

# **Disorders of Sex Development: Psychological Outcomes in DSD Research**

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Based on the following presentation:

Disorders of Sex Development: Psychological Issues and Outcomes. 2008 Annual Pediatric Academic Societies/Lawson Wilkins Pediatric Endocrine Society Scientific Meeting, Gender Medicine: Spanning the Specialties. Honolulu, Hawaii, 5/5/08

## INTRODUCTION

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- Assigning gender in a newborn is a daunting task
- Parents wait nine months: “It’s a boy” “It’s a girl”
- Despite media coverage, parents are caught off guard
- They look to us for help; case example
- Intense focus on this aspect of psychosexual development
- Did we get it “correct?”

- Two years ago, I drove to an outlying hospital to visit with parents who had just given birth to a child with a DSD. I had visited other Hospitals around Buffalo before when such an infant was born. I introduced myself as the psychologist who is involved in the team with Children’s Hospital where her baby would be transferred. We started to talk. The baby’s gender had not been assigned at this point and the mother told me, with her husband present, that this is their first child, that they had thought of all these things that could have gone wrong with their baby, “you know, extra toes, extra eyes, what have you, but not in our wildest imaginations did we think that we would have to wonder about the gender.” Now if I could have the first slide.
- Many of you in this room have experienced such a story, in your own hospitals and in your own community, but assigning gender whether in the traditional way as our first speaker said with physicians only or even with the involvement of parents, it is always, as all of you know, a very daunting task. Parents wait 9 months for “it is a boy” or “it is a girl.” And despite, even today, with coverage and the media, Oprah Winfrey, other talk shows, parents are still caught off-guard and they look to you and to me for help. Some years ago, a mother whose child was diagnosed with CAH with Prader 5 genitals came to talk with me about the experience she had when her child was born, the assignment of female gender was made, but upon leaving the hospital, she was told she could raise her child as a boy as a girl. I don’t think that is the kind of help that parents are looking for from us. While a decision has to be made in concert with the right information to the parents and enlist their help, we are still , I

think, in the kitchen and in the heat of the kitchen, trying to make the best judgments we can and best advice we can offer to families.

- Now, there is an intense focus at this time on the aspects, I call it psychosexual development, specifically gender identity. This historically has been where we have been, the issue of assigning gender; male or female. So it is not uncommon that we would want to know, parents as well as us, do we get that correct? In other words, is the assignment of gender the one that is established in adulthood? What information do we have to answer that question? Did we get it correct?
- There are recent data from a series of articles published in the Archives of Sexual Behavior a couple of years ago that help answer this question. The speaker who just preceded me on this panel, Dr. Drop and Dr. Dessins, a colleague of his, provided information on the long term outcome of gender identity in adult women with a diagnosis of CAH. We do get it right a majority of the time if you believe the data from Dr. Drop's review as well as the others. Next slide please.

## LITERATURE REVIEW ADULT GENDER IDENTITY OUTCOME Published Data

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- Most of the time we get it correct
- 46,XY DSD, disorders of androgen synthesis/action
  - CAIS : 0/156
  - Micropenis (M) : 0/79
  - Micropenis (F) : 0/10
- 46,XX DSD, disorder of androgen excess
  - 46,XX CAH (M): 0/33

- In this slide you will notice that I'm using the new terminology, DSD, which replaces the old terms such as hermaphroditism, sex errors of the body, and so forth. As you seen in this slide, there are no reported self-gender reassignments out of 156 cases of 46XY DSD's disorder of androgen synthesis, complete androgen insensitivity. None in micropenis initially assigned as male and even in the small group of 10 who were initially assigned as females. Those 10 have not been reported to self-gender reassign. Let me be clear here, this is not an endorsement to assign micropenis kids as females, because I think the consensus report and the consensus of most endocrinologists would be to assign them as males, but nevertheless, the literature points to the fact that the 10 genetic males with micropenis have been assigned and reared female. They are a young group, and we must wait the final outcome but as of now there has not been any reported self-gender reassignment. There also has been, in 46XX DSD's disorders of androgen excess (CAH) no gender reassignment to female in those 33 individuals (46,XX) assigned male at birth. Although there are reports that about 4 out of those 33 were having various degrees of gender dysphoria. Again this is not an endorsement for assigning these individuals as males, but this is what the review of the literature shows.
- Now, while we get it right most of the time, gender reassignment or gender self-reassignment does occur and it occurs in these conditions.

