DSD Support Tool
A Guide for Parents

An education tool that takes support of children born with Differences/Disorders of Sex Development and their families to heart.

2018 Callens, Sharp, Sandberg
University of Michigan

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This tool will take you on a journey and provide information about your child's condition and decisions that need to be made

"Your Current Understanding" questionnaire will ask what you already know about DSD

"What is DSD?" will provide an overview on DSD and how they can happen

"Support for Families" explains the importance of having a support team. "Sharing Information with Others" questionnaire asks questions about your support team




Sometimes gender assignment becomes a decision that needs to be considered*

Your child's specific characteristics or DSD diagnosis can also help provide clues about how to make decisions

Tests can provide specific answers to questions that come up in exams; the "Additional Genetic Testing" questionnaire dives into specific concerns

Examinations become an important part of doctor visits and it is important to learn about them

Sometimes surgery may be necessary for the health of your child*

Chromosomes	☐ XX	☐ XY		☐ Other
Diagnosis	☐ CAH	☐ CAIS	☐ 5αRD-2	☐ 45, X Turner
	☐ MRKH	☐ Swyer	☐17βHSD-3	☐ 47, XXY Klinefelter
	☐ XX, testicular DSD	☐ PAIS	☐ Partial GD	☐ 45,X/ 46,XY Mixed GD
		☐ Denys-Drash, Frasier, or WAGR		☐ Ovotesticular DSD
Description	☐ small vagina	☐ hypospadias		☐ gonads
	☐ urogenital sinus	☐ undescended testes		☐ bladder exstrophy
	☐ enlarged clitoris	☐ small penis		☐ cloacal exstrophy




Both your child's and your own well-bring are very important

Parents who may be in situations similar to yours share their stories

"What have you learned?" questionnaire will ask the same questions you were asked in the beginning of the workbook

We have provided a list of questions your team may ask you and you may want to ask you team

DSD Support Tool: A Guide for Parents

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Ann Arbor, MI

Acknowledgements:

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Disclaimer:

The information contained in this workbook is developed to help you make higher quality health decisions. The information is not intended or implied to be a substitute for professional medical advice, diagnosis, or treatment. All content, including text, graphics, images, and information in this workbook is designed to be used in partnership with your child's healthcare providers for general information purposes only.

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WELCOME TO THE DSD SUPPORT TOOL

We are glad you have found us. Having a child you love and cherish with a difference that you did not expect brings with it not only many questions and concerns, but also the need to understand.

OUR WORK

We have created an educational workbook for parents and other family members to explore. This workbook first provides basic information about DSD and continues with more specifics about your child's condition and its management. Specific topics include how you can share information with other people (including family, friends, and your child while he or she grows up) and whether you and the medical team may consider further testing (including genetic tests). Next, this workbook will help you in making decisions about your child's care, even if that decision is to just "wait and see". This will be accomplished by asking about your thoughts, feelings, and beliefs with regard to the different topics and decisions via questionnaires and decision guides.

OUR GOAL

As you learn more about your child's condition, we hope you will take the time you need to gather information, ask questions, learn about options, talk to others who have similar experiences, and make medical decisions guided by both the best medical evidence and other factors that are important to you and your family. Remember that each child is different and that doctors do not yet have all the answers about the best management options. You play a critical role in deciding what is right for your child and your family. An important goal is to have your child grow up happy, healthy, and loved.

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Family Name: _____ Date: _____
Month/Day/Year

Relationship to Patient:_____

Before you begin this workbook, your child's healthcare team has some questions designed to help us gain a better understanding of the kinds of things that may concern you. Please answer the following questions and bring them to your next clinic visit. You will be asked the same questions at the end of the workbook to see how your understanding may have changed over time about DSD and confidence about its management.

Your Current Understanding

Do you believe the following statements are true or false? Please write T for true of F for false on the line. If you are unsure, you may leave the space blank.

1. _____ Differences/Disorders of Sex Development (DSD) are all conditions in which babies did not develop along the most common sex development pathways.
2. _____ Most DSD have a known genetic cause that can be found with genetic testing.
3. _____ DSD are usually not life threatening conditions.
4. _____ In most DSD, genital surgery is medically necessary.
5. _____ Genital surgery is only performed on babies or young children.
6. _____ Genital surgery has risks.
7. _____ Most children with DSD often grow up questioning the feelings they have about themselves as boys or girls.
8. _____ People with DSD are just as likely as people without DSD to be attracted to members of the same sex.
9. _____ My child's DSD needs to be kept a secret from my child.
10. _____ Most people with DSD are not able to have biological children.

11._____ When it is not clear if a baby should be reared as a boy or girl, doctors should decide and then tell the family.

12._____ If surgery is done early enough, there is no need to tell anyone about the DSD.

Your confidence in gathering information to make decisions for your child

Please rate how certain or confident you are that you can do the things that we list below.

How certain are you that you can…

1. Face all the care decisions that might come along the way?

☐ Not at all ☐ A little ☐ Somewhat ☐ Quite a bit ☐ A great deal

2. Get all the information you need (e.g., searching for extra info on your own or with help) to make decisions?

☐ Not at all ☐ A little ☐ Somewhat ☐ Quite a bit ☐ A great deal

3. Learn all about the risks and benefits that matter to you most in these decisions?

☐ Not at all ☐ A little ☐ Somewhat ☐ Quite a bit ☐ A great deal

4. Figure out how involved you want to be in decisions?

☐ Not at all ☐ A little ☐ Somewhat ☐ Quite a bit ☐ A great deal

5. Work with your partner (your child's other parent) to make decisions that you both agree on?

☐ Not at all ☐ A little ☐ Somewhat ☐ Quite a bit ☐ A great deal

6. Identify questions that you want to ask doctors?

☐ Not at all ☐ A little ☐ Somewhat ☐ Quite a bit ☐ A great deal

7. Talk to doctors about what matters most to you?

☐ Not at all ☐ A little ☐ Somewhat ☐ Quite a bit ☐ A great deal

8. Ask a doctor for more information if you don't understand what he/she said?

☐ Not at all ☐ A little ☐ Somewhat ☐ Quite a bit ☐ A great deal

9. Figure out what to do when you hear information that does not agree with the things you have already heard?

☐ Not at all ☐ A little ☐ Somewhat ☐ Quite a bit ☐ A great deal

10. Answer questions about your child's DSD if family members ask you about it?

☐ Not at all ☐ A little ☐ Somewhat ☐ Quite a bit ☐ A great deal

11. Talk to your child about the DSD when your child grows up?

☐ Not at all ☐ A little ☐ Somewhat ☐ Quite a bit ☐ A great deal

12. Ask your doctor to put you in touch with families with the same or a similar diagnosis?

☐ Not at all ☐ A little ☐ Somewhat ☐ Quite a bit ☐ A great deal

13. Call, email, or write to a support organization to ask for information or support?

☐ Not at all ☐ A little ☐ Somewhat ☐ Quite a bit ☐ A great deal

WHAT IS DSD?

Your child's sex development has been affected by one of many conditions, known as Differences/ Disorders of Sex Development (DSD).

There are many ways to get from point A to point B. Similarly babies can follow different sex development paths in the womb. Some paths are more common than other paths.

All sex development paths lead to a combination of sex characteristics. These sex characteristics include, for example, sex chromosomes (X and Y) and how the genitals look on the outside.

<u>Most Boys Typically Have</u>

- XY Chromosomes
- A penis
- Testes and no uterus
- Hormones: A lot of testosterone and a little estrogen

<u>Most Girls Typically Have</u>

- XX Chromosomes
- A vagina and clitoris
- Ovaries and a uterus
- Hormones: A little testosterone and a lot of estrogen

When sex development takes a less common path, there may be a different combination of these sex characteristics

Children with a condition called congenital adrenal hyperplasia (CAH) usually have XX chromosomes, ovaries, and a uterus. Because they produce a lot of testosterone, the clitoris may be larger and/or the vagina and urine tube may share an opening.

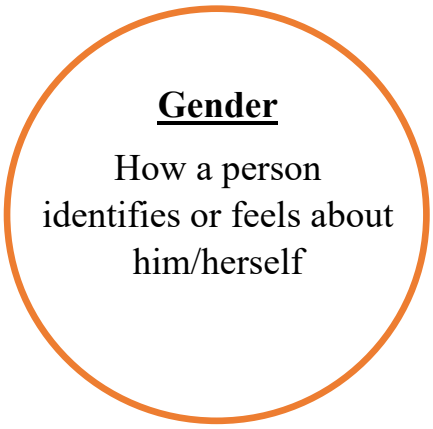
Children with a condition called complete androgen insensitivity syndrome (CAIS) have XY chromosomes and testes. Because the body does not respond to testosterone, the genitals and reproductive structures develop as a clitoris and vagina.

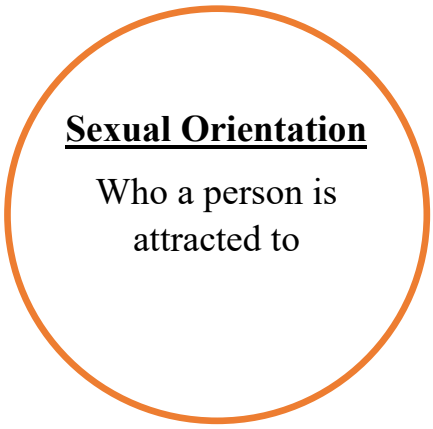
In general, the amount of testosterone that your baby produces, and can react to, will influence how the genitals will look.

Variations of DSD

Sex development is a complex process and many combinations or variations are possible. We call these variations “DSD”.

To clarify, DSD refers to the biological or physical sex characteristics of a person. These include the sex chromosomes, hormones, gonads (ovaries or testes), and genitals. These do not include gender or sexual orientation.





Why did my child take a different path?

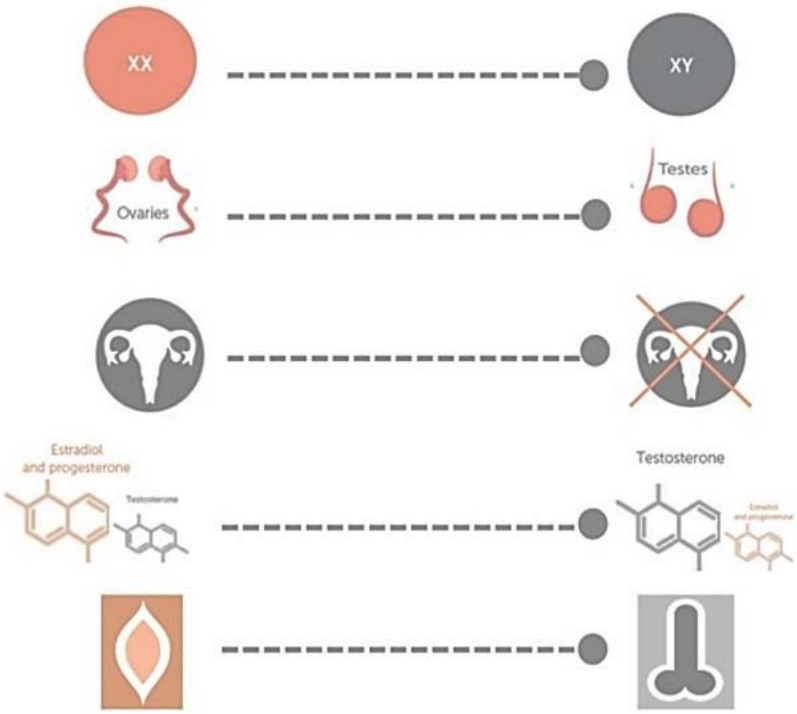
There are many reasons why babies take different pathways. Sometimes, they involve genes. Genes are pieces of information in every cell of the body that serve as the instruction manual for how bodies develop. Changes in genes may sometimes cause unexpected combinations of sex characteristics to develop. They can also affect the way babies produce or respond to hormones. Often, changes in genes occur randomly and are not inherited from the biological parents.

How common is a DSD?

Some DSD are relatively rare. Other DSD are quite common. Although DSD are already present before birth, they can go unnoticed for months or years. Not all DSD lead to visible differences.

Is DSD life-threatening?

Most DSD do not affect general health. Some unfortunately do. Children with one type of DSD may require different care than those who are affected by another type of DSD. That is why it is further important to understand which DSD condition (or "diagnosis") your child has.



SEX DEVELOPMENT BASICS

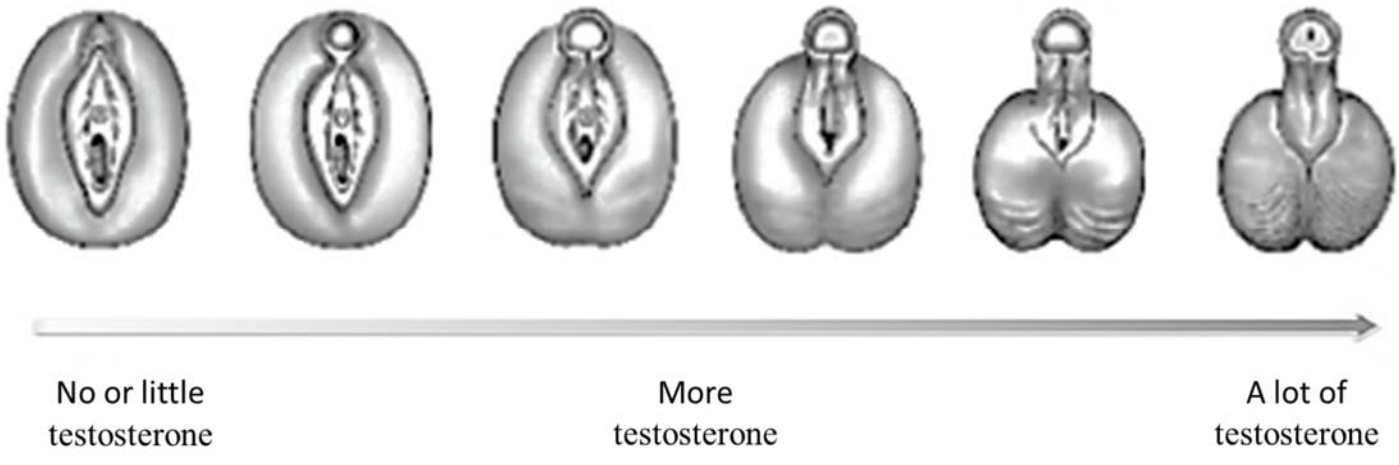
Why do some fetuses grow into typical girls, while some grow into typical boys?

1. Sex Determination

The first step is called “sex determination.” It lasts 5-6 weeks starting from when the egg (ovum) of the biological mother is fertilized by sperm of the biological father.

Usually, the egg has one X chromosome and the sperm carries either an X or a Y chromosome. The fertilized egg (the embryo), can have either two Xs, or an X and Y. There could also be a combination (called “mosaicism”) — like XX in some cells and XY in others. Sometimes, there are 47 chromosomes (47, XXY) or only 45 chromosomes (45, X). Many combinations are possible.

During the first 5-6 weeks of growth in the uterus, all babies have the same internal and external sex structures. Part of the internal sex structures are called gonads. The gonads usually develop further into testes or ovaries which usually produce sperm or eggs for reproduction later in life. The external sex structures are called the genitals. In some babies, they develop further into a penis and the scrotum (the pouch containing the testes). In other babies, they develop further into a vulva, which includes the clitoris, the vagina, and the labia (any of the folds of skin bordering the vagina).



2. Sex Differentiation

The next step is called “sex differentiation.” It starts at 6 weeks when a cascade of genes found on the Y chromosome, including the SRY gene, signals the gonads to develop into testes. If these genes are missing, do not work, or there is no Y chromosome, then the baby will usually not grow testes, but ovaries. Some gonads develop into ovotestes (when there are aspects of both), other gonads do not develop further (also called “streak gonads”).

Gonads differ in the hormones they produce in the womb. Testes produce a lot of testosterone, which typically guides the genitals to develop into a penis and scrotum. When there is none or little testosterone, or when testosterone cannot work, the genitals will develop into a clitoris, vagina, and labia. Remember, there is a big spectrum between typically male and typically female and many variations of genitals are possible depending on the amount of testosterone to which the baby responds to in the womb. Finally, testes also produce anti-Müllerian hormone (AMH). This AMH makes sure that there is no development of a uterus. Without AMH, a uterus usually develops.

SUPPORT FOR FAMILIES

Just like all children, children with a DSD need love and support from their parents. In addition, they need care from their doctors. A psychologist, counselor, psychiatrist, social worker, or nurse specialist can be very helpful in helping you understand what the medical team is doing (diagnostic process) and how your child's biological and physical sex development factor into making decisions about your child's long term care. It is also essential to talk about your child's emotional well-being, as well as your own well-being, now and in the future. They will give you support in dealing with tricky or stressful situations, such as how to manage information about your child's DSD, how to talk about it with other people and, importantly, how you might talk to your child about DSD in the future.

The amount and type of information you may share with others (e.g., baby sitters, child care providers, friends) will depend on many factors: your child's medical needs (e.g., if your child needs medicine), your personal preferences and values, and what you and your child feel comfortable sharing. As your child grows older, it is important to let him/her decide, as much as possible. One of the main challenges is how to respect their child's privacy until he/she is ready to decide what can be shared. This can leave parents feeling isolated. For some parents, having trusted friends or family members who know about the DSD can be helpful.

Although your own family and friends offer support in their own way, they, themselves, are not living with a DSD. Talking with other people who have a DSD or who are parenting a child with a DSD may help with feelings that no one else understands what you are going through. If you feel like talking with other families, check with your doctors to see if they host family days,

or if they can connect you with families or family groups that have been through similar experiences. However, it is important to remember, every family may deal with this in very different ways. Support groups can provide a confidential space where it can be comfortable to discuss feelings about DSD. Advocacy groups are interest groups dedicated to changing the standards of care and participating in these groups can also help you further learn about DSD.

Sharing information with others – psychologists, friends, family, support groups – may give you more time to get used to your child's DSD and more confidence in regards to sharing this information with your child later. How much you share is always up to you. And not all information has to be shared at once. Educating children about their difference is a lifelong process and their questions should be answered in ways that they can understand during each period of development. This helps them grow up with a healthy understanding of their bodies and what to expect. If you are comfortable and confident about this, then your child will be too.

