

## 11. The National Children's Study.

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DR. GUERRA: This morning we will begin with one of our very generous substitute speakers. A few days ago when this individual was visiting me in my office, after having finished a committee meeting on the fetal and infant mortality review work that we do in the public health department, he mentioned that he'd been serving on an important task force at the national level that is doing a very long-term study in assessing many different factors that impact on the health and well-being of children and families.

And yesterday, as you recall, we received word just a couple of hours before Dr. Woodie Kessel was to give his talk in the afternoon that he would not be able to do so. So I said "Well, let me call Dr. Don Dudley," who immediately and very graciously accepted to substitute for Dr. Kessel.

So Dr Dudley is here with us this morning, without the benefit of slides, without the benefit of having had a chance to think about what he wants to say, because of the incredibly short notice and the fact that he was working all day yesterday. Nonetheless, he is here, and to do so on a Saturday morning is above and beyond the call of duty.

Dr. Don Dudley is from San Antonio. He graduated from medical school here and then continued his training at the University of Iowa in obstetrics and gynecology. After that he did a fellowship in maternal and fetal medicine at the University of Utah. His area of expertise and particular interest is in preterm births.

Dr Dudley is going to talk to us about a very important project that was started a few years ago, I believe through NICHD, the National Institutes of Child Health and Human Development, at the NIH. This project is designed to get a better understanding of so many of the things that affect children directly or indirectly during those critical stages of their development and that may have long term consequences.

With that, let me introduce to you Dr. Don Dudley. And again, Don, we really appreciate your being here with such short notice and so early on a Saturday morning.

DR. DUDLEY: So there I was in the clinic with 35 pregnant ladies yesterday, and Dr. Guerra's office called me and said, Can you talk today at 1:30? That was yesterday. I said, "I don't think so." Then they asked, "Well, how about tomorrow at 8:00?" "I can swing that. What do you want me to talk about?" "The National Children's Study." I said, "Okay."

So now we're going to have this multimedia, interactive talk on the National Children's Study. It's multimedia because I have a sheet of paper, and I have you and you have me. After I finished clinic around five o'clock yesterday, I had to drive to Austin. My kid's in the high school band, and we had a game in Austin. So I got to bed around three o'clock this morning. Hey, I'm an obstetrician; I can do this.

Okay. So I'm going to tell you a little story. About a year ago I got a telephone call asking if I would like to serve on a federal advisory committee for the National Children's Study? First of all, I didn't know what the National Children's Study was, and secondly I didn't even know what a federal advisory committee was, and so my immediate response was, "Sure."

It sounded important, so I thought, well, let's go on and do it. And as it turns out, it really is important. Now, we have a very mixed audience here this morning. Some may be familiar with the National Children's Study and others may never have heard of it. Some of you are with the NIEHS and may even chair one of the work groups I'm going to talk about. So if anyone has anything to add as I go along, please chime in. If you have any questions or any thoughts, just pop up, because I don't have a prepared text.

What I want to do first is to read very quickly the précis for the National Children's Study. This will give you an idea of what we're dealing with.

"The Children's Health Act of 2000 authorized the National Institute of Child Health and Human Development and a consortium of federal agencies to conduct a national longitudinal study of environmental influences on children's health and development.

"Children have special vulnerability to a wide variety of exposures in their total environment. This study will investigate the interaction of biologic, genetic, social and environmental factors to better understand the role of disease etiology and to increase the understanding of the origin of health disparities. It will be the most comprehensive study ever undertaken to examine the effects of the environment on children, both helpful and harmful. With a longitudinal study design and a life stage approach, this study will include approximately 100,000 children across the U.S., identified early in pregnancy and followed through birth, childhood, and into adulthood.

"The successful completion of a study of this magnitude will require, among other things, well-defined scientific questions, careful integration and communication with community groups and health care providers throughout the country, and a state-of-the-art data collection and management system. The planning process will emphasize strong partnerships with federal and nonfederal scientists and with community, parent, advocacy, and industry groups.

This study will provide a rich national resource for study and evaluation of a wide array of child health questions and form the basis of child environmental health guidance and policy over the next generation.”

