his severe intellectual and developmental disabilities and complex health issues. His life is one with many hurdles and challenges, with spinal surgery on the horizon in just a few short months. It's a burden he must carry but who that has challenged us and its partners to support expanded newborn screening and work to ensure every baby will receive screening as recommended by the American College of medical genetics. In order to do so it must continue to take shape and grow and overcome the hurdles that present themselves. Newborn screening is a great program with great promise and one that has constantly been asked to prove itself over the years. Each time it has risen to the challenge thanks to dedication and support from the Maternal and Child Health Bureau. And the thousands of babies diagnosed with newborn screening are the true testimony and proof that it works. Ultimate victory in new worn screening requires quality education and training for both professionals and the public, effective, appropriate follow-up and treatment for the children throughout their life spans that are diagnosed with disorders. Continued research is essential in order to continue to strive to achieve a program that can accomplish this and add more disorders to the panel that await consideration. My family today has truly endured defeat but we have claimed victory as well with our children and are honored to be part of this program. And at the end of each day we must all remember this is a program whose sole purpose is to save lives and each day newborn screening allows more victories and more Bright Futures. Thank you and congratulations on 75 years. [Applause]

BRADFORD THERRELL: Thanks, Jana. I'm always inspired when I hear her talk about overcoming these adversities. HRSA continuing to meet the challenge in newborn screening. 2003 as I mentioned the secretary's advisory committee was organized. The HCMG report came out in 2006 talking about a core panel of disorders that should be screened in all the states. Funds for national newborn screening clearinghouse have been set aside by HRSA and the Federal government in 2009. And also HRSA has been assuming a leadership role in improving newborn screening information technology. So that is sort of where we are today. Here is what it looks like in terms of numbers of tests mandated in the different states. You can see it was running along at four or five tests in every state through about 2000. And that's where HRSA funds kicked in to the American Academy of Pediatrics to develop a blueprint for the country followed by the HCMG report. You can see that beginning in 2000, the number of conditions that were being screened rose dramatically until today on average more than 35 disorders in every state. That means some states do more than the core panel and some states may only do the core panel but still we're moving forward and some states screen as many as 50 different conditions. So what next? Well, we're moving forward with -- secondary testing and so on. If you look at this issue in discover magazine a few years ago it said now that genetic testing really begins, it starts with a single drop of blood taken

from each newborn and it ends when scientists predict everyone's physical and mental future. That's a pretty big charge. And so people have begun to look at what scientists are doing with their blood. You can see you see a lot of adverse press about stories of newborn screening blood spots. We're working to overcome that at the present time. The advisory committee is looking at more and more conditions. Here is a list of some things being considered. The ones marked in red have been looked at and evidence presented and those are basically being reviewed for better evidence except for skid which has recently been adopted by the advisory committee. We're looking in the laboratory in terms of chip technology and maybe we're going to an NB SCHIP at some point and maybe moving to a laboratory on a chip in terms of nanotechnology. Some people have been thinking about hand-held instruments that can be used at the bedside. A lot of activities going on in research on newborn screening and there has been a lot of emphasis put on the Middle East and the flags around the outside of this slide show you the countries that are involved in HRSA and NIH and others have been involved with these programs in the Middle East. The same is true for the Asia Pacific. Over the Internet and listservs and that sort of thing providing information to the developing world. So in summary, newborn screening is an essential and productive public health prevention activity. You've heard that over and over today. HRSA has played a major role in developing and sustaining newborn screening. I didn't talk very much about hearing screening but it has been a real influence on the hearing screening programs. Expansion of newborn screening is inevitable and the secretary's advisories committee will play a major role in shaping national policy with HRSA help. Equal access for all newborns will require continued HRSA foresight and support and so I look forward to that moving forward and so that the next time I give this kind of talk I can show you that everybody is doing 50 or more disorders rather than just 35. With that I'll end and thank you for your attention. [Applause]