## LITERATURE REVIEW ADULT GENDER IDENTITY OUTCOME Published Data

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- **BUT:** Gender reassignment does occur.
  - 46,XY DSD, disorders of androgen synthesis
    - 5 alpha : 62/110
    - 17 Beta : 19/49
  - Female to Male
  - Two exceptions

- Out of 110 individuals with 5 alpha reductase, 62 have gender reassigned. 19 out of 49 individuals with 17 beta dehydrogenase have reassigned and this has all been in one direction. It has been from those individuals who were initially assigned as female at birth. They eventually reassigned themselves to the male gender. There are exceptions to this direction; these 2 exceptions are the following.

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Two exceptions:

46,XY, DSD, disorders in androgen action  
PAIS: F to M (3/99) and M to F (6/99)

46,XX, DSD, androgen excess  
CAH: F to M (4/250)

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- In partial androgen insensitivity, the direction goes both ways. Out of 99 cases, I was able to find in the world literature in English, 3 assigned from initial assignment as female to male and 6 the other way. The other exception is in genetic females with congenital adrenal hyperplasia where there were 4 out of 250 or 2 % of individuals who assigned themselves male.
- Now there are some other lessons to be learned from this review of selected conditions of DSD's.

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While self-gender change occurs, it varies in frequency by syndrome from a high of 67% (due to very small numbers) to a low of 2% for 46,XX, CAH individuals. This is higher than the general population.

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- While self-gender change occurs, it varies in frequency by syndrome from a high of 67% in 2 out of 3 reported cases of classical cloacal exstrophy (an extremely small number) from the initial female gender assignment to male reassignment to a low of 2% for the individuals with congenital adrenal hyperplasia. I must add though that this low of 2% is, nevertheless, a higher gender reassignment than in the general population of transsexuals.



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Self-gender reassignment is not  
100% in any syndrome.

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- The lesson here is that self gender reassignment does not occur 100% in any syndrome which means that even in those cases or those syndromes where there was gender reassignment, not all of them reassigned. They stayed in the initial gender of assignment.

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The factors that coalesce to result  
in gender re-assignment have  
yet to be elucidated.

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- So, we still have a lot to learn as to why some people self-reassign for the same condition and some don't. I will extend this to say we still have a lot to learn to complete the puzzle of psychosexual development, specifically, gender identity; that is how a person like you and I form our gender identity. Gender identity development is still a big unknown.
- Now these data have important implications for deciding gender assignment at birth and what you tell parents.

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## These data have important implications for policies of gender assignment at birth

- high degree of confidence in some
- in others???

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- Based on this review of literature and depending on the diagnosis, you would inform the parents that if assigned one way, say female, their child at a later date might self gender reassign later in life. In a different condition, say CAIS, one could tell the parents that there is a very high degree of confidence that self-gender reassignment will not occur.

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# NOW WHAT?

## Quality of life

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- Remember that story I told you at the very beginning; the mom and dad were saying we never in our wildest imaginations thought we would have to consider gender of our child. Later on, as I followed them up and saw them, they said, “Dr. Mazur, OK we have a little girl now. Tell me. How is she going to be as she grows up? Is she going to have friends? Is she going to be attractive to individuals? Is she going to form romantic attachment attraction? Is she going to be satisfied with her life? Is she going to be having an education? In essence, what this woman, this mother was asking is what all of us would ask of our children. And that is the quality of life. What will be the quality of life of our children?

## Thanks to Colleagues

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**Ellen Bean**, University of Buffalo

**Dianne Berg**, University of Minnesota

**John Breckner**, Canisius College

**Cindy Paxton**, Children's Hospital of Orange County

**Natashia Robbins**, University of Michigan

**Tricia Rynski-Giambelluca**, Children's Hosp of Buffalo

**David E. Sandberg**, University of Michigan

**Mery Taylor**, Children's Hospital of Orange County

**Nicole Vincent**, Children's Hospital of Orange County

**Amy Wisniewski**, University of Oklahoma

- This next slide shows the names of the people I really owe a great debt of thanks to for their unselfish efforts to help me with this presentation. You will recognize some of these names and one of them, Amy Wisniewski is in the audience today. Some of these are new names. I have engaged all these people in a kind of a nutty project, I guess. I've asked them all to review various syndromes from 1955 to the present with regard to not only gender but to extend the previous work I just showed you. I asked them to review what we know about other domains of quality of life. I asked this in an effort to help answer that mother's question about the quality of life of her child. This is a work in progress. Besides offering a big "thank you" to these people, what also is very important to me personally is that a number of these people are young and are very interested in providing good clinical and research services to individuals with a diagnosis of a DSD and their families. They will be around for years to come to help further the effort to provide not only research information, but also the best quality of care as we move forward,