Let me tell you, this is a stunning thing to attempt. So here we are, I get this phone call and we have our first meeting of the federal advisory committee meeting in March. Legally, the NIH has to have a federal advisory committee to provide advice to the director of NICHD.

So we're dropped into this meeting, and we're told about 22 working groups involving 350 people, working on hypotheses. What is going on? My analogy is, imagine that you're an Australian aborigine and you're dropped in the middle of Game 7 of the World Series. You wouldn't have a clue. Then after five minutes, you're asked to explain the game of baseball. That was kind of our experience, because the Children's Health Act of 2000 had directed Lane Alexander, of NICHD, to put together a longitudinal study of over 100,000 children over 30 years. So just think about that. That's pretty daunting in itself.

At the time, at the Department of HHS the new director, Tommy Thompson, had put a complete ban on the formation of federal advisory committees. Now Dr. Alexander has this mandate. He's got to do something, so he creates something called the Interagency Coordinating Committee, or the ICC. The ICC got together, and this involves members from EPA, National Institute of Environmental Health Sciences, CDC, and NICHD, as well as Dr. Kessel from the HHS.

The U.S. Congress says, “Here's your study design: 100,000 children, 30 years. Learn something.” How many of you have done a study where you start with a study design, but you don't even yet have a question to ask? And your study design is 100,000 children over 30 years. What the ICC said was, “Well, we need to get together in working groups to determine the questions we want to answer with this study,” and they started working on this like crazy. So by the time Dr. Alexander convinced Tommy Thompson to establish a federal advisory committee, they'd already been working about six months, and we came in, kind of like the cart behind the horse, just trying to figure out what we were supposed to do.

This is an old list (as of last January) of some of the people on the Interagency Coordinating Committee. Gwen Cohen, Adolfo Correa, Sarah Keim from NICHD; Woodie Kessel, Carole Kimmel from EPA; Mark Klebanoff from NICHD, Matthew Longanecker from NIEHS, Pauline Mendola from EPA, Mark Rigas, Peter Scheidt, who is the executive secretary of the Advisory Committee, Ken Schoendorf, who is from National Center for Health Statistics and CDC, Sherry Selevan and Marshalyn Yeargin.

Now, this is a very interesting group of people, and I thought what am I doing here? I'm just a country obstetrician, and I'm working with these people that have institutes named after them.

For the Advisory Committee, Don Mattison is the chair. David Bellinger is from Harvard. Willa Doswell is a nurse in the department of health promotion and development, School of Nursing, at the University of Pittsburgh. Alan Fleischman, is a senior vice president at New York Academy. Lynn Goldman, is at Johns Hopkins. Judith Graham, is director of the American Chemistry Council. Shiriki Kumanyiki, is from Pennsylvania. Phil Landgriegan, is the chair of the Department of Community and Critical Medicine at Mount Sinai. Grace Lemasters is from Cincinnati. Rod Little is a biostatistician from Michigan. Bob Michael is from the University of Chicago and has written a book on the sociology of sexual relations; and this has always been the source of interesting comments at our meetings. Jonathan Samet, is very big in international smoking prevention. Ann Spence is a pediatrician. Steven Spielberg (the other Stephen Spielberg) is vice president of the pediatric medical program at Johnson & Johnson. Lucina Suarez is with the Texas Department of Health in Austin. Dan Swartz, is executive director of the Children's Environmental Health Network.

This is a prestigious group of human beings, and why am I here? I think they needed a sacrificial obstetrician, and I was the most likely subject. When the group gets together, there are about 400 of the best scientists in the country; it's quite imposing. The Interagency Coordinating Committee is NICHD-directed. So Dr. Alexander runs the show. He's usually there at the meetings for about 30 minutes and tells us "Keep going." He likes to know what's going on, but we are the advisory committee. So the advisory committee and the ICC have had this kind of tug of war on who's running the show. I think it's pretty clear that they're running the show, because they're there and they're doing the work. We just come in every three months and say "Yes, that looks okay."