** Check out the Questions to Ask section in the back of the workbook for a list of questions you can ask about Support Groups. Advocacy Groups, and Sharing With Others*

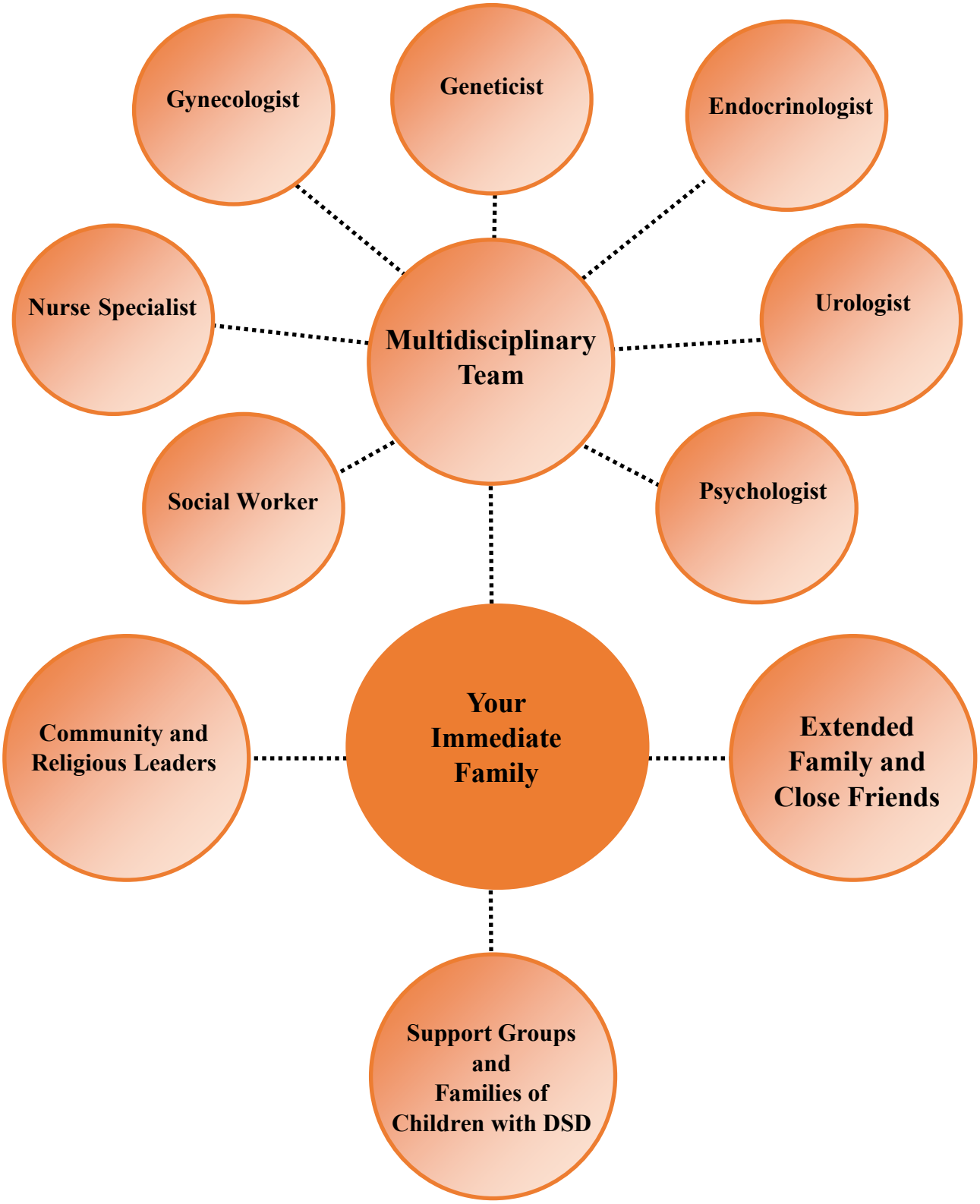


Figure 1: People who could be involved in your support system.

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Family Name: _____ Date _____
Month/Day/Year

Relationship to Patient:_____

Sharing Information with Others and Reaching Out for Support

After reading the "Sharing Information and Support" section, we would like to ask you some questions. Show how you feel about the following statements by filling in the bubble that best describes how you are feeling (closer to the statement means you agree more with what is being said). Please consider bringing this with you to your next clinic visit.

Example Question:

Reason to carpool to work		Reason not to carpool to work
I enjoy talking to others during my commute	○○○○○●○	I enjoy quiet and solitude during my commute

The example above indicates that the respondent generally enjoys quiet and solitude during their commute.

How do you feel about sharing information with others?

Reasons to not share with others		Reasons to share with others
I generally do not like to share information with others about my family's health.	○○○○○○○	I generally like to share information with others about my family's health.
I am worried about how others will react if I share information with them.	○○○○○○○	I am not worried about other's reactions if I share information with them.
My culture has an influence on my decision to share information with others.	○○○○○○○	My culture is not a factor in my decision to share information with others.
I generally keep things to myself and find information on my own.	○○○○○○○	I generally reach out to others for support and information.

How much information do you want to share with others?

1. Close family

☐ None ☐ A little ☐ Some ☐ A lot

2. Extended family

☐ None ☐ A little ☐ Some ☐ A lot

3. Close friends

☐ None ☐ A little ☐ Some ☐ A lot

4. Co-workers

☐ None ☐ A little ☐ Some ☐ A lot

5. Daycare providers/babysitters/teachers

☐ None ☐ A little ☐ Some ☐ A lot

How much are you interested in…

1. Talking with parents of children who have a similar condition?

☐ None ☐ A little ☐ Some ☐ A lot

2. Talking with adults who have a similar condition?

☐ None ☐ A little ☐ Some ☐ A lot

3. Visiting a support group website?

☐ None ☐ A little ☐ Some ☐ A lot

4. Visiting an advocacy organization's website?

☐ None ☐ A little ☐ Some ☐ A lot

EVALUATION OF A BABY WITH A DSD

A diagnosis requires a team of professionals and several tests

When doctors evaluate your child for a DSD, they first complete an evaluation for life-threatening conditions. This includes keeping some babies in the hospital for the first few days of life.

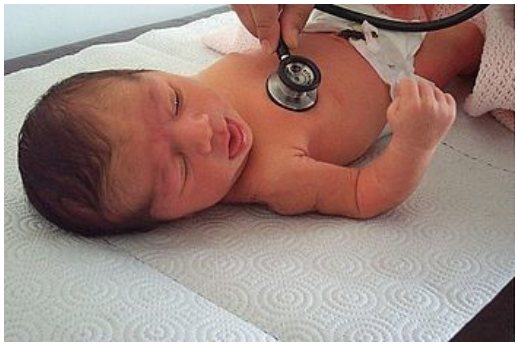
Finding a team of doctors with experience caring for children and families affected by a DSD can help you feel comfortable and confident that your family is receiving the best care available. Usually, these teams are based in specialized centers. These centers can arrange for more specific tests. These teams are also multidisciplinary, including specialists from various disciplines. Usually, there are specialists in endocrinology (hormones), urology/ gynecology (kidneys, bladders, genitals and internal reproductive organs), and psychology (emotional well-being). Other team members usually include geneticists and genetic counselors, nurses and nurse specialists, social workers (help with emotional, financial, and social matters), and child life specialists.

GENITAL/ PHYSICAL EXAMS AND MEDICAL PHOTOGRAPHY

Advice given by Dr. Charmain Quigley

1. Newborn and infancy

Your baby should be examined only by medical personnel who are directly involved in your child's care. Whenever possible, all specialists involved in the assessment and management (e.g., pediatric endocrinologist, urologist, geneticist, and pediatrician) should be present at the same time and undertake the physical/genital exam together. This will minimize the number of exams required. In addition, the number of people present during the exam should be kept



to a minimum, to avoid overwhelming your child and your family. If any teaching of medical students or residents is planned, your permission should be sought well in advance of the exam. Similarly, if medical photography is planned, your informed consent must be obtained beforehand.

What can you do?

If you do not want teaching or medical students attending, before the exams, explain that you would prefer to have only the people who are directly involved in your child's care present.

**Check out the Questions to Ask section in the back of the workbook to find questions you can ask your healthcare providers regarding Physical or Genital Exams/Photography)*

You can be there during the exams and are encouraged to ask questions. The doctors should describe their findings to you and to other medical professionals in attendance (with the caveat that information and answers may be limited before a definitive diagnosis is made) in clear, easy-to-understand words. At the very least, privacy curtains or screens should be drawn and the exam should be performed in a closed room or other private space. If you give permission for medical photography, let the doctor explain again the privacy and confidentiality rules related to these photos, for what purposes photographs will be used, and how they will be stored.

2. Toddler and childhood years

For children who are old enough to be aware of an examination of their genitals, this can be perceived as an invasion of privacy and others not respecting their boundaries. Thus, even greater care should be taken to minimize the number of exams performed and number of doctors present in the room.

What can you do?

You can explain to your child in advance that the doctor may want to look at his/her genitals (use your preferred words and communicate them with the doctors), and that it will be okay because you (or another parent or family member) will be there the whole time. A child who is old enough to understand what is going on, will also be asked by the doctor for his/her permission to participate in exams (called “assent”). Doctors will never force an exam against your child’s wishes. When the exam has been agreed to, you can help your child undress and put on an examining gown or perhaps a piece of clothing brought from home, such as a large T-shirt, so that your child is not fully naked during the exam. Some toddlers and young children may feel more comfortable if they are examined while seated on a parent’s lap, rather than on an examination table.

If you think this approach might make your child feel safer during the exam, suggest this to the doctor(s). Ask them to explain to your child what is about to happen before they touch your child, and provide reassurance to your child that the examination will stop if requested. As a parent, you can help your child feel positive about the experience by showing confidence in interactions with the doctors and providing reassurance to your child during the process. Generally, the results of the exam will not be discussed with your child in the exam room because your child may not have a clear understanding of his/her condition. For this reason, it is often helpful to have someone in your family or a close friend attend the appointment. That way your child can play in the waiting area while you discuss findings and implications with the doctor.

3. Teenage years

Teens start to have an understanding of the associations between genitals and sexual function and may be experiencing their own increasing sense of sexuality. This can make the process of genital exams feel uncomfortable.

What can you do?

Ask the doctor before your upcoming appointment whether your teen needs a genital exam, so that he/she can discuss any fears or concerns with you and be prepared. Some teens feel more comfortable being examined by a doctor of the same gender, so it may be helpful for you to communicate this with the healthcare team, if this is what your teen wishes. At this stage of life, your child's consent for examination is required, not just yours. Your child can also choose not to have you in the room. Another medical professional (generally of the same sex as your teen) might then be present as a chaperone. Your child should be encouraged to tell the physician if they feel discomfort, have questions, or wish the doctor to stop the examination. After the exam, the doctor should share the results with your teen. As parents, you may want to consider allowing your teenager to choose how much information he/she shares with you about the completed exams, as long as the information is not medically critical.

TESTING

Medical care often involves different types of tests and evaluations. In order to diagnose and manage a DSD doctors use different types of tests. This can include checking genetic information and what type of hormones your child's body is producing. Other tests try to determine how the internal sex organs (such as the uterus and gonads) have formed and how the external genitals might continue to develop. Some of these assessments can be important for predicting responses to future medical treatment (usually some form of hormone replacement) as well as what to expect if you and your family decide to proceed with surgical treatment. Well-being assessments might further give the team an idea of how you feel and think about some of the challenges involved in rearing a child with a DSD.

GENETIC TESTING

The Genetic Puzzle

Because there is no genetic test that can detect everything that might cause a DSD, there is a chance that a couple of genetic tests are needed if you and the medical team decide to have complete testing.

Things to Consider

In order to correctly diagnose a DSD, genetic testing is often necessary. However, there are some important factors to consider before tests are done. In some cases, learning that your child does not have typical male or female chromosomes can be difficult for parents. In addition, just learning the details about your child's diagnosis can be challenging.

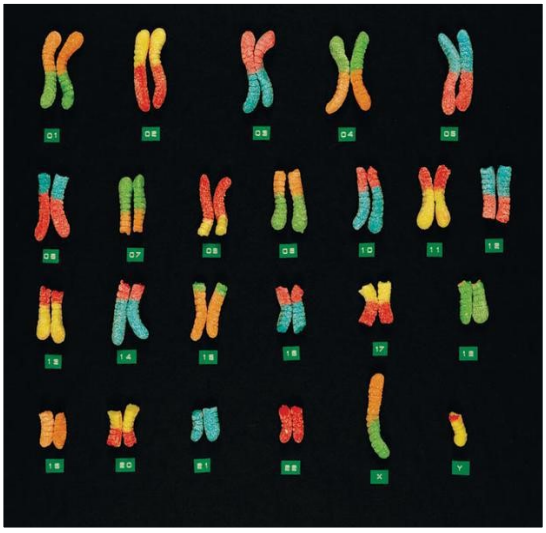
With any genetic testing there is also the risk of finding unanticipated results. Some types of genetic testing might reveal that your child carries genes for a disorder (one that is

related to DSD or not). Along with how to manage your child's condition, this could raise questions about who else in the family has these genes and how you would like to share this information with other family members. In addition, some tests can pick up other changes in chromosomal material for which there is very little medical information available to predict what type of (other) problems may develop in your child. If the child's parents are undergoing genetic testing as well, testing could also reveal that the biological parents are genetically related (called consanguinity) or reveal information about family relationships. For example, the test could show that a father may not be the biological father of the child. It is also possible that the genetic testing may not detect a DSD or change the treatment of your child.

Genetic Tests

Usually, before any test, the team will ask you about your child's medical history. The doctor can use this family health history to become familiar with the conditions that may run in the family. The more people in the family there are with the same condition, the higher the chance that genes are involved in causing the condition. But, even if there is no family history, there could still be a genetic cause. Sometimes, a DSD is caused by changes in genetic material that are not inherited.

1. Chromosome Pattern Test

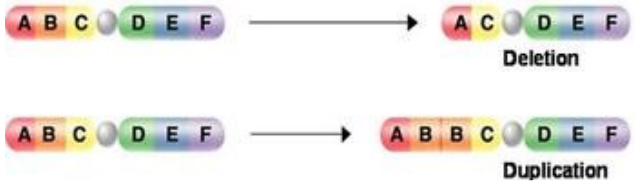


In genetic testing for DSD, doctors will typically begin by checking your child's chromosomes (or karyotype). Each person usually has 46 chromosomes or 23 chromosome pairs, including one pair of sex chromosomes, XX or XY. This information is written down as 46, XX or 46, XY.

Sometimes, there is an atypical number of chromosomes. For instance, there could be 45 chromosomes (if there is only one X, written as 45, X).

Sometimes there are 47 chromosomes (if there is an extra X chromosome, written as 47, XXY). Other people have combinations of sex chromosomes that differ from cell to cell. This is called “mosaicism.” For instance, some cells of the body have 46, XX and others 46, XY or some cells have 45, X and others 46, XY. Many combinations are possible.

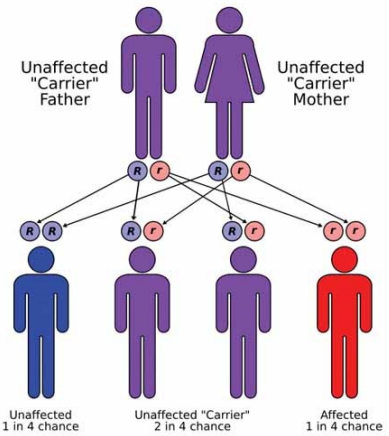
2. FISH Test



A test that is commonly performed together with the chromosome pattern test is the FISH (Fluorescence in situ hybridization) test. It can be used to check whether a specific gene linked to sex determination (the SRY gene) is present and if it works.

3. Chromosomal Micro Array

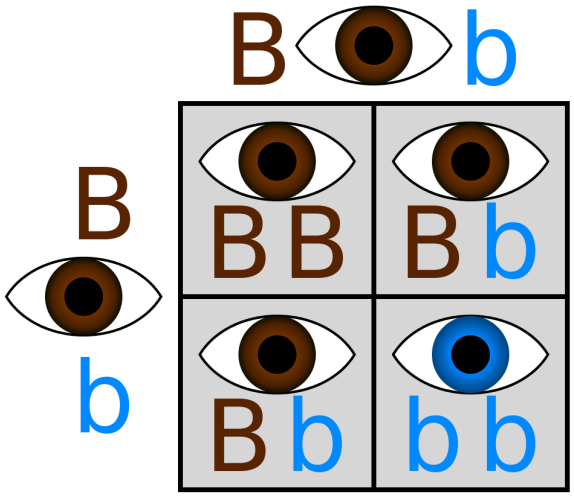
A Chromosomal Microarray Analysis (CMA) looks at the chromosomes in a more detailed way, via a blood sample, and the results from testing take roughly 3-4 weeks. CMA uses a gene chip (a “microarray”) to look for imbalances in the amount of chromosomal material, by comparing the material from your child with that of a “control” group (a group of individuals with no known genetic disorders or abnormalities). If a difference is found, the test can show where the difference is located on the chromosomes and what the reason is for that difference. Sometimes, a small amount of material is missing (deleted) from a chromosome (called microdeletion).



Sometimes, a small amount of material is present in an extra copy (duplicated) on a chromosome (called micro duplication). Too much or too little chromosomal material can lead to differences in the overall development of a child, such as physical and mental differences, including developmental delay and autism.

4. Targeted Gene & Carrier Testing

Targeted gene testing helps determine if there are changes in certain specific "targeted" genes (and their sequences) that influence sex development (such as SRY, SOX9, SF1, WT1, and many more). We all carry two copies of each of these genes, one from our biological mother and one from our biological father. Some DSD require only one of these two gene copies to be affected by unusual changes in order for someone to have a DSD. This is called a dominant condition. Other DSD require both copies to be affected. This is called a recessive condition. For this to happen, both the biological mother and father have an affected copy and each transmitted that affected copy to their baby. It is also possible that only the mother or only the father passed on an affected copy. In this case, the biological mother or father is called a "carrier." Being a carrier means that people do not have a genetic condition themselves, but have the ability to pass on the affected gene to their offspring. Carrier testing can thus determine if the child and other biological family members (e.g. brothers, sisters, parents) "carry" a certain targeted gene change. This may have medical consequences for these family members. If planning future pregnancies and both partners are carriers for the same recessive genetic condition, they have a 1 in 4 or 25% chance of having an affected child in each pregnancy. The American College of Medical Genetics currently does not support carrier testing in children. If tests find changes in these targeted genes, the results may not predict how mild or severe your child's (or other biological family members') health problems will be. If they did not find changes in targeted genes, they rule out some important DSD diagnoses, but do not rule out all DSD caused by changes in other genes.



5. Whole Exome Sequencing (WES)

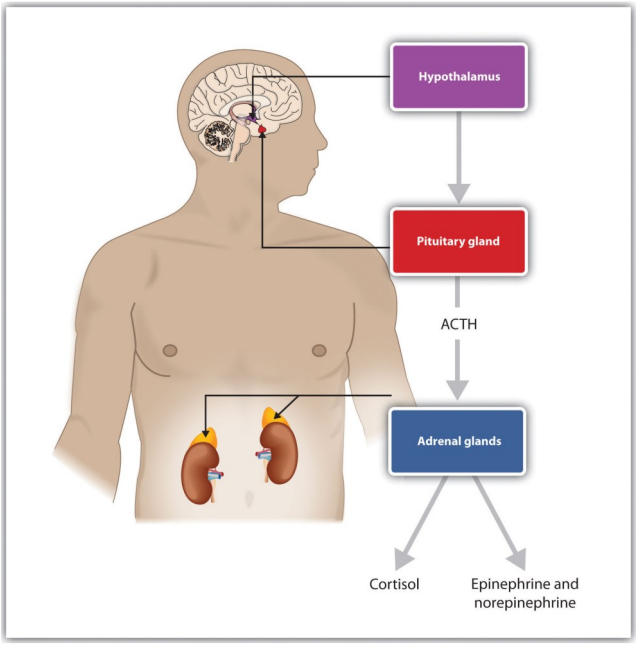
A person's collection of genetic material (genome), is their own personal blueprint for life. Whole Exome Sequencing (WES) only screens a person's exome (1% of the genome). Compared to other genetic tests, WES looks at more genes and has a higher chance of finding a genetic cause for your child's DSD if previous tests failed to find one. However, 75% of patients do not receive a DSD diagnosis from WES. The test is usually done via a child's blood sample and other biological family members can also be tested. Results from testing take roughly 4-6 months. The WES test will compare your child's exome (or that of other family members) with that of a "control" group (a group of individuals with no known genetic disorders or abnormalities), and try to detect differences. Sometimes, these differences can be the cause of your child's DSD. It is possible that WES will not find gene differences that are actually present. WES is a new and expensive genetic test. Not all health insurance companies will pay for the cost of the test. All WES tests will be discussed with your insurance company before testing. If your insurance does not cover the test, it could cost several thousand dollars.

HORMONE EVALUATION

Hormones are chemical messengers in the blood that alert different parts of body to preform certain actions. Your doctor will want to know what hormones your child's body is producing and how much of those hormones are present. Hormone evaluations can help your doctor come to a diagnosis, determine if your child is at risk for a potential crisis (such as salt wasting in certain types of CAH), and help make decisions about managing your child's health. The part of the body that controls hormones is called the endocrine system.

How Does the Endocrine System Work?

Most hormone tests will assess a part of the hypothalamic-pituitary-adrenal (HPA) axis, which is a major part of the neuroendocrine system that controls reactions to stress and regulates many body processes. These include digestion, immune system functioning, mood and emotions, sexuality, energy storage, and energy use.



The HPA axis is named after its three components: the hypothalamus, the pituitary gland, and the adrenal glands. The hypothalamus regulates the body and brain and is considered the control center for the body's automatic responses. When excited, the hypothalamus activated the pituitary glend which releases corticotrophin-releasing hormone (CRH) to activate the pituitary gland.