## **DSD CONDITIONS**

### **Consensus Statement, 2006**

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#### ➤ **Sex chromosome DSD**

- 45,X (Turner syndrome and variants)
- 47,XXY (Klinefelter syndrome and variants)
- 45X/46XY (mixed gonadal dysgenesis)
- 46,XX/46,XY (ovotesticular DSD)

#### ➤ **46,XY DSD**

- Disorders of gonadal (testicular) development (eg, Swyer syndrome)
- Disorders in androgen synthesis or action (eg, 5 $\alpha$  RD2 deficiency, androgen insensitivity)

#### ➤ **46,XX DSD**

- Disorders of gonadal (ovarian) development (eg, ovotest DSD)
- Disorders of androgen excess (eg, 21-OH CAH)

- In this next slide are some of the conditions that we looked at And here is what we found.

**LITERATURE REVIEW**  
**ADULT GENDER IDENTITY OUTCOME**

Unpublished  
1955-2007

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**Gender reassignment occurs in:  
Sex chromosome DSD**

- Mixed Gonadal Dysgenesis
- Klinefelter syndrome

- Gender reassignment does occur in mixed gonadal dysgenesis and Klinefelter's syndrome. And many of you might know that in Klinefelter's syndrome there have been reports and at least one book written on individuals who have self-reassigned themselves.

## LITERATURE REVIEW ADULT GENDER IDENTITY OUTCOME

Unpublished  
1955-2007

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Gender reassignment does not occur in:

- 46,XX DSD, other (MRKH)
- Sex chromosome DSD (Turner syndrome)
- 46,XY DSD, disorder of testicular development (Swyer syndrome)

- But we don't find self-gender reassignment, in these conditions, in Mayer-Rokitansky, Turner's Syndrome and in Swyer's Syndrome to date.



## LITERATURE REVIEW: 1955 – 2007 Standardized QOL Measure

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- 3 out of 219 articles
- QOL is new

- Now, I mentioned quality of life before. Quality of life or health related quality of life is a relatively new term although it has been used for a number of years in pediatric psychology. It may be defined as the multi-dimensional concept trying to capture how a person is functioning, subjectively and objectively in many of the essential domains or aspects of being human. We looked at the literature to see what domains were reported on in addition to gender identity, gender role, and sexual orientation. We also wanted to know if the domain was measured using instruments that had the expected psychometric properties such as reliability and validity. We also looked to see if we could find articles that have used psychometric, quality of life tools.
- Right now we found 3 out of 219. We expect to find more, but there are not a whole lot.

## LITERATURE REVIEW: 1955 – 2007

### Domains other than gender identity

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- Sexual functioning: 85/219
- Gender role: 63/219
- Sexual orientation: 39/219
- Cognitive function: 41/219
  - (23/41 46,XX DSD, androgen excess, CAH)

- As you can see from the next slide, the traditional domains of psychosexual development and functioning were looked at the most. Not an unexpected finding given the history as I already mentioned. Here I want to point out that gender role is not the same thing as gender identity. It was mentioned before and many of you know this but truly bears repeating: a child with congenital adrenal hyperplasia will, on average, have an atypical gender role, but it doesn't equate with a wrong gender identity. A genetic female with a diagnosis of CAH can—an often does—demonstrate an atypical gender role (i.e. tomboy) and have established a female gender identity. This is vital information to give to parents, especially to parents who have had the experience of their child initially being called “a boy.” I moved away from my main point which we can return to now, but I wanted to make that remark about gender identity and gender role because it has real clinical utility as you can see from the example.

