Differences of Sex Development

sprout

Supportive Program
for a Range of Urogenital Traits

Ann & Robert H. Lurie
Children's Hospital of Chicago®

Sex development occurs in stages. It is an intricate process. Thus, there are many opportunities for differences to occur that lead to development that is not typical for a boy or a girl. When sex development follows a less common path, the result is a difference of sex development (DSD*). In many cases, knowing the specific cause for the difference may help providers guide better care for individuals with DSD.

Differences of sex development occur more frequently than most people realize. Estimates vary depending on the exact definition used for a DSD, but they occur in one in 2,000–5,000 individuals. While many times these differences are found at birth, some are not found until later in life even though these conditions are present since early in fetal development. Human development is a complicated process. Slight differences in the usual process can result in a difference of sex development. Because these developmental differences occur before birth, they are called congenital.

Three key times for DSD to occur in development

AT FERTILIZATION

Before we talk about fertilization, let's step back and review chromosomes.

Chromosomes are tiny packages of genetic instructions found in every single part of your body. Your chromosomes give instructions for how to build all the different parts of your body. Two special chromosomes have most of the instructions on how to build the reproductive system: we call these the X and Y chromosomes. There are different genes ("instructions") on the X and Y chromosomes that tell the reproductive system how to develop. Typically, an egg cell contains an X chromosome, and a sperm cell contains either an X or a Y chromosome. When an egg and a sperm combine, the two most common patterns are XX and XY.

Usually, an individual with the XX pattern develops along the typical female pathway and an individual with the XY pattern develops along the typical male pathway. Sometimes, however, a child gets an extra chromosome from a parent, or a chromosome is absent, resulting in patterns like XXY, XO or XYY. These differences lead to a DSD.

**DSD is a term in evolution. Commonly used terms to describe DSD conditions include difference of sex development, disorder of sex development and intersex.*

IN EARLY FETAL DEVELOPMENT

When a fetus is just forming in the uterus, two organs are present that we call the gonads. These are identical in everyone until midway through the second month of pregnancy. At that time, certain signals direct the gonad to develop into an ovary or a testicle. Any variation in these complex signals can lead to variation in the way the gonad(s) develop. For example, a gonad may contain both ovarian and testicular tissue or may not produce the usual levels of hormones.

IN LATER FETAL DEVELOPMENT

After the gonads develop, they start to make hormones and send signals that tell the rest of the reproductive system how to develop. This includes both internal and external organs — typically a uterus, fallopian tubes, clitoris and labia in a girl or the penis and scrotum in a boy. At first, every fetus has the potential to develop either set of organs on the inside or outside. Variations in the usual process of development can lead to a range of differences. For example:

- A structure that may look like a small penis or a large clitoris
- A penis with the opening at the base instead of the tip and no testes in the scrotum
- An individual with testicles and male-typical internal structures, but who looks like a typical female on the outside

Several different types of tests may be recommended to help us find the cause for the difference. Understanding the cause helps us to guide families about what to expect for their child and allow us to provide treatment options. However, sometimes the precise cause cannot be determined.

A DSD may bring a complex set of physical, medical and emotional challenges affecting both the child and the parents. Our approach to care at Ann & Robert H. Lurie Children's Hospital of Chicago is to address all of these needs in a sensitive manner. Our goal is a happy, healthy child and the best possible future for each individual in our care.

Detection and diagnosis

DETECTION

Prenatal detection

Increasingly, parents may learn of a possible DSD before birth. For example, a family may learn the child's chromosomes from amniocentesis, or prenatal ultrasound may detect differences in the genital development. In these situations, prenatal consultation with our team is recommended.

Detection in infants

Some children are born with genitalia that is not clearly male or female. This situation is referred to as atypical (or ambiguous or non-binary) genitalia. Many babies with atypical genitalia are otherwise healthy, while some have other serious medical concerns. When a difference in genital development occurs, the labor and delivery team or pediatrician consults our DSD specialists.

For a newborn, the process of diagnosing the specific condition and determining medical needs begins right after birth. The team accomplishes this evaluation at the hospital and provides any urgent care that may go along with the condition. For example, a baby may not have enough cortisol, a life-sustaining hormone. Urgent conditions must be treated early to avoid serious complications. As our medical team addresses any health issues, we also gather information to understand how the baby's reproductive and urogenital systems function. In some situations, this information may be used to help parents designate the sex of rearing (whether to raise the baby as a boy or girl). In rare cases, a decision may be made to raise the child without a specific designation of male or female.

Sometimes, a possible DSD diagnosis is raised after the baby has gone home from the hospital. In these situations, the team may recommend admission to the hospital or outpatient consultation with our DSD specialist.s

Detection in children and adolescents

A DSD can also be found after infancy. As an example, sometimes during hernia surgery for girls, testicles are found to be present in the pelvis. Other times a DSD may be diagnosed if puberty does not occur in a typical way (e.g., not starting a menstrual period), or if a girl starts to develop characteristics such as facial hair or unexpected growth of the clitoris at puberty.

DIAGNOSIS

Diagnosing differences of sex development and planning healthcare involves many specialists. Our multidisciplinary team provides compassionate and respectful care during this sensitive time.

Test and exams

We implement a comprehensive approach to diagnosis, including a physical examination and clinical testing. This information allows our team to understand the patient's genetic instructions, how hormones are working and the exact anatomy of the internal and external genital structures.