The pituitary gland, often referred to as the master gland, is responsible for controlling the hormones in the body. This pea-sized part of the brain releases hormones to stimulate other areas of the body including gonadotropin and growth hormones that regulate normal growth, sexual development, and reproductive function. The pituitary gland also releases the adrenocorticotropic hormone (ACTH) to trigger the adrenal glands. The adrenal glands sit on top of the kidneys, like little blobby hats. The kidneys are used to filter the blood and are in the center of the body. This makes it an ideal location for a hormone that needs to affect the entire body, because all blood passes through the kidneys. The adrenal glands release several hormones including cortisol and aldosterone. These hormones are important for regulating the

Hormone Tests

How are hormones evaluated?

Hormones are typically evaluated by taking a blood sample. Some hormone levels are looked at as part of a standard newborn screen. Depending on the test, your child may need to stop taking certain medications (e.g. if they contain steroids).

There is a small risk in having your child's blood taken. Veins and arteries vary in size from one patient to another and from one side of the body to the other. Taking blood from some children may be more difficult than from others. Other risks of having blood drawn are small but may include: excessive bleeding, fainting or feeling light-headed (more frequent in adults than young children), blood accumulating under the skin (hematoma), and/or infection (a slight risk any time the skin is broken).

1. Standard Evaluation

Early on in treatment or evaluation your doctor will most likely test your child's levels of:

- 17-hydroxyprogesterone- a building block for cortisol, the body's "stress" hormone
- Testosterone- a hormone commonly associated with male sex development that often causes virilization (masculination)

- Gonadotropins- a term for several hormones that are produced in the pituitary gland and act on the gonads (ovaries or testes). The levels of these hormones can be used to predict how the body will develop at puberty
- Anti-mullerian hormone- plays a role in inhibiting the development of the Mullerian ducts early in development. Later in development the Mullerian ducts can develop into fallopian tubes, a uterus, the uterine cervix, and the upper regions of the vagina
- Serum electrolytes- function in keeping water flowing in and out of cells and in nerve impulses. Sometimes referred to as salts, they include sodium, potassium, chloride and bicarbonate

By looking at the levels of these hormones (and any others that were looked at) your doctor will be able to make some determinations about how your child's body is functioning and developing. In some cases it may be necessary to perform more intensive hormonal evaluation through stimulation tests. The three stimulation tests often preformed as part of DSD care are: ACTH, hcG and GnRH stimulation tests.

2. ACTH Stimulation Test

In this test, synthetic ACTH is given to your child to stimulate the adrenal glands to produce cortisol (the stress and energy hormone) and aldosterone (the salt balance and blood pressure hormone). If there is not enough cortisol and aldosterone, your child may show signs of weakness, poor feeding, poor weight gain, and low blood pressure. If not treated medically, this can be life-threatening.

How is the test performed?

Your child's blood will be drawn at the beginning of the test, the synthetic ACTH will be given, then, about 90 minutes later, blood will be drawn again. Longer versions of the test are also available but are rarely performed. Because of the small size of babies and children, sometimes blood cannot be obtained at all time points. The synthetic ACTH may in some .

babies lead to a temporary rash, high blood pressure, and lower/higher heart rate. Usually, something called a Heparin Lock will be used to avoid repeated needle sticks are not needed. You will typically get the results for the cortisol level back in one day. It can take one to two weeks for the other results. From testing cortisol levels, the endocrinologist (hormone doctor) will be able to determine if the adrenal glands and pituitary gland are working properly. They can probably tell you if there is an appropriate increase in cortisol after the synthetic ACTH is given or if there is no increase in your child's cortisol level. If there is no increase, more testing may be needed to make a diagnosis and to specify what kind of hormone replacement is necessary.

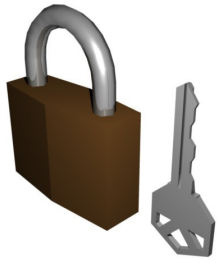
3. hCG Stimulation Test

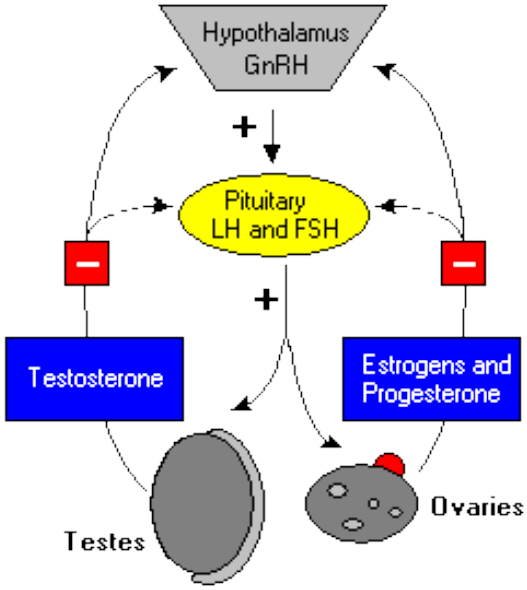
If your child has testes, during the first three months of life, your child's testes can produce large amounts of testosterone naturally as part of a "mini puberty." After three months, testosterone levels begin to decrease to the low levels seen throughout childhood. If your baby is being evaluated after this early peak of testosterone has passed, specific stimulation tests may be used.

One way to stimulate the testes to produce testosterone is to give your child a synthetic hormone called hCG (short for Human Chorionic Gonadotropin), administered in a series of injections.

<u>How is the test performed?</u>

On day one, blood is drawn to measure the levels for testosterone and other androgens associated with testosterone. Then hCG is administered by a shot into a muscle in the arm, leg, or bottom. Two more injections, on day 2 and 3, are usually given to stimulate the testes. These shots can be done at the endocrine clinic or at your child's primary care provider's office. A second blood draw is done after the third shot and again 24 hours later to see how much testosterone and other androgens have been made.





There are many variations of this test. This test may cause fussiness and an increased number of erections (if an erection lasts longer than 4 hours, the baby/ child needs to be taken to the emergency department immediately). Usually, the test results will be back in a week and could show that your child's testes produce normal, low, or no levels of testosterone. The additional blood tests assessing other androgens may also help in determining the specific DSD diagnosis. For example, some children produce normal testosterone, but have problems converting it to other androgens, which are also necessary for the development of the male external genitals.

Other children may produce normal testosterone, but the cells in their bodies (called receptors) are not able to respond to these hormones. There is a key, but it does not fit on the lock, because the lock has changed. Usually, doctors will recommend genetic testing to study the specific characteristics and structure of the lock.

4. GnRH Stimulation Test

GnRH (short for Gonadotropin-Releasing Hormone), is produced in the hypothalamus and signals the pituitary gland to produce Luteinizing Hormone (LH) and Follicle Stimulating Hormone (FSH). In males, LH stimulates the testes to produce testosterone and FSH supports the maturation of sperm. In females, FSH and LH stimulate the ovaries to produce estrogen and progesterone and regulate the menstrual cycle.

How is the test performed?

In a GnRH stimulation test, synthetic GnRH is given as a shot to make the pituitary gland release LH and FSH. Before the test, your child may need to stop taking certain medications. Your child's blood will be drawn at the beginning of the test, the synthetic GnRH will be

given, then, about 90 minutes later, blood will be drawn again to measure LH and FSH. Longer versions of the test are also available but are rarely performed. Because of the small size of babies and children, sometimes blood cannot be obtained at all time points. Results are usually available in a couple of days. Hypogonadism occurs when the gonads (testes or ovaries) produce little or no hormones. This can be caused by some DSD conditions, but it can also be caused by tumors. When hypogonadism centers on the testes or ovaries, it is called primary hypogonadism. When it centers in the pituitary gland and hypothalamus areas of the brain, it is called central or secondary hypogonadism. To treat hypogonadism, your doctor needs to know if it is primary or secondary.

When the LH response is higher than normal, it may indicate primary hypogonadism. When the response is too low, it may indicate secondary hypogonadism. Doctors may suggest an MRI scan of your child's brain and further genetic testing. Sometimes, your child can produce enough LH, but the body does not respond to it (there is a key, but it doesn't fit into the lock), and genetic tests can be used to the problem with the LH "lock" (called a receptor). These and other tests may also be important to determine which type of hormone treatment your child may need to start puberty later in life.

EXTERNAL AND INTERNAL SEX ANATOMY TESTS

External and Internal Sex Anatomy

Here we explain some of the exams that doctors use when trying to define how your child's external genitals and internal sex organs have developed before birth and are developing over time with or without medical treatment and/or genital surgery. The results of these exams can be difficult to interpret.

Doctors will usually do an external genital exam first. They will measure how the genitals have developed, investigate whether there are testes and where they might be located (in the genital area, groin area, or in the belly), and check the location of the tube that carries urine from the bladder to the outside of the body (urethra). Sometimes, the urethra and vagina are fused together and only have one opening, called a urogenital sinus. Sometimes, the urethra does not end at the tip of the penis, but somewhere on the shaft or at the base of the penis. This is called hypospadias.

Doctors will also check for a uterus (womb) and whether your child has functioning ovaries, testes, or ovotestes (where there is a combination of ovaries and testes). Ultrasound tests and scans (e.g. MRI, genitogram) may sometimes show these internal sex organs, but the results of these scans are usually difficult to interpret. Another way of looking is through small incisions in the skin of the belly, and passing a small "telescope" (laparoscope) through those incisions. Sometimes, a sample of tissue (biopsy) is taken for examination in a laboratory. Doctors may also suggest looking at the bladder and vagina with a special "telescope" (cytoscope).

Description of External Genitals

Usually, the doctor will measure the length and width of your child's penis/clitoris, check

how the labia/scrotum have developed, investigate whether there are testes and where they are located (in the genital area or groin area), and check the location of the urine tube and vaginal opening (if they are fused together, it is called a “urogenital sinus”). A genital exam can be important to predict the responses of your child’s body to medical treatment (for instance, the size of the clitoris can sometimes become smaller, or the size of the penis larger, with hormone therapy) and will possibly also give you and the healthcare team a better idea of what to expect (or not to expect) if surgery to change the appearance and/or function of your child’s genitals is an option Because some exams are more thorough (e.g. exams of the genitals and bladder/bowel), and can cause physical and psychological distress for babies and children (for instance if they need to lay still for some time), doctors can suggest to do these exams under anesthesia (the medicine that prevents any immediate discomfort or sensation during the exam).

Anesthesia

The FDA warns against the use of repeated and/or lengthy anesthesia (over three hours), when not medically necessary, in children under 3 years old because it may effect brain development. If your child has previous anesthesia exposure and is under 3 years old, or if you are concerned, it is important to talk with your doctor about the risks and benefits of performing an exam under anesthesia. It may be helpful to ask if this exam can be combined with another procedure that your child may need anesthesia for (for example: a cystoscopy or laparoscopy).

When using anesthesia, there may be short term side-effects, such as drowsiness or disorientation after the exam, and your child may be restless or cry. Many parents worry that their child is in pain, but that is usually not the case. Generally, your child is reacting to the anesthesia wearing off. Crying may actually assist in removing the anesthesia from your child's system. The best thing you can do is try to comfort your child and wait. If your child is hungry, you may offer clear liquids. Breast fed infants may be given breast milk.

Examination of Internal Sex Organs

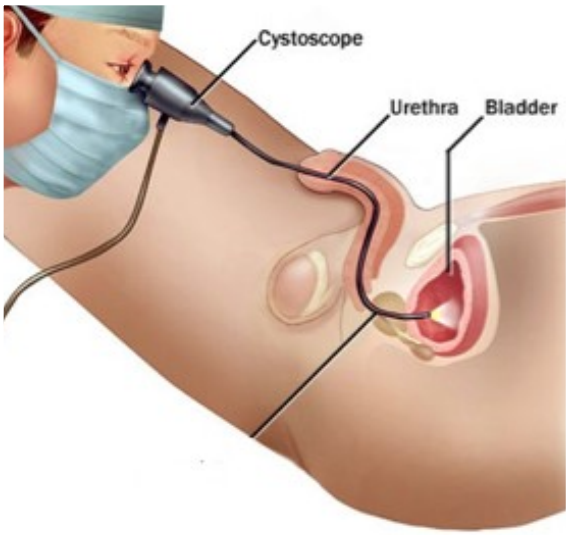
1. Pelvic Ultrasound

This imaging test is very similar to the ultrasounds that women receive during pregnancy. It produces pictures of the inside of the body using sound waves. An ultrasound is performed by first putting a gel on your child's lower belly and then using an ultrasound probe to touch your child's belly. Ultrasound images can show the structure and movement of your child's internal organs, as well as blood flowing through blood vessels. The key to getting useful information is to have this test performed and interpreted by a professional with experience in the evaluation of babies and children. Ultrasound examinations do not use radiation and are safe for use in children. A pelvic ultrasound is however not really suited for examining the vagina or urogenital sinus. Also, because the uterus is very small before puberty, it may be hard to see on an ultrasound.

2. Magnetic Resonance Imaging (MRI)

MRIs give more information than pelvic ultrasounds about your child's internal (reproductive) organs and better identify any problems that may exist. However, again, like in pelvic ultrasounds, MRI's are not good at visualizing the vagina or urogenital sinus. Often a uterus is very small before puberty, and not large enough to image well. MRI does not use radiation and is therefore safe for use in children. However, sometimes, a contrast dye might be injected to get a better picture of some specific areas of your child's lower belly. This sometimes causes allergic reactions (such as rashes, hives, nausea, flushing, and dizziness). Some babies may have general anesthesia when they have an MRI so that they do not move during the test. In other babies, a sedative will help to calm them, but will not completely put them to sleep. To have an MRI, your child will be placed in a large scanning device and must be relatively still so that the MRI machine can make a good picture. The machine can be very noisy and might upset your child. The exam usually takes 20-30 minutes to complete.

3. Cystoscopy and Vaginoscopy



Doctors can insert a special “telescope” into the bladder and opening of the vagina or urogenital sinus (cystoscope for the bladder and vaginoscope for the vagina and urogenital sinus) to get a clear image of the insides of these structures. The “scopes” can also take pictures. Sometimes, there are under-developed sex structures with no real function (called remnants or remains), which can put your child at risk for infections and internal obstruction, which may need to be removed (with a laparoscopy, see next section). Usually, however, these structures are very small, do not cause problems, and can be left in place.

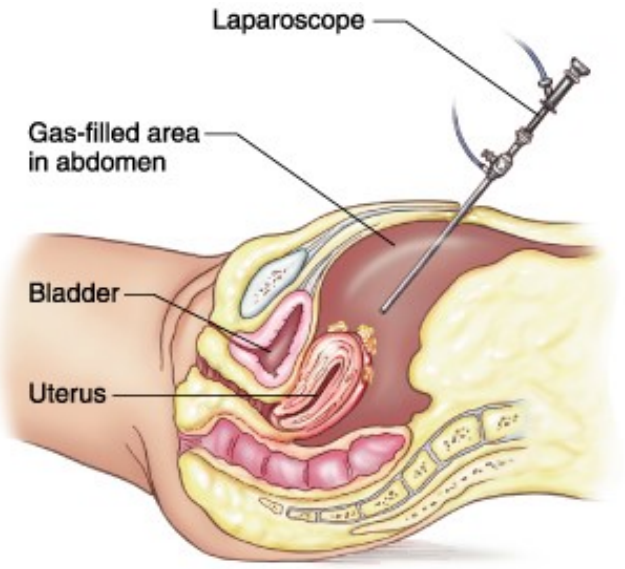
Your child will be given general anesthesia (which will help your child sleep during the prodecure). Some children will have a reaction to the anesthesia. When performed by a pediatric urologist/gynecologist (or similarly trained surgeon), these procedures are usually relatively quick and harmless.

Rarely, scopes can introduce germs into the urinary tract, which can cause infections. They may also worsen an existing urinary tract infection,. Therefore, most doctors will prescribe antibiotics for your child to take before and after the scopes to prevent infection. Although rare, scopes may cause bleeding because of damage to the blood vessels or pain because of damage to the bowel, bladder, and nerves.

4. Laparoscopy, Including Gonadal Biopsy and Gonadectomy

For some procedures, such as a gonadal biopsy (taking a small sample of your child’s gonads for evaluation) or gonadectomy (removal of the gonads), small incisions (cuts) into the belly or groin area are made to insert a laparoscope (a special telescope) and other

instruments necessary to perform the procedure. Your child will be given general anesthesia and his/her belly will be inflated with a carbon dioxide (CO2) gas. To allow ventilation with the CO2 in the belly, your child will also be intubated, in other words, a tube will be inserted into the child's airway. This may cause a sore throat. After the surgery, the incisions are closed with a stitch or glue. In general, school can be restarted the day after or some days after a laparoscopic procedure.



Laparoscopic surgery can further help doctors to determine the specific diagnosis and provide some indication of future fertility of your child when a biopsy of the gonad is taken and further investigated under a microscope. The procedure can also be useful for removal of the gonads that have a high tumor risk. The risks of laparoscopy are small, but include:

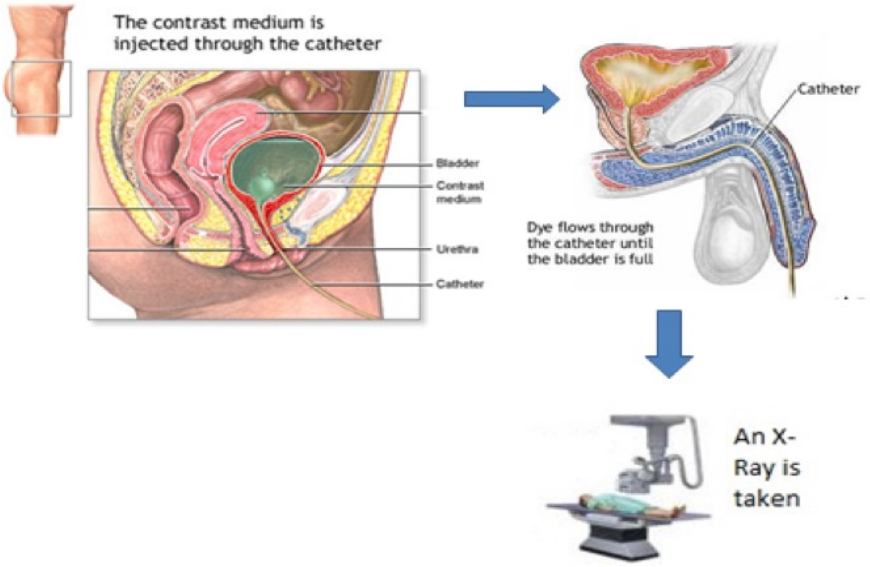
- Bleeding
- Infection
- Damage to the bowel, bladder, blood vessels, and nerves
- Some babies will have a reaction to anesthesia
- When a biopsy is taken of the gonad, it is very uncommon, but biopsies can result in unintended damage to or loss of the gonad.

5. Genitograms

Genitograms use contrast dye injections and X-rays to get a clearer picture of your baby's bladder ("a cystogram"), vagina, urine tube, or urogenital sinus. Sometimes, your doctor may prescribe antibiotics for your child to take before and after the test to prevent urinary tract infections (UTI). The test can only be done when your child has not had a UTI for at least 2 weeks before the test is scheduled.

During the test, a catheter will be inserted in the urinary tube or urogenital sinus and filled with a contrast fluid. A series of X-ray pictures are taken. Once the bladder is full, small babies and infants usually start to urinate (if not, the doctor might stimulate them to urinate). During urination, more X-ray pictures will be taken (called a "voiding cysto-urethrogram" (VCUG)), so that doctors have a clearer image of the bladder and lower urinary tract in motion, as well as the flow of the urine. While your child is urinating, the catheter will usually slide out spontaneously without your child feeling any discomfort. A few additional X-ray pictures will be obtained to complete the exam. The whole procedure takes approximately 20-30 minutes.

There can be a slight irritation from the catheter insertion and there is a risk of UTI after the exam. Some babies also have a slight allergic reaction to the contrast dye, such as rashes, hives, nausea, flushing, and dizziness. There is radiation exposure from the X-rays. While a small amount of radiation exposure is not harmful, the more X-rays and scans are performed, the higher the risk that the exposure becomes harmful. Therefore, you may want to ask your doctor about the amount of radiation used during the procedure and the risks related to your child's situation. It is always a good idea to keep a record of your child's past history of radiation exposure, such as previous scans and other types of X-rays, so that you can inform your doctor.