## LITERATURE REVIEW: 1955 – 2007

### Domains other than gender identity

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|                             |        |              |
|-----------------------------|--------|--------------|
| ➤ Parental response to DSD: | 20/219 | (7/20 MRKH)  |
| ➤ Individual's response:    | 18/219 | (12/18 MRKH) |
| ➤ Career:                   | 8/219  | (5/18 MRKH)  |
| ➤ Spirituality:             | 2/219  |              |

- Back to my main point.
- In this slide notice the small number of articles since 1955 addressing these areas of functioning: parental response to DSD, individual's response to DSD, and so on. Dr. Berenbaum's work on career development in women with CAH is here as well as other people's work on congenital adrenal hyperplasia. This number will obviously go up when you start adding in cognitive functioning in Turner's Syndrome. However look at the little investigation into parental response. We say it takes a village to rear a child. We often say that the most important people in a child's life are their family, their parents. Yet, what do we know about parental response, parental decision making to their child's condition. 7 out of 20 published reports on parental response is in the Mayer-Rokitansky literature; 12 out of 18 for individual's response to their diagnosis.
- People talk about stigma and shame. There were reports out of Germany about individuals with a DSD diagnosis involved in self-cutting, and various high risk behaviors. I'll also mention Dr. Drop and his group back in the 90's I believe talked about family functioning. But we don't know a whole lot about that. Careers, we have some information thanks to Sherri's work on CAH and one report on MRKH but what kind of career or what kind of education is my child going to have who has other DSD conditions? What about disclosing to a partner? What about this issue of

fertility, infertility?

- I mention spirituality on this slide here because I think it is an interesting concept. It certainly has been avoided for a long time by psychology, but how people cope with adversity is very important. How do people cope with various events that come into their lives can be very helpful.

## EXAMPLES

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- Patients searched for “meaning” to interpret their situation (individuals with MRKH)
- “God has given us Emily for a reason” (parents of infant with PAIS)
- Overlap of domains

- Here are 2 examples, one from the Mayer-Rokitansky literature that patients actually tried to understand or interpret as some meaning for their life based on the condition that they have. The second example found on this slide is from the story that I told you at the very beginning. This is what this family said, “God has given us Emily for a reason.” These are the parents of the child with partial androgen insensitivity. Now is that something that bodes well for this family or not well? I think we need to look into it, investigate it more than we have. There can also be overlap of domains in terms of functioning and how they cope, how parents respond, how an individual responds. There’s not much out there in this domain to study and understand

## NATIONAL CONFERENCE ON CHILD HEALTH PSYCHOLOGY April, 2008

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A Pilot Study: Religiosity, Spirituality, Religious Coping in Adolescents with Sickle Cell Disease (S. Cotton et al. University of Cincinnati and Cincinnati Children's Hospital Medical Center)

---HrQoL positively associated with one's religious beliefs

- I came back from a meeting in Miami not too long ago, the National Conference on Child Health Psychology.
- There was a poster that showed that health related quality of life in adolescents with sickle cell disease associated with one's religious beliefs. NIH is funding this project for 5 years. There is beginning to be literature in this area as well as significant body of adult literature in this area. As already hinted at in the about DSD examples, this is a domain we need to look into along with some other domains, which together will paint a better picture of an person's quality of life with a diagnosis of a DSD than we have now.

# SUMMARY

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## RESEARCH NEEDED

- In domains other than gender identity:
  - Family functioning
  - Individual response: shame, etc.
  - Socialization
  
- In populations other than DSD:
  - Childhood development
  - Friendships
  - QOL in other chronic medical conditions

- Now in summary, obviously I want to talk about research.
- I don't think that we are going to solve, at least in my lifetime, the puzzle of how we form our gender identity. Historically, and I'm going to use a phrase that might be out of fashion now, but historically individuals with a diagnosis of a DSD were seen as 'experiments of nature' that gave us a window into the interplay between hormones, prenatal and postnatal and a person's gender identity development. Therefore, it is certainly understandable that historically we have spent a great deal of time investigating this aspect of human development. And, furthermore, I don't mean to imply that we should abandon this search but there are other aspects that need to be explored as illustrated on this slide. We know that some children with a diagnosis of a DSD have difficulties making friends, keeping friends. What do we know about the development of romance and attraction in these children? What about populations other than DSD, what do we already know about typical child development that might apply to and help us with individuals with a DSD and their families? What about friendships again and quality of life in other chronic medical conditions and will that have anything to help us in this particular area.