The goal for the working groups is to come up with eight to ten key hypotheses that could be answered by following 100,000 children over 30 years. Each of these working groups have been generating hypotheses to study to see if they meet muster. We have the study design; we need to get the questions. Once we get the questions we're going to generate a request for applications, and we will probably go with about ten vanguard centers to roll out the study. And this probably will happen in the year 2005. We're hoping to have the hypotheses ready in the spring of next year, an RFA out by the summer, and then to start the studies in roughly the summer of 2005. We've had several time lines and none have even been close to reality. If we start enrolling patients in 2005, that would be pretty good.

Some of the working groups don't have hypotheses, and they're what we call overarching working groups, because they kind of tie all the others together.

I want to say something about each one of the working groups very briefly, so that you get a sense of the scope of what the National Children's Study is going to involve.

There's an asthma working group. I don't have to tell anybody here that asthma is a major problem in the United States today. The asthma working group has come up with several hypotheses, looking at environmental influences on asthma. One of our real goals as an advisory committee is to try to push these people to move a little bit beyond what is known.

For example, we know that mercury is bad for pregnancies and for children. We already know that. Move past mercury. We're trying to get as contemporary as we can.

The federal advisory committee is an open meeting. Anything that happens at a meeting is fair game. It's in the registry. You can look it up if you want. It makes it kind of nice that you don't have to worry about keeping secrets.

There's a birth defects working group. It makes sense that there would be something to look at regarding birth defects. There's a community outreach and communications group. This is important because if you're looking to recruit 100,000 children across the United States, we need to be sure that it is a representative sample of the United States. So we want Native American children. We want Spanish-speaking children. We want rich kids from the north side of San Antonio and poor kids from the south side of San Antonio. You're not going to be able to do this if you can't get the community to buy in. If the community doesn't buy in, you're not going to recruit. So we're looking to add community advocacy groups to the federal advisory committee.

We're looking to set up a specific organization to reach out to communities—active community groups to tell them what's going on and to get buy-in from the community. If you're a parent and you're enrolling your child into a study for 30 years, the United States is a pretty mobile population. I suggested that we put GPS chips in all the kids. They laughed at me at first. I said, No, I'm serious, because it's going to be hard to track these kids for that long. If we start off with 100,000 and we end up with 20,000 we're probably doing pretty well after that amount of time.

There is a development and behavior group that is looking at early origins of adult health.

There is an ethics subcommittee. And the ethics subcommittee, to me, is probably the most important subcommittee that we have. The ethical issues of the study are broad and at times troubling. For example, how do you deal with child suicide in an ethical framework in a study like this? The ethics Committee is probably going to be one of the overarching subcommittees.

There is an exposure to chemical agents subcommittee. They've been very interested in environmental estrogens, for example. There is a fertility and early pregnancy group. They're by far the most developed group. They've already come up with two or three white papers that are probably going to be published. One of them is on the feasibility of enrolling patients prior to conception. Just think about that. This has dominated some of our discussions. What's the scope of the study? Is it going to be all patients? I mean, is it going to grow out from all populations in the U.S. Is it going to grow out from select populations? Are you going to enroll children, or are you going to enroll pregnant women? If you're going to enroll pregnant women, are you going to enroll them preconception? How are you going to enroll a 17-year-old before she's pregnant?

At our last meeting, which was the middle of September, we went through every one of these hypotheses and kind of graded them -- yes (proceed), maybe, and no. That's how we graded them; that's the best we could do.

We had 50 hypotheses to evaluate and only had a day and a half to do it.

There is a health disparities group and an environmental justice group. There is a health services group that came up with an hypothesis that I thought was probably the key to the whole shooting match. What they've proposed is looking at how health services impact on health. Well, yes, of course it impacts on health, but they're saying "What degree of health services are needed?" This group is probably going to come up with data that guides public health policy, and this was one that Dr. Kessel was keenly interested in.

There is an immunity, infection and vaccines group. Again, very topical, including questions like how do vaccines affect autism?

There is an injuries group, another very topical topic. These folks have some very interesting ideas about injury, causation of injury, and prevention of injury. Injury is a major cause of morbidity and the leading cause of death in children after the first birthday.