** Check out the Questions to Ask section in the back of the workbook for questions you can ask your team regarding Testing, Genetics and Hormone Replacement Therapy.*

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Family Name: _____ Date _____
Month/Day/Year
Relationship to Patient:_____

After gaining more knowledge on the different tests that can be administered and what they entail, please let us know how you are feeling by answering the following questions and please consider bringing your answers to your next clinic visit.

Extra genetic testing

Want testing results		Do not want testing results
I want all genetic test results, including those which are not related to DSD and won't change my child's management	○○○○○○○	I don't want to get genetic test results that are not related to DSD and won't change my child's management
I only want genetic results that are not related to DSD if they have an impact on my child's management	○○○○○○○	I don't want genetic results that are not related to DSD, even if they have an impact on my child's management
I am comfortable getting genetic test results that are not related to DSD, even if doctors don't know if they'll change my child's management	○○○○○○○	I am not comfortable getting genetic results that are not related to DSD, if doctors don't know if they'll change my child's management

Decide what's next

Do you understand what all the different options or possibilities are about extra genetic testing?

○ Yes

○ No

Do you have enough support and advice from others to make a choice?

○ Yes

○ No

Certainty

How sure do you feel right now about a decision regarding extra genetic testing?

Not sure at all ○○○○○○○ Very sure

Check what you need to do before making a decision

○ I want to discuss options/possibilities with others

○ I want to learn more about options/possibilities

○ I'm ready to take action

Use the following space to list questions, concerns and next steps

You may also think about **genetic testing for research**.

The purpose of genetic testing for research is to identify new genes that cause DSD and to further understand how those genes work. This information may not help your child directly, but can be important in the development of new tests that can be used in the clinic in the future for other affected children and their families. The results of genetic testing for research are usually not shared with you, but can be shared if you desire. All the benefits and risks of genetic tests will be explained in the informed consent forms that you will need to go through before you decide to participate in genetic testing for research.

What are you leaning towards?

I do not see the value in participating in research	○○○○○○○	I see a value in participating in research

Carrier testing

Finally, some genetic tests may reveal that your child's DSD condition is hereditary. If you are a biological parent, you may want to think about these tests, too.

○ I'm a biological parent

○ I'm not a biological parent

You may be a carrier for the DSD, meaning that you don't have the condition yourself, but passed it on to your child. Other people in your family might also be a carrier and may pass it to their offspring. This information may challenge personal and family relationships.

Show how you feel about the following statements		
I would blame myself if I learned that I passed on a genetic change to my child	○○○○○○○	I feel as though I could not do anything to prevent passing on a genetic change to my child
I am worried about family members and/or partners finding out that I am a carrier for a genetic change	○○○○○○○	I am comfortable sharing with other family members and/or partner that I am a carrier for a genetic change
I feel as though others will blame me if I share with them that I am a carrier for a genetic condition and ask them to consider testing themselves	○○○○○○○	I feel as though others will not blame me if I share with them that I am a carrier for a genetic condition and ask them to consider testing themselves
If I plan on having more children, I want to know if they could be affected by a genetic condition	○○○○○○○	If I plan on having more children, I am comfortable not knowing if they could be affected by a genetic condition

Now that you thought about your feelings, you may have a general idea of where you stand. On the scales below, show which way you are leaning now.

What are you leaning towards?		
I would like to know if I am a carrier of a genetic change	○○○○○○○	I don't want to know if I am a carrier of a genetic change
I would tell other family members that I am a carrier of a genetic change	○○○○○○○	I would not tell other family members that I am a carrier of a genetic change

Decide what's next

Do you understand what all the different options or possibilities are about carrier testing?

○ Yes

○ No

Do you have enough support and advice from others to make a choice?

○ Yes

○ No

Certainty

How sure do you feel right now about a decision regarding carrier testing?

Not sure at all ○○○○○○○ Very sure

Check what you need to do before making a decision

○ I want to discuss options/possibilities with others

○ I want to learn more about options/possibilities

○ I'm ready to take action

Use the following space to list questions, concerns and next steps

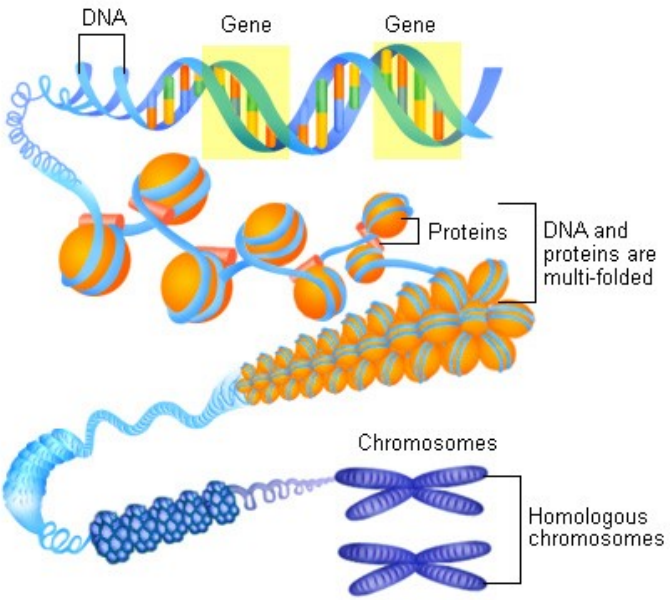
YOUR CHILD'S DSD

The following part of this support tool gives details about your child's DSD according to your child's chromosome pattern: XX, XY, or others, such as: X, XXY, XX and XY.

If a DSD diagnosis (with confirmed genetic cause) has already been found for your child, you can immediately access more detailed information as well as consider decisions for that specific diagnosis.

If you do not have a diagnosis, it is likely that you have a description of your child's condition, for instance a description of how your child's external genitals or internal sex structures look (e.g., a small penis, hypospadias, or a large clitoris and urogenital sinus, in which the urine tube and vagina open into one common channel).

Although some of the descriptions will look very similar in the different chromosome pattern groups, the management decisions may be quite different because of the chromosomes. If your child has a Y-chromosome (in some or all cells) you will need to consider decisions about the gonads (testes, ovotestes). On the next page are examples of different DSD diagnoses and descriptions.



XX DSD	XY DSD	Other
e.g., Possible Diagnoses Congenital Adrenal Hyperplasia Mayer-Rokitansky-Küster-Hauser syndrome (MRKH) 46,XX Testicular DSD **e.g., Descriptions** Urogenital sinus (the vagina and urine tube open into one channel) Small vagina Enlarged clitoris Bladder and Cloacal Exstrophy	**e.g., Possible Diagnoses** 17 Beta Hydroxysteroid Dehydrogenase Deficiency-3 5 Alpha Reductase Deficiency Partial or Complete Androgen Insensitivity Syndrome (PAIS/CAIS) Partial or Complete Gonadal Dysgenesis Gonadal Dysgenesis due to Denys-Dreash, Frasier or WAGR syndrome **e.g., Descriptions** Hypospadias (the urine tube doesn't end at the top of the penis) Small penis Enlarged clitoris Small Vagina Small Penis Undescended Testes Bladder and Cloacal Exstrophy Urogenital Sinus	**e.g., Possible Diagnoses** Klinefelter syndrome (47,XXY and Variants) Turner syndrome (45,X) 45,X/ 46,XY Mixed Gonadal Dysgenesis **e.g., Descriptions** Ovotesticular DSD

XX DSD

Confirmed diagnosis

- 46,XX Testicular DSD
- Mayer-Rokitansky-Küster-Hauser syndrome (MRKH)
- Congenital Adrenal Hyperplasia (CAH)

Description only

- Bladder and Cloacal Exstrophy
- Small Vagina
- Enlarged Clitoris
- Urogenital Sinus

XY DSD

Confirmed diagnosis

- 17 Beta Hydroxysteroid Dehydrogenase Deficiency-3
- 5 Alpha Reductase Deficiency
- Complete Androgen Insensitivity syndrome (CAIS)
- Complete Gonadal Dysgenesis
- Gonadal Dysgenesis due to Denys-Drash, Frasier or WAGR syndrome
- Partial Androgen Insensitivity syndrome (PAIS)
- Partial Gonadal Dysgenesis (due to SOX9, WT1, SF1 , …)

Description only

- Small Penis
- Hypospadias
- Undescended Testes
- Bladder and Cloacal Exstrophy
- Enlarged Clitoris
- Small Vagina
- Urogenital Sinus
- Management of the Gonads

Other

Confirmed diagnosis

- Klinefelter syndrome (47,XXY and Variants)
- 45,X/ 46,XY Mixed Gonadal Dysgenesis
- Turner Syndrome (45,X and Variants)

Description only

- Ovotesticular DSD

46, XX Testicular DSD

What is it?

Children with testicular DSD have two X chromosomes and testes. The testes produce androgens, such as testosterone, but a smaller amount of androgens than children with XY chromosomes.

- Most children with 46, XX testicular DSD (about 80%) will physically develop as typical boys, but there may be:
    - a small penis
    - undescended testes
    - hypospadias (i.e., when the urinary tract does not open at the tip of the penis, but on the shaft or base of the penis)
- In 80% of children with testicular DSD, the diagnosis is made after puberty, when small testes are noted or breast development (called gynecomastia) begins.
- Because there are two X chromosomes, and no Y chromosome, germ cells in the testes (the cells which usually grow into sperm) cannot function, resulting in a very low sperm count or no sperm at all. This means fertility is affected and often poor.

What causes it?

- Usually, 46, XX testicular DSD is not inherited. It results from a random new change in genes and occurs in people with no history of the condition in the family.
- In most children with 46, XX testicular DSD, a change in the SRY gene is the cause. This gene controls the development of the testes.

- Changes in other genes can also cause 46, XX testicular DSD, such as SOX-9.

Assigning a gender of rearing

- Almost all children with 46, XX testicular DSD grow up to be happy as boys/men.

Genital treatment?

- Sometimes, severe hypospadias can cause urinary problems. In most children, however, atypical genitals, such as mild hypospadias or a small penis cause no medical problems.
- Surgery to the penis in childhood may result in irreversible damage to sensitive nerves. This can lead to problems with spraying and/or dribbling and having to sit instead of stand, as well as appearance.
- Surgical revision is often necessary for complications, such as narrowing of the urinary tract or leaks.

What about the gonads?

- There is no increased risk of testicular cancer.
- If the testes are located in the abdomen or groin area instead of the scrotum, doctors may suggest performing an operation called orchidopexy in early childhood, to bring the testes down into the scrotum.
- Like all boys, doctors recommend regular follow-up of the testes with self-examination and annual checkups to examine for unusual lumps.
- Extra hormone therapy, usually testosterone, may be necessary for overall well-being and bone health.

- Some men have a difficult time finding appropriate hormone therapy that does not cause side-effects.
- Assessments of well-being and bone health may be suggested by the health care team as a way to ensure that the right dose of hormone therapy is being used.

Mayer-Rokitansky-Küster-Hauser (MRKH) Syndrome

What?

- Some girls only have a small vaginal opening (also called “dimple”) because the female internal sex organs (the Müllerian ducts) did not fully develop.
    - These include the uterus, cervix, and upper part of the vagina.
- Girls usually have normally functioning ovaries.
- Sometimes, the kidneys are atypically formed or positioned in atypical places in the abdomen. Sometimes, there is only one kidney that also may be unusually placed.
- Other problems may include skeletal problems, hearing loss, ringing in the ears (tinnitus), and/or heart problems.

Management

The exact cause remains unknown

- No specific genes have been associated with MRKH.
- Usually, MRKH is not inherited and there is no history of the disorder in the family.
- In some families, it is passed through generations. However, this is difficult to determine because the signs of MRKH vary among affected women from the same family.

Most women with MRKH will not be able to carry children themselves

- It is possible for some women without a uterus to have biological children via gestational surrogacy. Gestational surrogacy is done by implanting a

couple's IVF (in vitro fertilization) embryos into another woman (the surrogate) who will deliver their baby.

- Uterus transplantation is a relatively new and experimental procedure and involves the risks of an invasive organ transplant surgery, such as organ rejection and infection.

Some women with MRKH might have to think about vaginal treatment

- For most women, the clitoris and labia (and not the vagina) give the most sexual pleasure. Therefore, women with MRKH do not have to change their body in any way to be able to enjoy sex.
- To be able to have vaginal intercourse, women usually need a somewhat larger vagina.
- Usually, vaginal dilation is the first line of treatment.
- If vaginal dilation is not successful, vaginal surgery can be done, but dilation is also required after surgery.

Congenital Adrenal Hyperplasia (CAH)

What is it?

The adrenal glands sit on top of the kidneys and produce three types of hormones (messengers in the blood):

- Cortisol: controls the stress response in the body
- Aldosterone: controls blood pressure and salt balance in the body
- Androgens: influence the development of sex characteristics, such as underarm hair in puberty and growth of bones

CAH is a collection of conditions which limit the ability of the adrenal glands to produce cortisol (and sometimes aldosterone).

What causes it?

- The cause of CAH is an inherited genetic change, that both biological parents have passed on to their child.
- Often, there is a genetic change in the CYP21A2 gene.
- Because of this genetic change, enzymes (certain chemicals in the body) that are necessary to make the hormone cortisol and aldosterone are not produced. One of these enzymes is 21-hydroxylase, which is related to the CYP21A2gene.
- In CAH, the adrenal glands are unable to produce more cortisol and aldosterone, but they can produce androgens. Because the adrenal glands are continuously stimulated to produce cortisol and aldosterone, but cannot produce these hormones, they instead produce a lot of androgens.

- If the adrenal glands cannot produce enough cortisol, “adrenal crisis” can occur, causing dehydration and vomiting, low blood pressure, and low salt levels. Although this can be life-threatening, it can be avoided with life-long medication. Close follow-up is necessary to make sure your child has the right amount of the essential hormones.

Androgen effects?

Because your child produced a lot of androgens before birth, there may be a:

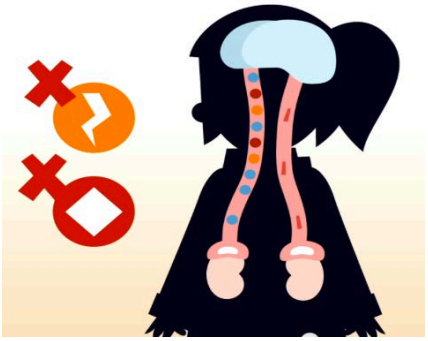
- Larger clitoris with or without a urogenital sinus (the vagina and urinary tract open into one channel, rather than separately). The vagina may also be narrow.
- Larger penis with or without hypospadias (the urinary tract does not open at the tip of the penis, but somewhere on the shaft or base of the penis).

Genital treatment?

- Sometimes, a urogenital sinus or severe hypospadias may cause urinary problems, when urine backs up to the kidney or bladder. In most children, however, atypical genitals cause no medical problems, and surgery is not urgent or medically necessary.
- Surgery to the vagina, clitoris, or penis in childhood may result in irreversible damage to the sensitive nerves. This can lead to problems with sexual pleasure and sensation in adulthood. Surgical revision is often necessary for complications, such as narrowing of the urinary tract or vaginal tightening.

Assigning a gender of rearing

- Because the sex anatomy is variable from baby to baby with CAH, doctors will usually consider how “masculine” or “feminine” the sex anatomy is, and what kind of fertility and sexual function in adulthood can be expected.
- Most children accept their gender of rearing assignment and will grow up happy as girls and boys even if their genitals or chromosomes are not typical.
- Some children who have been exposed to a lot of androgens during development in the womb have been raised as boys and are happy as boys, even if they have XX chromosomes.

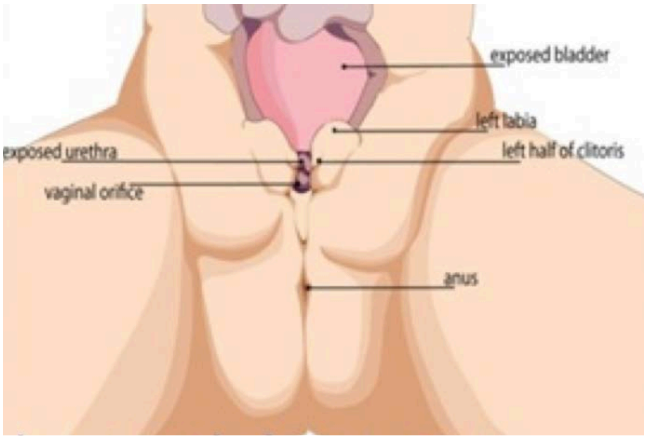


- Research tells us that of children with CAH raised as girls, around 95% of them will identify and be happy as girls.
- Gender role behavior in children with CAH is variable, but there is a tendency, even in children reared as girls, that they will prefer activities and hobbies typical to boys.
- Children with CAH and XX chromosomes have ovaries, and are usually able to conceive naturally in adulthood.

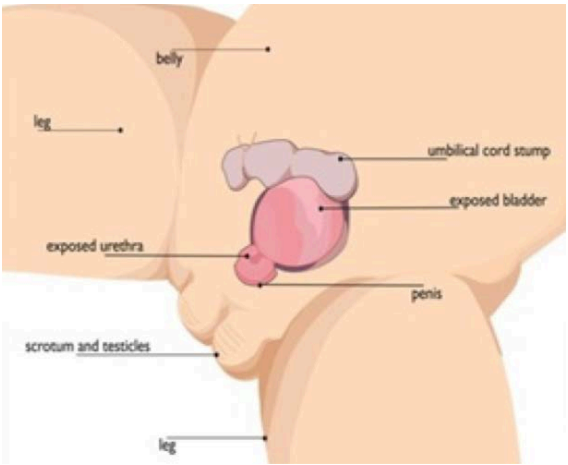
Cloacal and Bladder Exstrophy

What is it?

- During a baby's development in the womb, the wall of the belly (abdomen) and underlying organs sometimes do not form completely and the baby is born with the bladder or intestines on the outside of the body.
- The urinary tract (urethra) is usually shorter and its inner lining is visible on the top surface of the penis (in boys) or labia (in girls). This is also called epispadias.
- This may be associated with urinary incontinence and back-up of urine from the bladder to the kidneys (called vesicoureteral reflux).
- Surgery in which the bladder and abdominal wall are closed is an important first step to manage urinary incontinence and vesicoureteral reflux. Later, you and your child will also need to learn how to use a catheter to empty the bladder. Many children need more than one surgery.
- Life-long follow-up care is important to make sure the kidneys and bladder are functioning well.



Urinary tract of a girl with bladder exstrophy



Exposed inner bladder and urethra of a boy

What causes it?

- Bladder/cloacal exstrophy occurs in approximately 2.07 per 100,000 live births and is 5 times more common in boys than girls.
- The cause remains largely unknown, but may be inherited in some families.
- The risk of a family having more than one child with this condition is approximately 1 in 100. Children born to a biological parent with exstrophy have a risk of approximately 1 in 70 of having this condition.

Assigning a gender of rearing?

- Children with exstrophy with XY chromosomes will typically grow up to be happy as boys/men, and children with exstrophy with XX chromosomes as girls/women.
- However, because exstrophy can affect how children appear and develop, some may have problems with body image or self-esteem. Emotional and psychological support can be valuable to help children manage their condition.

Genital treatment?

- Most boys with exstrophy have a small penis. In girls, there may be a small and narrow vagina.
- Different treatment options exist to make the penis or vagina larger.
- Deciding between these treatment options or preferring not to have treatment is not a parent's decision to be made in childhood.
- It will be a personal decision of the young adolescent or adult and will be discussed in private with members of the health care team.

If your child has a small vagina

What is it?

- Some girls have an underdeveloped vaginal opening (sometimes called a "dimple"), because the female internal sex organs did not fully develop. These organs include the uterus, cervix, the Müllerian ducts, and the upper part of the vagina.

What causes it?