# SUMMARY

## DELIVERY OF CARE

### Team approach:

- Not just a list of professionals
- Long term follow up: issues revisited & collect data
- <http://www.accordalliance.org/>
- Researcher needed
  - Design and systematic collection of data
  - Clitoral surgery: to cut or not to cut
  - Effectiveness of team approach

- OK, a few words about delivery of care.
- Since 1955, there has been this idea about a team approach. But what does it mean? It is not just a list of professionals performing their jobs in isolation. This is not the traditional medical model of going from this professional to that professional. It takes a lot of interaction. I think that is important to mention when you put a team together it is not putting together simply a list of people that you have at your institution. It has to be people that are interactive with one another and interested in this particular topic.
- Long term follow up is needed. A little girl with complete or partial androgen insensitivity, if my previous clinical experience has any relevance, will eventually talk about the idea of having children adoption and this topic of infertility will be revisited at various points of development. Take for example when the child becomes a teen or young adult when you are interested in someone and they in you. How do you tell about your condition? Do you? When? How? Thought occurs: who is going to want me if I can't produce babies, if I can't, who is going to be attracted to me. How do I tell someone? Working with children with a DSD and their families is a long term commitment. The job isn't over when we make the diagnosis and gender is assigned.
- In this regard, there is an organization called Accord Alliance.com They are just starting up and this is an organization whose mission is to help carry the and I'll use my own words, carry on some of the consensus report recommendations in terms of the team approach and they want to be able to spearhead or be involved in producing teams or providing guidance to people across the country or individuals across the country in producing this teamwork approach. I'm happy to find out, too, that the



Lawson Wilkins organization is sponsoring what is called SNOPEs. Dr. Wisniewski can speak to SNOPEs better than I but I believe it's goal is to bring groups of professionals together that are interested in working together to understand some of these issues that I've been talking and I think the Lawson Wilkins is the appropriate organization to do this. One other thing I can tell you about in April of 2009, the University of Michigan will be hosting a conference involved in people wanting to produce these teams in various areas and also bring together to decide what are the areas of research that need to be created in addition to the traditional ones that I've just mentioned. Now I mentioned this. I'm basically a clinician and I've read through the years we need a team, we need a team, we need a team. And I read you need a psychologist, we need a geneticist, we need this, we need that and I think I need a researcher on the team. I need somebody to help me collect systematic information and data on these various domains because if we don't have that as everyone in this room knows, the issue of clitoral surgery, to do it or to not do it, to cut or not to cut, if we don't begin to have systematic information on this, we are going to be here 20 years from now having some discussion about, well, is this the thing to do, is it not the thing to do. What do parents think? So we need somebody on these teams that can help design protocols that fit into, that have feasibility and generalize-ability in the clinical setting.

- One last word and then I am finished. What about the effectiveness of the team approach? We need to ask and investigate this question.

# SUMMARY

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## A paradigm shift needed

- My final slide. I think we need a paradigm shift. We need to basically look at things in a much broader lens so that the little girl and the parents whom I mentioned to you at the very beginning can have answers to their questions about the quality of life. Research and clinical service that looks through this broader lens can only result in better care.
- Thank you.

## Recommended Readings

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1. Berenbaum, S.A. (2006). Psychological outcome in children with disorders of sex development: Implications for treatment and understanding typical development. In *Annual Review of Sex Research* (D.L. Rowland and C.M. Davis, Eds.) 17, 1-39.
2. Cohen-Kettenis, P.T. (2005). Gender change in 46,XY persons with 5 alpha reductase-2 deficiency and 17 beta-hydroxysteroid dehydrogenase-3 deficiency. *Archives of Sexual Behavior*, 34, 399-410.
3. Dessens, A.B., Slijper, F.M.E., & Drop, S.L.S. (2005) Gender dysphoria and gender change in chromosomal females with congenital adrenal hyperplasia . *Archives of Sexual Behavior*, 34, 389-397.

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## Recommended Readings

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4. Mazur, T. (2005). Gender change and gender dysphoria in androgen insensitivity or micropenis. *Archives of Sexual Behavior*, 34, 411-421.
5. Meyer-Bahlburg, H.F.L. (2005). Gender identity outcome in female-raised 46,XY persons with penile agenesis, cloacal exstrophy of the bladder or penile ablation. *Archives of Sexual Behavior*, 34, 423-438.
6. Meyer-Bahlburg, H.F.L. (2005). Introduction: Gender dysphoria and gender change in persons with intersexuality. *Archives of Sexual Behavior*, 34, 371-373.
7. Zucker, K. (2005). Measurement of psychosexual differentiation. *Archives of Sexual Behavior*, 34, 375-388.

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- Thank you.