There is an information technology group. Think about it: 100,000 children, how many bits of information from each kid are you going to get? We're looking at billions and billions of bits of information. You can envision rooms with hard disks the size of automobiles with all the information on them.

There is a medicine and pharmaceuticals group. This group will look at the impact of drug exposure during pregnancy, something about which we know precious little. Wouldn't that be cool if we could get some information about this, since women do take drugs during pregnancy.

There is a pregnancy and the infant group. As an obstetrician, this is a group that I have a lot of interest in. They're working on one hypothesis on stress and pre-term birth and another on infection and pre-term birth.

There is a nutrition, growth, puberty and development group. Obesity and diabetes kind of fall in here. There's probably going to be a hypothesis on obesity.

There's a physical exposures work group. There's a recruitment and retention. I'm glad I'm not on that one; these guys are really going to have to work.

Then there's my favorite working group, which is repository. It's estimated that there will be two to 10 billion biologic and environmental samples from this study. How do you store these? I suggested that they build a building for it. Two to 10 billion. How do you number that many specimens? How do you catalog them? How do you store them in such a way that if I want to get the baby teeth from Subject Number 100591 to look at lead levels I can do so?.

There's a social environment study group that's looking at the impact of social services and social stressors on health outcomes.

Probably one of the most important groups is the study design work group. This has a lot of hooks from the ICC on it, and these guys are going to have to review every single one of the hypotheses to see if it meets muster for study design.

Our next meeting will be in December, and hopefully, we're going to be able to get people from these different working groups to begin to work together. There are other work groups that are going to probably be developed. We'll probably have another meeting in March, and hopefully by then we would have honed down the hypotheses so that we can generate a request for actual patients. As I said, we're probably going to start off with about eight to ten vanguard centers but envision perhaps 40 centers to do all the studies. We're looking at 2 to \$3 billion. And that's a lot of money.

What I'd like to do now is entertain any questions that you might have.

MS. DANIELS: What are some of the different hypotheses on how they're going to retain those kids for 30 years?

DR. DUDLEY: That's a really good question. For example one hypothesis that we're entertaining at this time is infection and the genesis of schizophrenia. One percent of the population has schizophrenia, and you can justify going out 30 years for that because that's more of an adult-onset disease. It doesn't really come on at the age of 12 or 15, for example.

MR. SANCHEZ: Why are you doing the study in the first place?

DR. DUDLEY: Because the U.S. Congress said to. It was mandated in the Children's Health Act of 2000. Somewhere along the line somebody lobbied and said to the Congress that we need to understand the role of environment and its contribution to childhood disease. Asthma's a big problem. Obesity's a huge problem. We're looking at huge public health issues, and we don't understand a lot of it. So when you say, Why are you doing it? The U.S. Congress said to do it.

DR. GUERRA: As these observations move along over an extended period of time, there's always the possibility that you will find something that provides some insight that needs to be put into a context for some interventions, or some medical measures, or whatever. The study design is not going to preclude that, is it?

DR. DUDLEY: No, no. For example, let's say during the course of the study we learned that eating caviar causes asthma. Well, then it's entirely reasonable for that to get published, and for health mandates to come out as a result of that. Children shouldn't be exposed to caviar.

The other thing is, let's say, for example, that five years from now a paper that comes out that says that environmental exposure to DVD players causes childhood obesity, and that wasn't even thought of at the time of the initiation of the study. We very strongly feel that there should be a mechanism in place to allow for investigators to come in and piggyback a study on that onto the National Children's Study. And the other thing that we're trying to build in also is a way to attract young investigators to come in. In 30 years, by the time the thing is done and conclusions are being drawn, a lot of people who are on the federal advisory committee or the ICC now are going to be dead or gone. So we need to have a lot of people come in.

There's another thing we're very much grappling with. Who owns the data and how available is the data going to be to people outside? For example, if someone in the audience has a real intense interest in the amount of smoking in the house and asthma, and that's a part of the study that hasn't been done, how accessible are those samples going to be to people who want to use those samples.

Our opinion on the federal advisory committee is that it should be as open as is humanly possible, and the data should be shared as much as possible. But there is a big bone of contention about who owns the data; who gets the credit?

DR. GUERRA: Thank you very much.