- Some girls have a condition called Mayer-Rokitansky-Küster-Hauser Syndrome.
- Other girls are insensitive to certain hormones (e.g. girls with partial or complete androgen insensitivity syndrome) or do not produce as much hormones (e.g., girls with partial gonadal dysgenesis) causing the vagina to not fully develop.
- The cause sometimes remains unknown.

Management

A smaller vagina causes no medical problems

- Girls with a small vagina have no medical problems and treatment in childhood is not medically necessary.

Some young women might have to think about genital treatment when they are ready to have sex:

- For most women, the clitoris and labia (not the vagina) provide the most sexual pleasure. So women do not have to change their body in any way to be able to enjoy sex.
- To be able to have vaginal sex, the vagina may need to be deeper (or longer) and sometimes wider.
- Usually, vaginal dilation is the first line of treatment, because vaginal tissue is very stretchy.
- If vaginal dilation is not successful, vaginal surgery may be an option.

If your child has an enlarged clitoris

What is the clitoris?

- The clitoris is the key for sexual pleasure for most women. It is packed with nerve endings and is very sensitive. When a woman is feeling excited, the clitoris fills with blood and swells up.
- The clitoris has an outside part that you can see (the glans) and an inside part (the legs and bulbs) that extends behind the labia (folds of skin) and surrounds the vagina. The outside part may be larger in some girls than typically seen in most other girls.
- Some girls with a larger clitoris may experience erections that can cause discomfort or embarrassment.

Should we do something about it?

In most children, a larger clitoris causes no problems and clitoral surgery is not urgent or medically necessary.

What are options?

- Surgery to the clitoris to make it smaller is called a "clitoroplasty" or clitoral reduction surgery. Doctors will try to avoid harming the tip (“glans”) and sensitive nerves, so that the clitoris remains sensitive for sexual pleasure later in life. However, there is always a risk of irreversible damage to the nerves in the clitoris. Sometimes, there is clitoris regrowth after surgery. Surgical revision may be necessary. With multiple operations, the risk of damage to the clitoris becomes higher.

- Some families choose to wait until their child is old enough to be involved in decision making.

When?

- It is important to take all the time that you need before deciding to have a surgery to reduce the size of your child's clitoris. There are many factors to consider and decision making with your providers and support team can be very helpful.
- Some parents who decide that they want their child to have surgery find it important that their child does not remember the procedure.
- Other parents might decide to wait until their child is old enough to participate in the decision.

Things to consider when thinking about genital surgery for your child

- How the genitals work now and how they could work in the future.
- How the genitals look today and how they will look after surgery.
- How sexual sensation and pleasure may or may not be affected.
- What need there will be for other surgeries in the future.
- What the benefits and side-effects may be in the short and long-term.
- What the healing time may be for surgery in childhood or later in life.
- What improvements in surgical procedures may develop in future years.
- How surgery may or may not affect your child's self-esteem and body image.
- How performing or not performing genital surgery may pose a risk for teasing or embarrassment.
- How your child's gender identity and preferences develop.

- How your own beliefs, culture and religion may influence your decisions.
- How your child might remember the surgery.
- How to share the decision about surgery with your child later, if you decide on surgery.
- How your child could be involved in decisions about her own body.
- Before making decisions about surgery, talk with your health care team, support groups or other families who have faced similar decisions and can give you some extra insight in their experiences (with and without surgery).
- Working together with your doctors and others, you can make informed choices to help your child thrive.

Results of genital surgery done in childhood

- Clitoral surgery is done to change the appearance of the genitals, but it may also change the function of the genitals.
- Some, but not all adults who had surgery as a child are happy about how their genitals look.
- Many adults who had clitoral surgery as a child have problems now with genital sensation and sexual pleasure (orgasm).
- Some, but not all adults who had surgery as a child regret not being involved in a decision about their own body.
- Some young women find it helpful talking to a psychologist or counselor about possible concerns related to genital appearance and function, before making a decision about clitoral surgery.
- Keep in mind, the right approach for one child/family is not necessarily right for another child/family.

17ß Hydroxysteroid Dehydrogenase Deficiency-3 (17ßHSD-3)

What is it?

Children with17ßHSD-3 have XY chromosomes and gonads (testes). The gonads are usually located in the groin area or belly. These gonads produce hormones called androgens (e.g. testosterone), but in a smaller amount than is typically expected.

- If little testosterone is produced, children with 17ßHSD-3 develop physically like most other girls. If more testosterone is produced, children will develop like most other boys.
- Children with 17ßHSD-3 have no uterus or cervix, because other hormones did not make it possible for these structures to develop.
- Sudden production of androgens by the gonads at puberty may cause male typical sex characteristics to develop. Examples of these changes are lowering of the voice and growth of the genitals.

What causes it?

- The cause is a genetic change in the HSD17B3 gene.
- This genetic change prevents the enzyme 17ß hydroxysteroid dehydrogenase-3 from working properly and producing androgens.

- Usually, both biological parents have passed on a changed HSD17B3 gene to their child. This makes the biological parents “carriers.” Being a carrier means that people do not have the condition themselves, but have the ability to pass on the affected gene to their biological children.

Androgen effects?

Depending on the amount of androgens produced before birth, there may be a:

- Larger clitoris with or without a urogenital sinus (the vagina and urinary tract open into one channel, rather than separately). The vagina may also be small.
- Small penis with or without hypospadias (the urinary tract does not open at the tip of the penis, but somewhere on the shaft or base of the penis).

Genital treatment?

- Sometimes, a urogenital sinus or severe hypospadias may cause urinary problems. In most children, however, atypical genitals cause no medical problems.
- Surgery to the vagina, clitoris or penis in childhood may result in irreversible damage to the sensitive nerves.
- This can lead to problems with sensation and sexual pleasure in adulthood.
- Surgical revision is often necessary for complications, such as narrowing of the urinary tract or vaginal tightening.

Assigning a gender of rearing

- Because the sex anatomy is variable from baby to baby with 17ßHSD-3, doctors will usually consider how “masculine” or “feminine” the sex

anatomy is, and what kind of fertility and sexual function in adulthood can be expected, to make a recommendation.

- Many children will grow up happy even if their genitals, chromosomes and/or gonads are atypical.
- Gender role behavior in children with these syndromes is variable, but there is a tendency, even in children reared as girls, that they will prefer activities and hobbies typical of boys.
- If the gonads are left in place, production of androgens at puberty may cause male sex characteristics to develop. If this happens, research tells that 40 to 60% of these children are happier to live in a male gender role (even if they were reared as girls).

What about the gonads?

- Many factors will influence a decision about the gonads. Keep in mind, what is right for one child with 17ßHSD-3 is not necessarily right for another child with 17ßHSD-3.
- The gonad cancer risk in children with 17ßHSD-3 is low before puberty (<1%), but becomes higher after puberty (around 17%).
- If gonads are removed, life-long hormone replacement is necessary for overall well-being and bone health.
- Some people with 17ßHSD-3 have a difficult time finding an appropriate hormone replacement that does not cause side-effects.
- Assessments of overall well-being and bone health may be suggested by the health care team as a way to ensure that the right dose of hormone replacement is being used.
- Fertility potential is uncertain.

5 Alpha Reductase Deficiency-2 (5αRD-2)

What is it?

Children with 5αRD-2 have XY chromosomes and gonads (testes). The gonads are usually located in the groin area or belly. These gonads produce hormones called androgens (e.g. testosterone), but in a smaller amount than is typically expected.

- If little testosterone is produced, children with 5αRD-2 will develop physically like most other girls. If more testosterone is produced, children will develop more like boys.
- Children with 5αRD-2 have no uterus or cervix, because other hormones produced did not make it possible for these structures to develop.
- Sudden production of androgens by the gonads at puberty may cause male typical sex characteristics to develop. Examples of these changes are lowering of the voice and growth of the genitals.

What causes it?

- The cause is a genetic change in the SRD5A2 gene.
- This genetic change prevents the enzyme 5α reductase-2 from working properly and producing androgens.
- Usually, both biological parents have passed on a changed SRD5A2 gene to their child. This makes the biological parents ‘carriers.’ Being a carrier means that people do not have the condition themselves, but have the ability to pass on the affected gene to their biological children.

Androgen effects?

Depending on the amount of androgens produced before birth, there may be:

- A larger clitoris with or without a urogenital sinus (the vagina and urinary tract open into one channel, rather than separately). The vagina may also be small.
- A small penis with or without hypospadias (the urinary tract does not open at the tip of the penis, but somewhere on the shaft or base of the penis).

Genital treatment?

- Sometimes, a urogenital sinus or severe hypospadias may cause urinary problems. In most children, however, atypical genitals cause no medical problems.
- Surgical revision is often necessary for complications, such as narrowing of the urinary tract or vaginal tightening.
- Surgery to the vagina, clitoris or penis in childhood may result in irreversible damage to the sensitive nerves. This can lead to problems with sensation and sexual pleasure in adulthood.

Assigning a gender of rearing

- Because the sex anatomy is variable from baby to baby with 5αRD-2, doctors will usually consider how “masculine” or “feminine” the sex anatomy is, and what kind of fertility and sexual function in adulthood can be expected in order to make a recommendation.
- Many children will grow up happy as girls and boys even if their genitals, chromosomes, and/or gonads are atypical, or if the combination of these biological sex characteristics is atypical.

- Gender role behavior in children with these syndromes is variable, but there is a tendency, even in children reared as girls, that they will prefer activities and hobbies typical of boys.
- If the gonads are left in place, production of androgens at puberty may cause male sex characteristics to develop. These can include growth of the genitals or lowering of the voice. If this happens, research tells us that 40 to 60% of these children are happier living in the male gender (even if they were reared as girls).

What about the gonads?

- Keep in mind, what is right for one child with 5αRD-2 is not necessarily right for another child with 5αRD-2.
- Gonad cancer risk in children with 5αRD-2 is low before puberty (<1%).
- If gonads are removed, life-long hormone replacement is necessary for bone health and overall well being.
- Some people with 5αRD-2 have a difficult time finding an appropriate hormone replacement that does not cause side-effects.
- Assessments may be suggested by the health care team as a way to ensure that the right dose of hormone replacement is being used.
- Fertility potential is uncertain.

Complete Androgen Insensitivity Syndrome (CAIS)

What is it?

Children with CAIS have XY chromosomes and gonads (testes). The gonads are usually located in the groin area or belly. These gonads produce hormones called androgens (e.g. testosterone). The bodies of children with CAIS are completely insensitive to the androgens they produce. Therefore, their bodies cannot respond to androgens.

- Therefore, children with CAIS will develop with a vagina and clitoris like most other girls.
- The bodies of children with CAIS were sensitive to other hormones during development in the womb. Due to exposure to these hormones, it was not possible for a uterus or cervix to develop. Children with CAIS will not be able to have biological children.

What causes it?

- The cause of CAIS is a change in the androgen receptor gene (AR gene).
- Like a key with a lock, hormones only fit certain receptors. Since there is a genetic change in the androgen hormone receptor ("the lock"), the hormone ("the key") does not fit closely and will not turn the lock.
- The genetic change is usually inherited via the unaffected biological mother, who passes on an altered copy of the AR gene on one of her X chromosomes. Sometimes, a new genetic change occurs in the biological

mother's egg cells before the child is conceived or during development in the womb.

Androgen effects?

Because the body's cells are insensitive to androgens, there will be:

- Female typical external genitals (clitoris, labia, vagina), but the vagina may be small.
- Natural breast development in puberty, because the body changes some of the androgens into estrogens.
- Little pubic or underarm hair in puberty.

Assigning a gender of rearing

- Doctors typically assign the gender "female" to children with CAIS.
- Many children with CAIS are happy as girls/women

Vaginal treatment?

- Some women with CAIS have a small vagina.
- To be able to enjoy vaginal sex, the vagina may need to be deeper (or longer) and sometimes wider.
- Vaginal dilation with the use of dilators is usually the first choice of treatment, because vaginal tissue is very stretchy and responsive to pressure.
- If vaginal dilation does not work, vaginal surgery can be done, but dilation will also be necessary after surgery.
- For many women, the clitoris and labia (and not the vagina) give the most sexual pleasure.

- Women with CAIS do not have to change their body in any way to enjoy sex.

What about the gonads?

- The gonad cancer risk in children with CAIS is low before puberty (<1%), but becomes higher after puberty (around 5-10%).
- Because the gonads naturally produce hormones, which are necessary for overall well-being, bone health and puberty, many doctors will recommend children keep them until puberty is complete.
- At that point, your daughter will also be old enough to be involved in decisions about her gonads.
- Some women want to keep their gonads (and have regular check-ups) and other women want to have them removed.
- If gonads are removed, life-long hormone replacement (usually estrogens) is necessary.
- Some women have a difficult time finding an appropriate hormone replacement that does not cause side-effects.
- Assessments of well-being and bone health may be suggested by the health care team as a way to ensure that the right dose of hormone replacement is being used.

Complete Gonadal Dysgenesis (Swyer Syndrome)

What is it?

Children with complete gonadal dysgenesis (CGD) have XY chromosomes and gonads. These gonads did not fully develop as testes, called underdeveloped testes or “streak gonads.” As a consequence, they do not produce the typical hormones, such as testosterone.

- Children with CGD will physically develop like most other girls, with a clitoris and vagina (which may be a bit smaller).
- At puberty, there will be limited natural breast development. Children with CGD do not produce estrogens, which promote breast development.
- Women with CGD have a uterus and some women can successfully carry pregnancies after receiving donated, fertilized eggs. Other women have a family by adopting children.

What causes it?

- Changes in a number of genes (e.g., SRY, SOX9, NR5A1, SF1, WT1, WNT4, NROB1 or DHH genes) can be the cause of complete gonadal dysgenesis.
- These genes usually provide instructions for the development and function of several endocrine (hormone-producing) tissues in the body, including the gonads.

- In most cases, complete gonadal dysgenesis is not inherited. It results from new changes in genes and occurs in people with no history of the condition in their family.
- Sometimes, complete gonadal dysgenesis can be inherited, if both biological parents pass on the same gene change (e.g. DHH gene change) or because either parent passes on an affected copy of the gene (e.g. NR5A1 or WNT4 gene change). It can be passed on by the biological father (e.g. SRY gene change on the Y chromosome), or via the biological mother (e.g. NROB1 gene change on X chromosome).

Assigning a gender of rearing

- Most children with CGD are happy as girls/women even if they have XY chromosomes and gonads.

Vaginal treatment?

- Some women with CGD have a small vagina.
- For many women, the clitoris and labia (and not the vagina) give the most sexual pleasure.
- Women with CGD do not have to change their body in any way to enjoy sex.
- Some women want vaginal sex and look for ways to make their vagina larger.
- Vaginal dilation with the use of dilators is usually the first line of treatment, because vaginal tissue is very stretchy and responsive to pressure.
- If vaginal dilation does not work, vaginal surgery can be done, but dilation will also be necessary after surgery.

What about the gonads?

- Since ultrasound and blood tests cannot reliably detect cancer in an early stage, doctors might suggest taking a sample of tissue from the gonad (a biopsy) to assess the risk microscopically.
- Many doctors will recommend removing streak gonads before puberty is complete.
- If gonads are removed, life-long hormone replacement (usually estrogens) is necessary for overall well-being and bone health.
- Some women have a difficult time finding an appropriate hormone replacement that does not cause side-effects.
- Assessments of overall well-being and bone health may be suggested by the health care team as a way to ensure that the right dose of hormone replacement is being used.

Gonadal Dysgenesis due to Denys-Drash Syndrome, Frasier Syndrome or WAGR Syndrome

What is it?

Children with these syndromes have partial gonadal dysgenesis (PGD). The gonads (testes) are not typically or completely formed (also called dysgenetic testes). As a consequence, they do not produce as much of the typical hormones, such as testosterone.

- If only a small amount of testosterone is produced, children with PGD will develop physically like most other girls. If more testosterone is produced, children will develop like most other boys.
- Children with PGD do not have typical female internal sex organs, such as a uterus and cervix. In some children, there are typical male internal sex organs, such as a prostate.
- WAGR: This syndrome combines gonadal dysgenesis and Wilms' tumor (kidney cancer), with the absence of irises in the eyes and intellectual disability.
- Denys-Drash: The combination of gonadal dysgenesis, kidney problems, and Wilms' tumor (kidney cancer).
    - XY: partial or complete gonadal dysgenesis
    - XX: partial or complete gonadal dysgenesis
- Frasier syndrome: Includes gonadal dysgenesis and kidney problems developing in late childhood, but no Wilms' tumor.

- Usually complete gonadal dysgenesis in XY. XX only have renal disease (normal ovaries).

What causes it?

- Changes in the WT-1 gene can cause Denys-Drash Syndrome and Frasier Syndrome.
- These genes usually provide instructions for making proteins. Proteins play an important role in the development and function of several endocrine (hormone-producing) tissues in the body, including the gonads.
- This can be inherited or be the result of a new mutation.

Testosterone effects?

Depending on the amount of testosterone produced before birth, there may be:

- A larger clitoris with or without a urogenital sinus (the vagina and urinary tract open into one channel, rather than separately). The vagina may also be small.
- Small penis with or without hypospadias (the urinary tract does not end at the tip of the penis, but somewhere on the shaft or base of the penis).

Genital treatment?

- Sometimes, a urogenital sinus or severe hypospadias may cause urinary problems. In most children, however, atypical genitals cause no medical problems.
- Surgery to the vagina, clitoris, or penis in childhood may result in irreversible damage to the sensitive nerves. This can lead to problems with sexual pleasure and sensation in adulthood.

- Surgical revision is often necessary for complications, such as narrowing of the urinary tract or vaginal tightening.

Assigning a gender of rearing

- Because the sex anatomy is variable from baby to baby with these syndromes, doctors will usually consider how “masculine” or “feminine” the sex anatomy is, and what kind of fertility and sexual function in adulthood can be expected, to make a recommendation.
- Many children will grow up happy even if their genitals, chromosomes and/or gonads are atypical.
- Gender role behavior in children with these syndromes is variable, but there is a tendency, even in children reared as girls, to prefer activities and hobbies typical of boys.

What about the gonads?

- Gonadal cancer risk in children with gonadal dysgenesis is high before puberty (30-50%).
- Since ultrasound and blood tests can not reliably detect cancer in an early stage, doctors might suggest taking a sample of tissue from the gonad (a biopsy) and look at it under the microscope to assess the risk.
- Many factors will influence a decision about the gonads. Keep in mind, the right approach for one child is not necessarily right for another child.
- If gonads are removed, life-long hormone replacement is necessary, for overall well-being and bone health.
- Some adults have a difficult time finding an appropriate hormone replacement that does not cause side effects.

- Assessments of wellbeing and bone health may be suggested by the health care team as a way to ensure that the right dose of hormone replacement is being used.

Partial Androgen Insensitivity Syndrome (PAIS)

What is it?

Children with PAIS have XY chromosomes and gonads (testes). These gonads are sometimes located in the groin area or belly. They produce hormones called androgens (e.g. testosterone). The bodies of children with PAIS are partially insensitive to the androgens they produce, so these androgens cannot perform many actions in the body.

- If the body is somewhat more sensitive to these androgens, children with PAIS will develop physically like most other boys. If the body is somewhat less sensitive to androgens, children with PAIS will develop more like other girls.
- Because the body of children with PAIS is sensitive to other hormones, there is no development of internal sex organs, such as a uterus or cervix.

What causes it?

- The cause of PAIS is a change in the androgen receptor gene (AR gene).
- Like a key with a lock, hormones only fit certain receptors.
- Since there is genetic change in the androgen hormone receptor ("the lock"), the hormone ("the key") doesn't fit 100% and will not completely turn the lock.
- The genetic change is usually inherited via the unaffected biological mother, who passes on an altered copy of the AR gene on one of her X chromosomes. Sometimes, a new genetic change occurs in the biological

mother's egg cells before the child is conceived or during development in the womb.

Androgen effects?

If the body is not completely sensitive to androgens, there may be:

- A larger clitoris with or without a urogenital sinus (the vagina and urinary tract open into one channel, rather than separately). The vagina may also be small.
- A small penis with or without hypospadias (the urinary tract does not end at the tip of the penis, but somewhere on the shaft or base of the penis).

Genital treatment?