Testing has to be done at specific times and often over several days or weeks. We ensure that families understand the nature of these tests such as:

- Blood test to determine chromosomes, called a karyotype
- Blood tests for hormone levels
- Blood tests for electrolytes such as sodium, potassium and blood sugar levels
- Imaging such as ultrasound

This testing can be complicated. We encourage families to ask questions about any of this information throughout the process.

For infants, these tests and exams help the team, in collaboration with the child's family, to make a sex designation (as a boy or girl). Our goal is to determine results as quickly as possible, but most importantly, for this work to be done correctly. Some of the testing may require multiple days or weeks for results.

For children and adolescents, we understand that sensitivity during tests and exams is important and as a result we minimize genital examination as much as possible.

Ongoing care

Our team specializes in supporting patients and families in understanding DSD conditions and treatment. We work closely with families to ensure that they understand their child's condition and create an environment that allows for questions throughout the process.

Sex designation

When a child is born with atypical (sometimes referred to as ambiguous or non-binary) genitalia, it may be recommended or suggested to delay the decision to raise the baby as a boy or a girl until the team has gathered information and had the opportunity to explain it and counsel parents. This may allow parents to make the best long-term decision for their child. Although this can be challenging for some families, it is important to note that most babies who are born with DSD have perfectly healthy bodies. We encourage families to bond with, and enjoy, their beautiful new child while our specialists collect and assess information as diligently and efficiently as possible.

Treatment

In some DSD conditions, hormone therapy may be recommended. Two types of hormone treatments may be needed or considered. The first type replaces life-sustaining hormones that a child is not producing on their own. Two examples are cortisol and aldosterone. Cortisol is the hormone that allows the body to respond to physical stress, and aldosterone helps to maintain the body's water and salt balance. Without these hormones, a child may develop an adrenal crisis, which is life threatening, but treatable once identified.

The second type replaces hormones such as estrogen and testosterone. In some DSD conditions, the body is not able to make enough of these hormones. As a result, the child may not develop breast tissue or have growth of the penis as typically expected at puberty. The pediatric endocrinologist gathers information about the child's hormone status to determine which of these treatments may be necessary or helpful.

In some cases, surgical procedures may be considered. In the past, these procedures were sometimes done without consideration for the reversibility of the surgery or the patients' future sexual function. This is no longer the standard of care and is not in line with the current surgical practice of the team at Lurie Children's. Decisions about surgery are complex and rarely urgent. We presently use the expertise of our multidisciplinary team to ensure that patients are provided with compassionate care and that information is provided to parents and patients in a transparent way that helps determine if any surgical care should be considered.

Mental health support

Mental health support is a core component of our program. Many patients and families benefit greatly from working with a psychologist to better understand the DSD condition. Our psychologists have specialized training and can help patients and their families at any stage in their care.

Our psychologists often provide support to families in multiple ways, such as:

- Supporting the family of a newborn or toddler while they learn about DSD and their treatment options
- Helping parents explain DSD-related issues to their family and friends
- Supporting parents as they adjust to caring for a child with a chronic medical condition
- Partnering with parents to develop age-appropriate ways to explain DSD to their children
- Helping children overcome worry and stress related to taking medication, undergoing tests or medical procedures, and hospital stays
- Helping children cope with worry and stress related to gender identity or body changes associated with puberty
- Helping children and adolescents foster skills to manage interpersonal relationships and maintain healthy self-esteem
- Facilitating peer-support opportunities for families with DSD through social gatherings designed to promote a sense of community
- Promoting wisdom in shared experiences through our program's involvement in Lurie Children's ParentWISE program

There are several ways that patients and families access our mental health services. Some families choose to meet with a psychologist once or twice a year while others choose to meet more regularly.

Fertility preservation for patients with DSD

Some DSD conditions result in infertility. Desires for fertility are deeply personal, but to many individuals and families this is a significant concern. Our DSD team carefully considers this aspect of DSD care from the time of diagnosis, whether the child is an infant or an adolescent. Our team works closely with Lurie Children's Fertility and Hormone Preservation and Restoration Program. We offer options for established techniques for fertility preservation, and we also participate in research programs that can offer investigational fertility preservation techniques.

Resources

Many families also find significant support from trusted family members, friends, support groups, advocacy organizations and their religious support system.

Below are resources with additional information:

- Accord Alliance
  https://www.accordalliance.org/
- Interconnect Support Group
  https://interconnect.support/
- Beautiful You MRKH Foundation
  https://www.beautifulyoumrkh.org/
- CARES Foundation
  https://caresfoundation.org/
- DSD Families
  https://www.dsdfamilies.org/
- Hormone Health Network
  https://admin.hormone.org/
- The Magic Foundation
  https://www.magicfoundation.org/
- Description and animation of sex development:
  https://pie.med.utoronto.ca/ "Sex Development module"

Get more information with these recommended books:

- Handbook for Parents:
  https://www.accordalliance.org/dsdguidelines/parents.pdf
- Disorders of Sex Development: A Guide for Parents and Physicians
  (A Johns Hopkins Press HealthBook) by Amy B. Wisniewski, Steven D. Chernausek and Bradley P. Kropp (Feb 21, 2012)
- Congenital Adrenal Hyperplasia: A Parents' Guide
  by C. Y. Hsu and Scott A. Rivkees (Sep 19, 2005)

All, for your one.®

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