- Sometimes, a urogenital sinus or severe hypospadias may cause urinary problems. In most children, however, atypical genitals cause no medical problems.
- Surgery to the vagina, clitoris, or penis in childhood may result in irreversible damage to the sensitive nerves. This can lead lead to problems with sexual pleasure and sensation in adulthood.
- Surgical revision is often necessary for complications, such as narrowing of the urinary tract or vaginal tightening.

Assigning a gender of rearing

- Because the sex anatomy is variable from baby to baby with PAIS, doctors will usually consider how “masculine” or “feminine” the sex anatomy is, and what kind of fertility and sexual function in adulthood can be expected, to make a recommendation.

- More than 90% of children accept their gender of rearing assignment and will grow up happy as girls or as boys even if their genitals, chromosomes, and/or gonads are atypical.
- Gender role behavior in children with PAIS is variable, but there is a tendency, even in children reared as girls, that they will prefer activities and hobbies typical of boys.
- If the gonads are left in place, production of androgens at puberty may cause male sex characteristics to develop. These can include growth of the genitals or lowering of the voice. If this happens, research tells us that 40 to 60% of these children are happier living in the male gender (even if they were reared as girls).

What about the gonads?

- The gonad cancer risk in children with PAIS is low before puberty (<1%) but becomes higher after puberty (around 10-15%).
- Fertility potential is uncertain.
- Individuals being raised as girls may have gonads removed before puberty to avoid “masculine” pubertal development.
- Many factors will influence a decision about the gonads. Keep in mind, the right approach for one child with PAIS is not necessarily right for another child with PAIS.
- If gonads are removed, life-long hormone replacement is necessary for overall well-being and bone health.
- Some people with PAIS have a difficult time finding an appropriate hormone replacement that does not cause side-effects.

- Assessments of overall well-being and bone health may be suggested by the health care team as a way to ensure that the right dose of hormone replacement is being used.

Partial Gonadal Dysgenesis

What is it?

Children with partial gonadal dysgenesis (PGD) have XY chromosomes and gonads (testes). These testes are not typically or completely formed, and are also known as dysgenetic testes. As a consequence, they do not produce as much of the typical hormones, such as testosterone.

- If little testosterone is produced, children with PGD will develop physically like most other girls. If more testosterone is produced, children will develop like most other boys.
- Children with PGD do not have female typical internal sex organs, such as a uterus and cervix. Sometimes, there may be male typical internal sex organs, such as a prostate.

What causes it?

- Changes in different genes (e.g. SRY, SOX9, NR5A1, SF1, WT1, WNT4, NROB1 or DHH genes) can be the cause of gonadal dysgenesis.
- These genes usually provide instructions for making proteins. These proteins play an important role in the development and function of several endocrine (hormone-producing) tissues in the body, including the gonads.
- Usually, gonadal dysgenesis is NOT inherited. It results from new changes in genes and occurs in people with no history of the condition in their family.
- Sometimes, gonadal dysgenesis can be inherited if both biological parents pass on the same gene change (e.g. DHH gene change) or because one of either parent passes on an affected copy of the gene (e.g. NR5A1 or WNT4

gene change). Sometimes it is passed on via the biological father (e.g. SRY gene change on the Y chromosome), or sometimes via the biological mother (e.g. NROB1 gene change on X chromosome).

Testosterone effects?

Depending on the amount of testosterone produced before birth, there may be:

- A larger clitoris with or without a urogenital sinus (the vagina and urinary tract open into one channel, rather than separately). The vagina may also be small.
- A small penis with or without hypospadias (the urinary tract does not end at the tip of the penis, but somewhere on the shaft or base of the penis).

Genital treatment?

- Sometimes, a urogenital sinus or severe hypospadias may cause urinary problems. In most children, however, atypical genitals cause no medical problems.
- Surgery to the vagina, clitoris, or penis in childhood may result in irreversible damage to sensitive nerves. This can lead to problems with sexual pleasure and sensation in adulthood. Surgical revision is often necessary for complications, such as narrowing of the urinary tract or vaginal tightening.

Assigning a gender of rearing

- Because the sex anatomy is variable from baby to baby with PGD, doctors will usually consider how ‘masculine’ or ‘feminine’ the sex anatomy is, and

what kind of fertility and sexual function in adulthood can be expected, to make a recommendation.

- Many children will grow up happy as girls and boys even if their genitals, chromosomes, and/or gonads are atypical.
- Gender role behavior in children with PGD is variable, but there is a tendency, even in children reared as girls, to prefer activities and hobbies typical of boys.

What about the gonads?

- The gonad cancer risk in children with PGD is high before puberty (30-50%).
- Since ultrasound and blood tests can not reliably detect cancer in an early stage, doctors might suggest taking a sample of tissue from the gonad (a biopsy) and look at it under the microscope to assess the risk.
- Many factors will influence a decision about the gonads. Keep in mind, the right approach for one child with PGD is not necessarily right for another child with PGD.
- If gonads are removed, life-long hormone replacement is necessary for overall well-being and bone health.
- Some people with PGD have a difficult time finding an appropriate hormone replacement that does not cause side-effects.
- Assessments of overall well-being and bone health may be suggested by the health care team as a way to ensure that the right dose of hormone replacement is being used.

If your child has a small penis

What?

Some boys are born with a small penis. This is sometimes called a micropenis or microphallus (when the penile length is smaller than 2 cm at birth).

Why?

- There are many reasons why this can happen.
- In some boys, there was not enough testosterone produced during development in the womb. This may have prevented the penis from fully growing. Doctors may check this with hormone tests.
- In other boys, the cause of a small penis remains unclear (also called “idiopathic” micropenis).

Management

A smaller penis causes no medical problems

- Most boys with a small penis (without other genital differences such as hypospadias or undescended testes) have no medical problems and genital treatment in childhood is not medically necessary or urgent.
- Many boys with a small penis grow up to be happy and healthy men who can father children and experience sexual pleasure.

What about genital treatment?

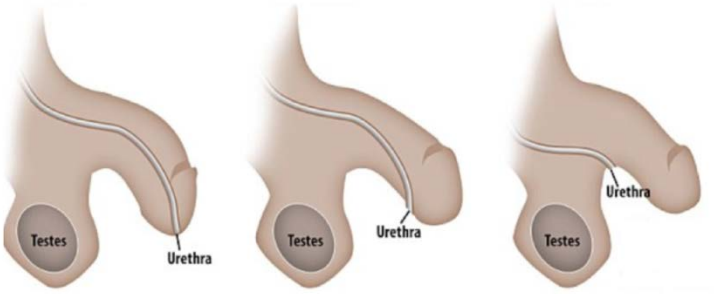
- The penis size can sometimes be increased by using testosterone during childhood.

- Testosterone is usually given as three injections, 1 month apart, by endocrinologists.
- This testosterone will advance penis growth during childhood, but it will not influence the final penis length in adulthood. It seems there is a predetermined length for every boy.
- This means that a child with a small penis will probably become an adult with a small penis.
- Surgery to make the penis larger (called phalloplasty) is very difficult, has a relatively high complication rate, and is not performed in childhood. It is only performed in late adolescence or adulthood, when your son is able to take part in the decision to undertake those risks.

If your child has hypospadias

What is hypospadias?

- The urethra (urinary tract) opens somewhere on the shaft or the base of the penis instead of at the tip
- Most boys with mild hypospadias have no difficulty urinating, even if the urinary opening is at a different place.
- If the penis is curved upwards or downwards (called chordee), it can be more difficult to urinate while standing



Typical penis: Urethra opens at tip of penis

Hypospadias: Urethra opens on underside of penis

Severe hypospadias: Urethra opens at base of penis

Should we do something about it?

Why?

- Some boys with hypospadias learn to urinate while standing up and some men and boys prefer to urinate while sitting down.
- Doctors may suggest surgery to change the appearance of the penis to look more similar to other boys, or to allow your child to urinate while standing.
- If the hypospadias is severe and there is a problem with urinating, genital surgery may be needed to avoid urinary problems. If there is severe chordee (a curve of more than 60 degrees), erections may be painful. Surgery for severe hypospadias and chordee release can make the penis look longer, but it cannot actually make it bigger.

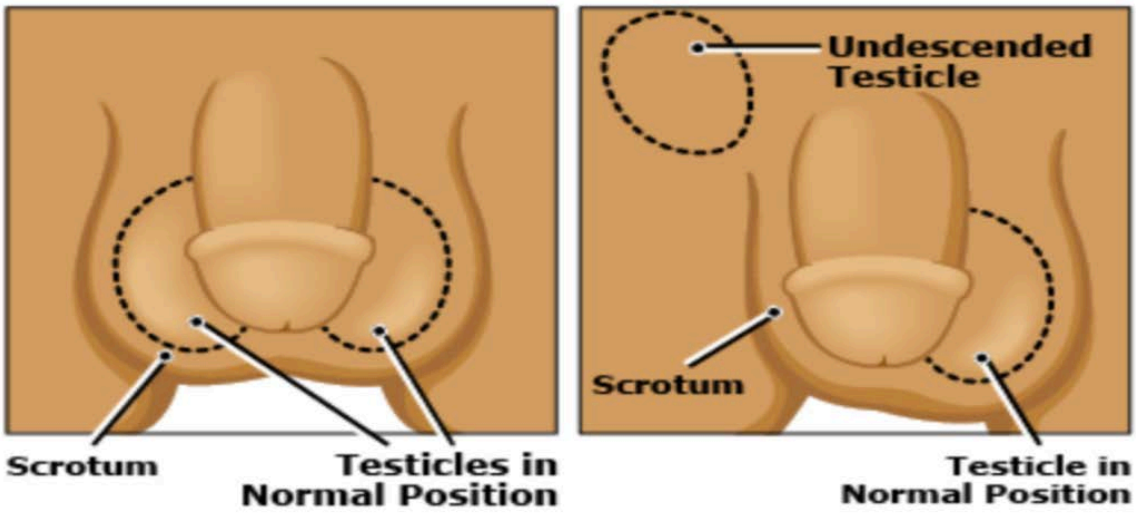
When?

- If surgery is not medical urgent or necessary, some doctors recommend doing this surgery in childhood, before one year of age, because the surgery is easier to perform at a younger age.
- Other doctors recommend waiting until your child is older, so he can be involved in this decision.

Other information

- 1 in 250-300 men have hypospadias
- Doctors will tell you if surgery is medically urgent or necessary. For example, when urine backs up into the bladder or kidney, it can cause urinary problems for your child.
- Most children with mild hypospadias will have no urinary problems.

If your child has undescended testes (cryptorchidism)



What?

- The testes typically form inside the belly and move down (descend) into the scrotum before birth. Sometimes, one or both testes do not descend.
- This occurs in 1 out of 3 premature babies and in approximately 1 out of 33 babies born to term.

Should we do something about it?

- In about half of the babies, the undescended testes descend on their own by 6 months of age.
- If descent does not happen by then, it is important to get treatment because testes that remain undescended may not work properly given that they are in the wrong position. This could affect future fertility or lead to other medical problems.

- When the testes are located in the belly or groin area instead of the scrotum, the cancer risk is also higher and it is difficult to keep an eye on them through examination and imaging tests.
- Doctors will suggest performing an operation called "orchidopexy" in childhood, to bring the testes into the scrotum.
- Regular follow-up of the testes by self-exam and doctor checkups (and sometimes ultrasound) helps to monitor the cancer risk. Sometimes an additional testes biopsy after puberty may be necessary.

Management of the Gonads

What? Why?

- If your child has Y chromosomes and the gonads are not fully developed or typically working, cancer cells may develop. That is why these gonads need to be monitored or checked.
- Some diagnoses have a higher gonad cancer risk than other diagnoses.
- In some diagnoses, the risk only becomes higher after puberty; in other diagnoses, the risk is already high during childhood.
- Gonads that are located in the belly or groin area have a higher risk than gonads located lower in the body (e.g. scrotum).

If your child is reared as a girl:

- The small amount of androgens produced by the gonads at puberty may lead to male typical body changes, such as lowering of the voice or growing of the clitoris. Whether these changes occur and to what extent is difficult to predict.
- Some girls may be unhappy with their assigned gender as girls and will welcome these body changes.
- If the gonads are left in place until puberty, adolescent/young women can decide for themselves whether to proceed with removal or not.
- After puberty, some women prefer to keep their gonads. Others want to have them removed and will need lifelong hormone replacement therapy (usually estrogens) to maintain overall well-being and bone health.
- Some women have a difficult time finding an appropriate hormone replacement that does not cause side-effects.

- Unfortunately, there is no evidenced-based data regarding preservation of the gonads for future fertility.

If your child is reared as a boy:

- The small amount of androgens produced by the gonads at puberty may lead to male typical body changes, such as lowering of the voice and facial hair growth.
- When the gonads are located in the belly or groin area instead of the scrotum, the cancer risk is higher and doctors will suggest performing an operation called orchidopexy in childhood, to bring the gonads down.
- During the orchidopexy, a gonad biopsy (a small sample of tissue) may be collected and examined under the microscope. If cancer cells are detected, removal of the gonads is usually necessary. If no cancer cells are detected in the biopsy, doctors will often suggest regular follow-up of the gonads by self-exam and ultrasound, to monitor the cancer risk. Sometimes an additional biopsy after puberty is necessary.
- It is challenging (but not impossible) for some men whose testes have not been removed to father biological children.
- Extra hormone therapy (testosterone) is usually necessary to maintain overall well-being and bone health.
- Some men have a difficult time finding an appropriate hormone replacement that does not cause side-effects.

Klinefelter Syndrome

What is it?

Children with Klinefelter Syndrome (KS) have one extra X chromosome in addition to their 46, XY chromosomes (written as 47, XXY). Some children have the extra X chromosome only in some cells, while their other cells have 46, XY chromosomes. This is called “mosaic” KS (written as 46, XY/47, XXY).

- Most children with KS physically develop like most other boys.
- The testes are of a small to typical size at birth, but they do not grow further and do not produce as much testosterone, especially later in puberty. The penis, therefore, usually remains small. In addition, fathering children is usually not possible without surgical help.
- Children with mosaic KS may have milder signs and symptoms, depending on how many cells have an extra X chromosome.
- Some boys and men experience social anxiety or difficulties with social communication and interaction with peers. Others have difficulties with speech, spelling, reading, writing, and attention.
- Some men with KS also have sparse facial and body hair and may have enlarged breasts (called gynecomastia). They are usually tall and have less muscular bodies and weaker bones.

What causes it?

- KS is quite common and occurs in 1 out of 500 -1000 live births.
- KS and its variants are not inherited.
- The chromosomal change usually occurs as a random event during the formation of reproductive cells (eggs and sperm) in a biological parent. For

example, an egg or sperm cell may gain one or more extra copies of the X chromosome as a result of an error in cell division.

- Biological parents who have a child with KS have a 1 in a 100 chance that they will have another child with the condition.

Assigning a gender of rearing

- Most boys with KS grow up to be happy men, even if they have atypical chromosomes or smaller testes.
- Some boys with KS prefer less typical boys' activities and tend to be more quiet, shy, and sensitive than boys without KS.

Genital treatment?

- Although unusual, some boys with KS have hypospadias (i.e., the urinary tract does not open at the tip of the penis, but on the shaft or base of the penis). If the hypospadias is more severe, it may cause urinary problems. In most children, however, atypical genitals, such as mild hypospadias or a small penis cause no medical problems and surgery is not medically necessary or urgent.
- Surgery to the penis may result in irreversible damage to the sensitive nerves, which can lead to problems with sexual sensation and pleasure.
- Surgical revision is often necessary for complications, such as narrowing of the urinary tract or leaks.

Management of the testes?

- There is usually no increased testes cancer risk in men with KS.

- Because the testes are small and produce little testosterone, extra testosterone treatment will help bring on the usual changes of puberty, including a deeper voice, growth of the penis, and facial and body hair.
- This hormone treatment is lifelong.
- It may have benefits, including increased physical strength, improved bone density, and reduced breast growth.
- However, some men have a difficult time finding an appropriate hormone replacement without experiencing side-effects.
- Testosterone therapy cannot increase size of testes or help with fertility.
- Although breast cancer in men is uncommon, there is an increased risk of breast cancer in men with KS.
- Some men prefer to have cosmetic surgery to reduce their enlarged breasts.
- Physical therapy can build muscle strength and coordination. Extra speech therapy can help improve speaking, reading, and writing skills.
- Counselors and therapists can also give boys and men practical skills to help them feel more confident in social settings.

45, X/46, XY Mixed Gonadal Dysgenesis

What is it?

The chromosome pattern in children with mixed gonadal dysgenesis (MGD) is usually 45, X/46, XY. This means some cells in the body have one X chromosome, while other cells in the body have X and Y chromosomes. This is also called mosaicism.

Children with MGD have gonads. The gonads did not fully develop into testes or ovaries (also called “streak” gonads or dysgenetic gonads). Children can have a streak gonad on one side of the body, and a dysgenetic or well-developed gonad (ovary or testis) on the other side of the body. Streak gonads or dysgenetic gonads do not produce as much of the typical hormones, such as testosterone.

- If little testosterone is produced, children with MGD will develop physically like most other girls. If more testosterone is produced, children will develop like most other boys.
- Children with MGD do not have typical female internal sex organs, such as a uterus and cervix.

What causes it?

- Changes in a number of genes (e.g. SRY, SOX9, NR5A1, SF1, WT1, WNT4, NROB1 or DHH genes) can be the cause of mixed gonadal dysgenesis.

- These genes usually provide instructions for the development and function of several endocrine (hormone-producing) tissues in the body, including the gonads.
- Usually, mixed gonadal dysgenesis results from new changes in genes and occurs in people with no history of the condition in their family.
- Sometimes, mixed gonadal dysgenesis can be inherited, if both biological parents pass on the same gene change (e.g. DHH gene change) or one parent passes on an affected copy of the gene (e.g. NR5A1 or WNT4 gene change).
- It may also be inherited via the biological father (e.g. SRY gene change on the Y chromosome), or via the biological mother (e.g. NROB1 gene change on X chromosome).

Testosterone effects?

Depending on the amount of testosterone produced before birth, there may be:

- A larger clitoris, with or without a urogenital sinus (a single channel and single opening of the vagina and urinary tract). The vagina may also be small.
- A small penis, with or without hypospadias (the urinary tract does not end at the tip of the penis, but on the shaft or base of the penis).

Genital treatment?

- Sometimes, a urogenital sinus or severe hypospadias can cause urinary problems. In most children, however, atypical genitals cause no medical problems, and surgery is not urgent or medically necessary.
- Surgery to the vagina, clitoris, or penis in childhood may result in irreversible damage to sensitive nerves. This can lead to problems with

sexual pleasure and sensation in adulthood. Surgical revisions are often necessary to correct complications, such as narrowing of the urinary tract or vaginal tightening.

Assigning a gender of rearing?

- Because the sex anatomy is variable from baby to baby with MGD, doctors will usually consider how “masculine” or “feminine” the sex anatomy is and what kind of fertility and sexual function in adulthood can be expected.
- Many children will grow up happy as girls and boys even if their genitals, chromosomes, and/or gonads are atypical.
- Gender role behavior in children with MGD is variable, but there is a tendency, even in children reared as girls, to prefer activities and hobbies typical for boys.

Management of the gonads?

- Dysgenetic gonads may not make enough hormones, so your child may need supplementation.
- If the chromosome test shows Y chromosome material (as in 45, X/ 46, XY), the dysgenetic gonads may have a risk for cancer.
- The gonad cancer risk in children with MGD is high before puberty (30-50%).
- Since ultrasound and blood tests cannot reliably detect cancer in an early stage, doctors might suggest taking a sample of tissue from the gonad (a biopsy) and look at it under the microscope to assess the risk.
- Many factors will influence a decision about the gonads.

- Keep in mind, the right approach for one child with MGD is not necessarily right for another child with MGD.
- If gonads are removed, life-long hormone replacement is necessary, for overall well-being and bone health.
- Some people with MGD have a difficult time finding an appropriate hormone replacement that does not cause side-effects.
- Assessments of overall well-being and bone health may be suggested by the health care team as a way to ensure that the right dose of hormone replacement is being used.
- Dysgenetic gonads may not have capacity for adequate hormone production or fertility function, which limits the benefits of leaving them in place.

Turner Syndrome

What is it?

Children with Turner Syndrome (TS) are born with only one X chromosome (written as 45, X) instead of two chromosomes (written as 46, XX or XY). In some children, one X chromosome is only missing in some cells of the body, while other cells of the body have 46, XX, 46, XY, or X chromosome variations. This is called "mosaic" TS. These variants of Turner Syndrome may have gonadal dysgenesis (gonads do not develop completely).

What causes it?

- TS is quite common and occurs in 1 out of 2500 female births.
- TS and its variants are NOT inherited.
- The chromosomal change usually occurs at random during the formation of the reproductive cells (eggs and sperm) in the biological parents. For example, an egg or sperm cell may lose a copy of the X chromosome as a result of an error in cell division.
- Biological parents who have a child with TS do NOT have an increased chance to have another child with TS.
- Dysgenetic gonads may not make enough hormones so supplementation may be needed.

Management of the gonads?

- If the chromosomes test shows Y chromosome material (mosaic Turner 45, X/ 46, XY), the gonads (ovaries) may have to be checked for cancer cells.
- Since ultrasound and blood tests cannot reliably detect cancer in an early stage, doctors might suggest taking a sample of tissue from the gonad (a biopsy) and look at it under the microscope to assess the risk.
- Sometimes, gonads may need to be surgically removed.
- Unfortunately, there is no evidenced-based data regarding preservation of the gonads for future fertility.
- Dysgenetic gonads may not have hormone or fertility function so there is no benefit to leaving them in.

Ovotesticular DSD

What is it?

Some children with ovotesticular DSD have XX chromosomes, other children with ovotesticular DSD have XY chromosomes. There can also be a combination of XX and XY chromosomes (called mosaicism), meaning some cells in the body have XX chromosomes and other cells in the body have XY chromosomes.

The gonads can be a combination of ovaries, testes, or combined ovarian and testicular tissue (ovotestes). Around 2/3 of babies with ovotesticular DSD have ovotestes. In some babies, there is a testis on one side and an ovary on the other side. As a consequence, the hormones produced by the gonads, such as testosterone, vary from baby to baby with ovotesticular DSD.

- If little testosterone is produced, children with ovotesticular DSD will develop physically like most other girls. Some babies have a uterus, but the uterus is often small. The vagina may also be small.
- If more testosterone is produced, children with ovotesticular DSD will physically develop like most other boys. The penis is usually smaller, and often there are hypospadias (i.e. the urinary tract does not end at the tip of the penis, but somewhere on the shaft or base of the penis). The gonads have usually not descended down into the scrotum, but are located in the belly or groin area.

What causes it?

- The underlying cause of ovotesticular DSD remains unknown.
- It is not inherited.

- It usually results from a random new change in genes and occurs in people with no history of the condition in the family.
- In about 10% of children with 46, XX ovotesticular DSD, there is genetic change in the SRY gene. This gene controls the development of the testes.
- Changes in other genes, such as DMRT1, SOX9, or RSPO1 are also possible.

Genital treatment?

- Sometimes, severe hypospadias may cause urinary problems. In most children, however, mild hypospadias does not cause no medical problems and surgery is not medically necessary or urgent.
- Surgery to the penis in childhood may result in irreversible damage to the sensitive nerves. This can lead to problems with sexual pleasure and sensation in adulthood.
- Surgical revision is often necessary for complications, such as narrowing of the urinary tract or leaks.

Assigning a gender of rearing

- Because the sex anatomy is variable from baby to baby with ovotesticular DSD, doctors will usually consider how “masculine” or “feminine” the sex anatomy is, and what kind of fertility and sexual function can be expected in adulthood.
- Many children will grow up happy as girls and boys even if their genitals, chromosomes, and/or gonads are atypical.

- Gender role behavior in children with ovotesticular DSD is variable, but there is a tendency, even in children reared as girls, for them to prefer activities and hobbies typical of boys.

What about the gonads?

- The gonad cancer risk is low in 46, XX ovotesticular DSD.
- It is higher in 46, XY or 46, XX/46, XY ovotesticular DSD, due to the Y-chromosome.
- Since ultrasound and blood tests cannot reliably detect cancer in an early stage, doctors might suggest taking a sample of tissue from the gonad (a biopsy) and look at it under the microscope to assess the risk.
- If there is a testis on one side and an ovary on the other, both gonads can produce hormones. Some doctors will recommend removing at least one of them before puberty, to avoid changes that hormones can bring about. Ideally, this decision is based on the gender identity preferences of your child and should be postponed until late childhood, when your child can take part in this decision.
- In many children with ovotesticular DSD, one or both gonads have both testicular and ovarian tissue (ovotestes), and it may be more difficult to make a decision about which parts to remove, especially because it is difficult to separate these parts.
- If gonads are removed, life-long hormone replacement is necessary for overall well-being and bone health.
- If there is a uterus, some women with ovotesticular DSD can get pregnant via egg donation. Not many women with ovotesticular DSD will be able to conceive naturally.

- Fathering a child biologically is more difficult because not all men with ovotesticular DSD can produce sperm or only produce sperm of a low quality.

DECIDING ON A GENDER OF REARING

A person's sex includes all physical characteristics, chromosomes, genes, gonads (testes, ovaries, ovotestes), internal reproductive structures (uterus), and external genitals. Sex is fixed and cannot be "assigned."

Gender is a "social" concept. It is a reflection of how someone thinks and feels about him/herself as a boy/man or girl/woman (gender identity) and how he/she publicly expresses gender typed behavior and preferences (gender role). Children do not come into the world with a completely formed gender identity or gender role preferences. They develop these over time.

Some girls might prefer model building or playing with cars to playing with dolls and some boys may be more interested in fashion design or cooking than playing with cars. These girls would still identify themselves as girls and the boys as boys, even if they prefer activities that are usually considered typical for the other gender. We would say that their gender role behavior is atypical, but not incorrect or unhealthy. You cannot really assign a gender, but you can decide which gender of rearing you assign your child until his/her gender identity and preferences develop.

What can be important in making this decision?

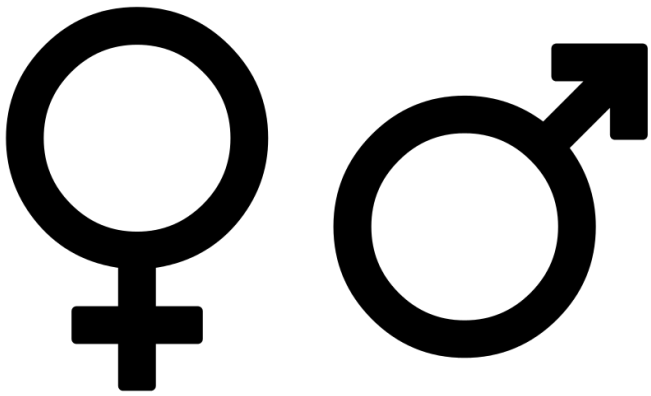
Unfortunately, we know little about the mechanisms involved in the development of gender identity. Is it determined by specific genes or by exposure to sex hormones, such as testosterone? Or is it something we have learned from the way we were brought up? It is probably a combination of many factors.

What we know:

- For most people, with and without DSD, gender identity will usually match their gender of rearing, but there is always a risk for gender unhappiness (also called gender dysphoria or distress). One in 2000 people in the general population experience gender dysphoria.
- In some DSD conditions, research shows a higher risk of gender dysphoria.
- If your child grows up being uncomfortable with and questions his/her assigned gender of rearing, no one is at fault. It just means that things turned out differently from the initial observations and discussions. With support, families can successfully handle gender distress and go through the process of gender transition.

When assigning a gender of rearing, a number of factors may influence your decision:

- Your child's likely gender identity given the DSD diagnosis (if known)
- Size and potential for growth of the genitals
- Hormone production and action
- Potential to have sexual activity later
- Potential to have biological children
- What other important people (family members, close friends, doctors) might think
- Your family's cultural background and values
- Your spiritual beliefs or religion
- How comfortable you are with your child's gender of rearing until he/she develops his/her own gender preferences



** Check out the Questions to Ask section at the end of the workbook for questions you can ask about Gender Assignment.*

Family Name: _____ Date _____
Month/Day/Year

Relationship to Patient:_____

The following questionnaire is for you to gather your thoughts about deciding on a gender of rearing. Show how you feel about the following statements by filling in the bubble that best describes how you are feeling . Please consider bringing this to your next clinic visit.

Deciding on the gender of rearing

Is or is not a factor in my decision		
My culture is a factor in my decision to raise my child as a boy or a girl.	○○○○○○○	My culture is not a factor in my decision to raise my child as a boy or a girl.
My religious/spiritual beliefs have an influence on my decision to raise my child as a boy or a girl	○○○○○○○	My religious/spiritual beliefs are not an influence on my decision to raise my child as a boy or a girl
The idea that my child may choose a different gender later in life makes me uncomfortable	○○○○○○○	I am comfortable with the idea that my child may choose a different gender later in life
My child's sex chromosomes play an important role in my decision to raise my child as a boy or girl	○○○○○○○	My child's sex chromosomes play no role at all in my decision to raise my child as boy or girl
My child's gonads (testes, ovaries, ovotestes, streak gonads) play an important role in my decision to raise my child as a boy or girl	○○○○○○○	My child's gonads (testes, ovaries, ovotestes, streak gonads) do not play an important role n my decision to raise my child as a boy or girl

My child's potential to have children in the future (if any) is an important factor in my decision	○○○○○○○	My child's potential to have children in the future (if any) is not an important factor in my decision
The appearance of my child's external genitals is important in my decision	○○○○○○○	The appearance of my child's external genitals is not very important in my decision
The type of genital surgeries that can be done (in childhood or later) to change the appearance and function of the external genitals influence my decision	○○○○○○○	The type of genital surgeries that can be done (in childhood or later) to change the appearance and function of the external genitals do not influence my decision
Hormone replacement therapy that my child can take is important in my decision	○○○○○○○	Hormone replacement therapy that my child can take is not important in my decision

Do you want to bring up your child as a boy or girl?

I am leaning towards…

Boy ○○○○○○○ Girl

Decide what's next

Do you understand what all the different options or possibilities are regarding the decision about gender of rearing?

○ Yes

○ No

○ Unsure

Are you clear about the benefits and risks and what matters most to you?

○ Yes

○ No

○ Unsure

Do you have enough support and advice from others to make a choice?

○ Yes

○ No

○ Unsure

Certainty

How sure do you feel right now about a decision regarding raising your child as a boy or girl?

Not sure at all ○○○○○○○ Very sure

Check what you need to do before making a decision

○ I want to discuss options/possibilities with others

○ I want to learn more about options/possibilities

○ I'm ready to take action

Use the following space to list questions, concerns and next steps

SURGERY

Figuring out if your baby should be raised as a boy or a girl is different from figuring out what to do about surgery. Some people might think that once you decide which gender to raise your child, you should do surgery to change the anatomy and/or gonads to match with that assigned gender of rearing. Doing surgery on sexual anatomy to try to "confirm" or "reinforce" your child's gender may not always be helpful or necessary.

** Check out the Questions to Ask section in the back of the book for questions you can ask your healthcare team regarding Surgery and Other Procedures!*

A difference should be made between medically urgent surgery (for instance, when urine backs up into the bladder or kidney) and elective non-urgent surgery. In general, most operations for DSD conditions are elective operations. It may not always be in the best interest of your child to have surgery. Elective surgery can create problems that may or may not influence your child's well-being.

Management of the Gonads

DSD patients with Y chromosome material in their karyotype have the greatest risk of developing a gastric cardia adenocarcinoma (GCC) precursor lesion, with a high potential to progress to GCC. If your child has Y chromosome material, doctors will suggest to monitor the gonads (testes, streak gonads, or ovotestes) closely or remove all or part of them because of gonad cancer risk. This cancer risk depends not only on your child's specific DSD condition and location of the gonads, but also on the age of your child.

Management of the Genitals

Severe hypospadias (when the urinary tract does not open at the tip of the penis, but somewhere on the shaft or base of the penis) or a urogenital sinus (when the vagina and urinary tract open into a common channel, rather than separately) can sometimes result in urinary problems. Often, however, atypical genitals do not cause medical problems and surgery is not necessary or urgent.

For children raised as girls, elective genital surgery may include:

1. Making the clitoris smaller (also called clitoral reduction or "clitoroplasty")
2. Reshaping the labia or removing parts of the labia (called "labiaplasty")
3. Any operation that changes the vagina (called "vaginoplasty;" e.g., surgery to make the vagina larger when the vagina is small or narrow)
4. Surgery for a urogenital sinus

For children reared as boys, elective genital surgery may include:

1. Release of "chordee", the thin band of skin that can hold the penis in a curved positon
2. Relocating the urine tube to end at the tip of the penis (called "hypospadias" surgery)
3. Reshaping the scrotum
4. (Re)construction of the penis (called "phalloplasty") if your child has a small penis

There are many things to consider when deciding if and when elective surgery should be performed.

Factors include:

- How the genitals work now and how they could work in the future.
- How the genitals look now and how they will look after surgery.
- How sexual sensation and pleasure may or may not be affected.
- How fertility may or may not be affected.
- What need there will be for other surgeries in the future.
- What the benefits and side-effects may be in the short and long-term.
- What the healing time may be for surgery in childhood or surgery later in life.

- How scars from the surgery may not grow while the child's body grows (i.e. genital appearance and function could get worse as your child grows).
- What improvements in surgical procedures may be possible in the future.
- How surgery may or may not affect your child's self-esteem and body image.
- How performing or not performing genital surgery may pose a risk for teasing or embarrassment.
- How your child's gender identity and preferences develop.
- How your child may remember the surgery.
- How your own beliefs, culture, and religion may influence your decisions.
- How to share the decision about surgery with your child later, if you decide on surgery.
- How your child could be involved in decisions about his/her own body.

Specific questions about the training of the surgeons include:

- How experienced is the surgeon in caring for children with DSD?
- How many times has the surgeon performed a certain procedure?
- How successful are his/her surgeries?
- How does he/she define success?
- Is there research supporting the surgeon's claims?
- Would he/she be willing to provide a referral for a second opinion?

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Family Name: _____ Date _____
Month/Day/Year

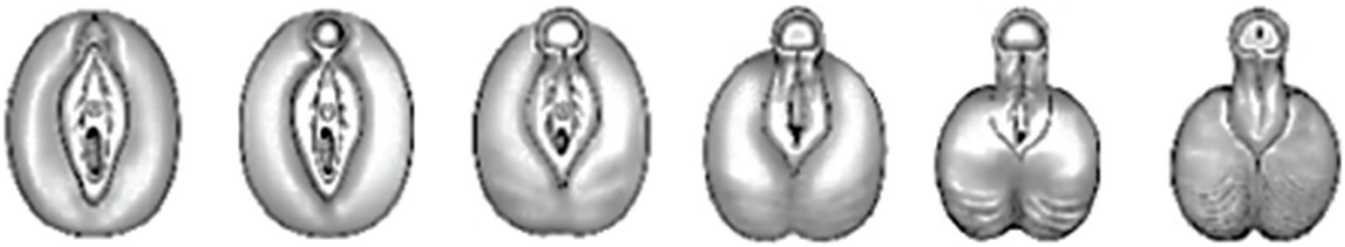
Relationship to Patient:_____

Surgery

After reading the surgery section, your DSD team would like to know more about your own thoughts regarding surgery, and would like to help guide you in the decision making process. Consider bringing this survey to your next clinic visit to talk more with the DSD team.

Could you indicate how the genitals of your child look by circling a number on the chart?

1	2	3	4	5	6
Typical vulva (appears like a typical girl)	Typical vagina and larger clitoris, testes may not be descended	Labia are partly joined, vagina and urethra open in common channel, larger clitoris	Labia are completely fused, vagina and urethra open in common channel, even larger clitoris, small phallus, opening is near base of shaft	Smaller penis and urethra located on underside, may have curvature	Typical penis and scrotum (appears like typical boy)



No or little testosterone — More testosterone — A lot of testosterone

Do you want elective genital surgery for your child?

Show how you feel about the following statements by filling in the bubble (closer to the statement means you agree more with what is being said).

Factors affecting my decision		
My culture has an influence on my decision to have my child have surgery	○○○○○○○	My culture has no influence on my decision to have my child have surgery
My religious/spiritual beliefs have an influence on my decision to have my child have surgery	○○○○○○○	My religious/spiritual beliefs are not an influence on my decision to have my child have surgery
That my child will have an appearance that looks more like that of typical boys or girls is an important factor to have my child have surgery	○○○○○○○	That my child will have an appearance that looks more like that of typical boys or girls is not an important factor to have my child have surgery
I worry that my child will be treated differently because of the appearance of his/her genitals	○○○○○○○	I do not worry that my child will be treated differently because of the appearance of his/her genitals
I worry that my child's future sex life could be affected if I do surgery	○○○○○○○	I worry that my child's future sex life could be affected if I do not do surgery
I feel prepared for the possibility of complications including future surgeries	○○○○○○○	I do not feel prepared for the possibility of complications including future surgeries

What matters most?

What are you leaning towards?

Choosing surgery for my child	○○○○○○○	Waiting for my child to choose, or not to choose surgery for him/herself

Is your decision on whether to raise your child as a boy or girl dependent on the outcome of surgery?

○ Yes

○ No

○ Unsure

How satisfied are you about various aspects of your child's genitals (if rearing as a boy is a possibility)?

1. Length of the penis

☐ Very satisfied ☐ Satisfied ☐ Dissatisfied ☐ Very dissatisfied

2. Position and shape of the urine opening

☐ Very satisfied ☐ Satisfied ☐ Dissatisfied ☐ Very dissatisfied

3. Shape of the glans (top of the penis)

☐ Very satisfied ☐ Satisfied ☐ Dissatisfied ☐ Very dissatisfied

4. Shape of the penile skin

☐ Very satisfied ☐ Satisfied ☐ Dissatisfied ☐ Very dissatisfied

5. Curve of the penis (straightness) of the penis upon erection

☐ Very satisfied ☐ Satisfied ☐ Dissatisfied ☐ Very dissatisfied

6. General appearance of the penis

☐ Very satisfied ☐ Satisfied ☐ Dissatisfied ☐ Very dissatisfied

How satisfied are you about various aspects of your child's genitals (if rearing as a girl is a possibility)?

1. Length of the clitoris

☐ Very satisfied ☐ Satisfied ☐ Dissatisfied ☐ Very dissatisfied

2. Position and shape of the urine opening

☐ Very satisfied ☐ Satisfied ☐ Dissatisfied ☐ Very dissatisfied

3. Shape of the labia

☐ Very satisfied ☐ Satisfied ☐ Dissatisfied ☐ Very dissatisfied

4. General appearance of the vulva (clitoris, vulva, labia)

☐ Very satisfied ☐ Satisfied ☐ Dissatisfied ☐ Very dissatisfied

5. Length of vagina

☐ Very satisfied ☐ Satisfied ☐ Dissatisfied ☐ Very dissatisfied

Decide what's next

Do you understand what all the different options or possibilities are regarding genital surgery?

○ Yes

○ No

○ Unsure

Are you clear about the benefits and risks and what matters most to you?

- ○ Yes
- ○ No
- ○ Unsure

Do you have enough support and advice from others to make a choice?

- ○ Yes
- ○ No
- ○ Unsure

Certainty

How sure do you feel right now about a decision regarding genital surgery?

Not sure at all ○○○○○○○ Very sure

Check what you need to do before making a decision

○ I want to discuss options/possibilities with others

○ I want to learn more about options/possibilities

○ I'm ready to take action

Use the following space to list questions, concerns and next steps

Family Name: _____ Date _____
Month/Day/Year

Relationship to Patient:_____

Surgery of the gonads

In DSD with a Y chromosome (e.g. XY pattern, or XY in some cells, but not in all cells), there is an increased risk for the development of a cancer in the gonads. The risk of developing gonadal cancer varies greatly from DSD diagnosis to diagnosis, but other risk factors include:

- Age of the child: in some DSD, the cancer risk can be already higher in childhood, while in other DSD, the cancer risk only becomes higher in puberty
- The location of the gonads: Gonads that are higher up (in the abdominal or in the inguinal region (the groin)), have a higher cancer risk than gonads that are lower (e.g. in the scrotum)

After removal of the gonads (called gonadectomy), lifelong sex hormone replacement is necessary for physical health and emotional well-being. Also, fertility options may be compromised, if the gonads were possibly able to produce eggs/sperm. While some children with DSD have fertility potential, many children with DSD may require future medical interventions for conception or may not be able to conceive at all.

What matters to you most? Show how you feel about the following statements by filling in the bubble that best describes how you are feeling (closer to the statement means you agree more with what is being said).

Worried		Comfortable
It worries me that my child when he/she is older, may not agree with my decision about gonadectomy	○○○○○○○	I am comfortable making a decision about gonadectomy on behalf of my child
Any amount of cancer risk is too much.	○○○○○○○	I am comfortable with routine monitoring of cancer risk
I worry that lifelong hormone replacement therapy would cause stress, including financial strains, for me and/or my child	○○○○○○○	I am comfortable with lifelong hormone replacement therapy for my child

I am worried that my child's gonads will have unwanted effects on my child (e.g. around puberty)	○○○○○○○	I think that my child's gonads will have wanted effects on my child (e.g. around puberty)
The location of my child's gonad(s) worries me	○○○○○○○	I am comfortable with the location of my child's gonad(s)
I think that the cancer risk is higher right now and I would like the gonads removed before puberty	○○○○○○○	I think that the cancer risk is lower right now and I would like to wait until my child is an adolescent and can decide for him or herself

Do you want gonadectomy (removal of the gonads) for your child?

I am leaning towards…

Choosing surgery for my child	○○○○○○○	Waiting for my child to choose, or not to choose, surgery for themselves

Decide what's next

Do you understand what all the different options or possibilities are regarding genital surgery?

○ Yes

○ No

○ Unsure

Are you clear about the benefits and risks and what matters most to you?

○ Yes

○ No

○ Unsure

Do you have enough support and advice from others to make a choice?

○ Yes

○ No

○ Unsure

Certainty

How sure do you feel right now about a decision regarding gonadal surgery?

Not sure at all ○○○○○○○ Very sure

Check what you need to do before making a decision

○ I want to discuss options/possibilities with others

○ I want to learn more about options/possibilities

○ I'm ready to take action

Use the following space to list questions, concerns and next steps

Genital Surgery in Infancy

Take your time

- In most babies and children with DSD, atypical genitals cause no medical problems and genital surgeries are not urgent.
- Doctors will tell you if surgery is medically urgent, for instance when urine backs up into the bladder or kidney and your child has urinary problems.

What kind of surgeries?

Girls:

1. Making the clitoris smaller (also called clitoral reduction or “clitoroplasty”)
2. Any operation that changes the vagina (called “vaginoplasty”):
    - Removing parts of the labia
    - Surgery to make the vagina larger
    - Surgery to separate the vagina and the urine tube, if there is only one channel (called a 'urogenital sinus')

Boys:

1. Release of “chordee”, the thin bands of skin that can hold the penis in a curved position
2. Relocating the urine tube to end at the tip of the penis (called “hypospadias surgery”)
3. Reconstruction of the penis (called “phalloplasty”)

Things you might want to consider when thinking about genital surgery for your child:

- How the genitals work now and how they could work in the future.
- How the genitals look like now and how they would look like after surgery.
- How sexual sensation and pleasure may or may not be affected.
- How fertility may or may not be affected.
- What the need will be for other surgeries in the future.
- What the benefits and side-effects may be on the short and long-term.
- What the healing time is when having surgery as a child or later.
- How scars may not grow as a child's body grows (i.e. meaning that the genital appearance and function could get worse as your child grows).
- What improvements in surgical procedures may be coming in future years.
- How surgery may or may not affect your child's self-esteem and body image.
- How performing or not performing genital surgery may pose a risk for teasing, stigma or embarrassment.
- Your child's happiness.
- How your own beliefs or culture and religion may influence decisions about surgery.
- Whether your child will have a memory of the event, and if not, if this will be viewed as positive or negative by your child.
- How to share the decision about surgery with your child later, if surgery is performed.
- How your child could be involved in decisions about his/her own body.

Of paramount importance is to look at the long-term outcomes of early genital surgery, which on the whole are not very satisfactory:

- Many adults who had surgery as a child are not happy about how their genitals look.
- Many adults have multiple surgeries and complications.
- Scar tissue after surgery may affect genital sensation and sexual pleasure.
- However, what is the right approach for one child/ family may not necessarily be correct for another.
- Before making decisions about surgery, talk with your health care team, support groups or other families who were faced with similar dilemmas and might give you some extra insight in their lived experiences (with and without surgery). Working together, you can make informed choices that will help your child thrive

Things to consider when thinking about genital surgery for your child

- How the genitals work now and how they could work in the future.
- How the genitals look today and how they will look after surgery.
- How sexual sensation and pleasure may or may not be affected.
- How fertility may or may not be affected.
- What need there will be for other surgeries in the future?
- What are the benefits and side-effects in the short and long-term?
- What the healing time may be for surgery in childhood or surgery later in life.
- How scars from the surgery may not grow while the child's body grows (i.e. genital appearance and function could get worse as your child grows).
- What improvements in surgical procedures may be coming in future years.
- How surgery may or may not affect your child's self-esteem and body image.
- How performing or not performing genital surgery may pose a risk for teasing or embarrassment.
- How your child's gender identity and preferences develop.
- How your own beliefs, culture, and religion may influence your decisions.
- How your child might remember the surgery.
- How to share the decision about surgery with your child later, if you decide on surgery.
- How your child could be involved in decisions about their own body.

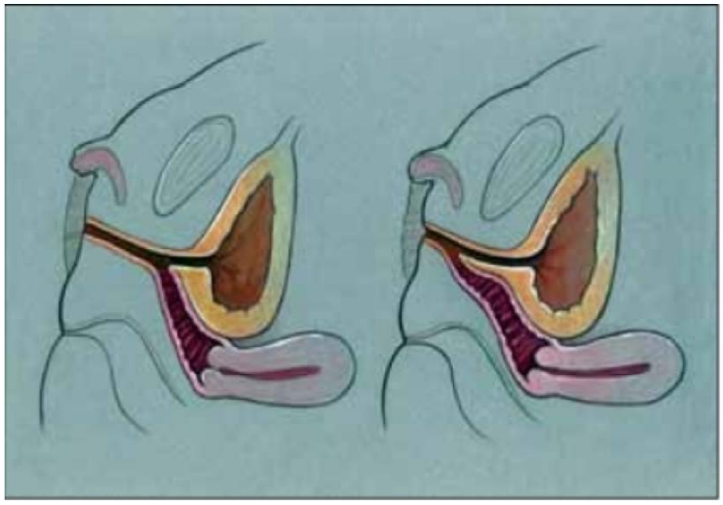
Results of this surgery done in childhood

- Surgery for hypospadias that does not cause medical problems, changes the appearance of the genitals, but may also change the function of the genitals.
- Some but not all adults who had this surgery as a child are happy about how their genitals look now.
- At least 1 out of 3 boys will need the surgery redone because of complications, such as narrowing of the urethra (“stricture”) and/or leaks (“fistulas”).
- Every surgery has risks of irreversible damage to the sensitive nerves of the penis.
- Some adults who had surgery as a child have problems with genital sensation and sexual pleasure.
- Some, but not all adults who had surgery as a child regret not being involved in a decision about their own body. Some find it helpful talking to a psychologist or counselor about possible concerns related to genital appearance and function, before making a decision about surgery.
- Keep in mind, the right approach for one child/family is not necessarily right for another child/family.

Surgery for a Urogenital Sinus

What is a urogenital sinus?

- Urogenital sinus: the vagina and urinary tract join into a common channel
- High confluence: the vagina and urinary tract join higher up in the body and have a long common channel
- Low confluence: the vagina and urinary tract have a short common channel



High confluence Low confluence

Vaginoplasty

This surgery repositions the vagina and urinary tract so that they have separate pathways out of the body. This is usually done to:

- Avoid urinary tract infections (if the urogenital sinus causes urinary problems)
- Allow for menstrual blood to pass through the vagina (if there is a uterus)
- Allow for vaginal sex
- Change the appearance of the genitals

If the urogenital sinus causes no medical problems, some doctors will recommend doing this type of surgery before your child is one year of age, because it is easier to perform in childhood. After surgery, vaginal dilation is usually necessary to

keep the vagina open. Many children will need more operations in puberty because of scar tissue tightening the vagina. Other doctors will recommend to wait until after puberty, to allow your child to be involved in this decision. Sometimes, the vaginal skin is more flexible after puberty and your child can perform the vaginal dilation herself.

Doctors will tell you if surgery is medically urgent. For instance, when urine backs up into the bladder or kidney or your child has urinary problems. Sometimes, a urogenital sinus causes no medical problems and surgery is not urgent.

Phalloplasty

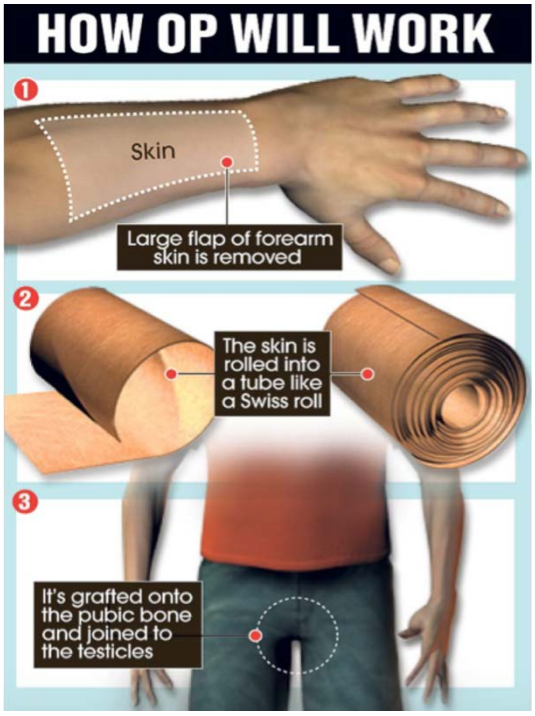
What?

Phalloplasty is surgery that reconstructs the penis, for example when a man has lost his penis because of an accident. Phalloplasty can also be done to make the penis larger in adolescent/adult men with a small penis. The surgery can not be done for children, as they are still growing.

Why?

In most men, a smaller penis causes no medical problems and genital surgery is not necessary. Surgery might be suggested by your surgeon when your adolescent/adult son indicates that he is very unhappy with his genital appearance and/or has problems with sex.

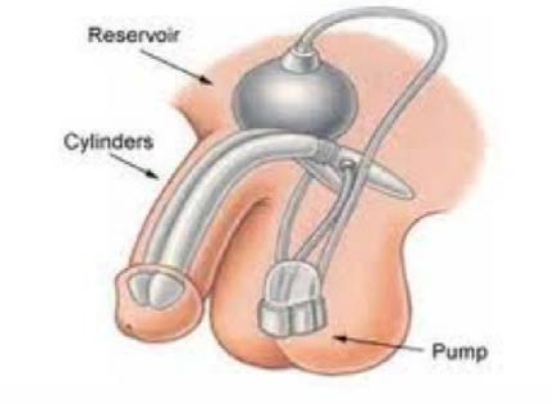
Some boys with a small penis grow up to be happy, healthy men and experience sexual pleasure without problems. Talking with a psychologist or counselor may help your son explore questions and possible concerns about genital appearance and future sexual function.



What will happen?

Phalloplasty involves taking tissue with the blood vessels from another part of the body (such as forearm, leg, chest, or belly), rolling it into a tube and attaching it –using the blood vessels to the existing penis or penile tissue. The urinary tract will be relocated to end at the tip of the penis.

Tissue taken from another part of the body and used for the surgery (called the donor site) may take a while to heal and may be less sensitive to touch, pressure, heat/cold, than before. There will also be scar tissue. Tissue taken later to rebuild the donor site (called a skin graft), will result in a second scar.



- Without an erectile prosthetic (a flexible rod or a pump), the penis cannot become erect.
- In a second surgery, this erectile prosthetic device needs to be implanted in the scrotum (the pouch containing the testes). The penis has to have healed first, which usually takes up to a year.
- At least 1 out of 3 men will need extra surgery because of complications, such as narrowing of the urinary tract ("stricture") and/or leaks ("fistulas").
- Other surgery risks include reduced blood flow to the penis, which results in loss of all or part of the penis, or rejection of the erectile prosthetic.
- Every surgery has a risk of damage to the sensitive nerves of the penis.
- Some men say their penis is not as sensitive as they hoped it to be, and experience problems during sex.
- Some but not all men are still not happy with how their genitals look after surgery or are bothered by the scars.

Keep in mind, the right approach for one man is not necessarily correct for another man. Before making decisions about surgery, we advise your son to talk with the health care team, support groups, or other men who have faced similar decisions

and can give some extra insight into their experiences (with and without surgery). Working together with doctors and others, your son can make an informed choice.

MORE INFORMATION

Well-being Assessments

For many chronic conditions, support from others (family, friends, etc.) can be very helpful in dealing with many of the challenges that may arise. The different challenges experienced at different life stages in DSD, are similar to other chronic conditions. Sometimes, families feel they cannot really share the information they have been told with their social environment (if they feel the need to talk about it at all). It might be helpful to talk to other families who have been through similar experiences (see the "Additional Resources section") or to a psychologist or behavioral health specialist who has experience working with DSD patient and their families.

Your Psychological Well-Being

In order for your child to thrive, it is essential to evaluate your own psychological well-being. The psychologist in the team may ask you to fill out questionnaires to survey your emotions and thoughts about what you have been through or what you are dealing with. The psychologist will also give you support and advice in dealing with tricky or stressful situations, such as how to manage news about your baby's birth, how to discuss your child's condition with other people, including your other children who will ask whether they have a brother or a sister. One effective way to approach this is first to learn about - and learn to talk about - the diagnosis and what caused it. Practice explaining this with someone close to you and with your child's doctors. Psychologists and specialist nurses can be of great help. If you are comfortable and confident sharing information, then your family and friends will be too. More importantly, practicing these conversations might help you feel more

comfortable talking to your child about his or her condition in the future. If you feel okay with the situation, your child probably will too.

Your Child's Psychological Well-Being

When your child is old enough (usually starting from around 8 years of age), the psychologist might start exploring what your child knows about their medical diagnosis and how your child processes what is going on. This can help ensure your child is feeling happy and healthy. Psychologists can answer some of the questions that your child might have.

Typical topics that are covered include:

- How is it going at school
- Friend and family relationships
- Your child's hobbies and activities
- Future dreams

Sometimes, questionnaires can be used to survey your child's emotions and psychological well-being.

The psychologist might also help you explain to your child:

- More about his/her condition in an age-appropriate way
- Explore the benefits and risks of the medical treatments that (and what it all really means)
- Prepare a long-term care plan

PARENT STORIES

Sharing information with your child

This may sound challenging now, but we do encourage you to be open with your child about his or her DSD starting early. Parents who wait often find it harder to discuss things with their child later. Sometimes, if you wait, the information that your child learns later may suddenly change the picture he/she has about him/herself. Another risk of waiting is your child may get information through other means, perhaps by overhearing conversations or from teasing by other children. These chunks of information, if left unexplained, may frighten your child or give him/her the feeling that he/she is unloved. When talking with your child about the condition and its management, consider your child's age. Choose your words carefully so that your child can understand and know they are loved. This lowers the risk of teasing. Some teens and children wish they had told their friends everything when they were younger. Your child's healthcare team can work with you to find the right balance for your child and family.

In general, the best approach is probably to follow the questions your child brings up him/herself. These questions should be answered in ways that they can understand during each period of development. The answers will become more detailed as your child grows older. This helps them grow up with a healthy understanding of their bodies and what to expect. If you are comfortable and confident about this, then your child will be too.

Infants and Toddlers

Many – if not all – babies and toddlers below the age of 3 years are interested in exploring their own body. They enjoy positive sensory experiences (including those of the genitals). They love skin contact and snuggling. We encourage you to bond with your child, and allow him/her the pleasure of body contact and to explore his or her different body parts, including the genitals.

When your child becomes a toddler and learns to talk, you can gradually start introducing words for the different body parts and genitals. Tell the healthcare team what you and your child's preferred words are, so that there is a common language. This can help your child learn to participate in discussions and exams even if they do not understand everything (yet). The goal is to make your child feel good or proud about his/her body and all its parts. It can help to frame exams as a positive adventure. At the same time any resistance to exams needs to be fully respected. Small children need help from you to believe their world is a safe place and that you, as parents, are protecting them.

As children grow (between ages 2 and 5 years), they learn to understand gender. They learn that some people are girls and some are boys, and they learn to say "he" or "she." They can use these words to label friends, family, and themselves as a boy or girl. Children also begin to learn "gender stereotypes"—narrow understandings of what males and females are like (e.g., a 3-year-old child may think that trucks are male toys because boys usually play with trucks. A 5 year-old child may think that a person putting on make-up has to be a female. That child may also think that only males lift weights, so everyone lifting weights must be a male). Stereotypes can be a problem, because many times they are not accurate and do not apply to all people. Stereotypes might make girls who do not like nail polish and prefer to build things feel that there is something wrong with them. Boys who play with dolls may be called "sissies". As a parent, you can help your child to explore new things and give your child many different experiences, whatever his/her gender.

"Atypical" gender play in early childhood does not mean that your child experiences gender unhappiness and certainly does not make a child gay or lesbian. All children need to be active, creative, and sensitive. Note that by age 6 or 7 years, most children understand and believe that a person's gender is constant. They know it will not change throughout

life (e.g., most children this age know that a man is still a man, even if he dresses like a woman). If your child expresses the wish to belong to the other gender at this point, he/she may experience signs of gender dysphoria, and should receive guidance and support from an experienced counselor. When young children (age 4-6 years) see other children naked, they begin to notice differences, but in a nonjudgmental way. They have no standard expectations (yet) for how genitals should look and by exploring many different bodies, they are introduced to a wide variety. However, children at this age are also eager to understand differences and to make sense of them. This is often experienced by parents as many of their "why" questions. We challenge you to use these opportunities, guided by your child's interest, to teach your child how the world functions.

A parent story

Until he was about 4 years old, my son [with a tiny penis and only one visible testicle] bathed with cousins and played naked in the sprinkler and wading pool in the backyard. If there were any kids there who had not seen him before, I would hover a bit, and listen for any questions. A couple of times children asked things like: "Why does he look like that?" or "What's wrong with him?" I made sure to be close enough to answer… "Oh, that's how he was born, and it's normal for him." Then I would shift to…"We're all different from each other in lots of ways right?" And then point out something like hair or height or glasses/no glasses differences in the group. In answer to the "what's wrong with him," I said "Nothing's wrong with him. That's how he was born, and it's normal for him. There are other children with privates like his, too."

Children aged 6-10 years old

At this age, children are very busy and eager to find their social roles and to comply with rules and expectations within their friend groups and with their parents. They will meet other people in their social surroundings, who are all different, and some with special health care needs. This may be a good time to start talking about chronic health issues because children at this age are able to have "islands of understanding" and may begin to be able to explain their development differences or health issues to others.

You can explain differences in body shapes and sizes by the way your child's body was constructed. For instance, there might be a missing womb in a girl, or the penis developed differently in a boy because the organs did not receive all the information when the body developed. You might also give your child some tips about how to talk to others about being different, without giving him/her the impression that this is something they need to be ashamed of. Children have different ways of handling this: some children like it better when these private issues are kept in the family or only shared with close friends; other children wish to proudly present their being special to a wider environment. Both options and many others that give your child a sense of control and self-worth are good.

By age 8-10 years old, children may ask more questions about family planning, sex, or reproduction ("Where do babies come from?" or "Will I have a baby?"). A basic understanding of the reproductive functions of the body will help your child to further understand his/her DSD and the potential consequences. Educating children from a young age about the variation in families (e.g., some have adopted children, some couples have no children, some children live with their grandparents, or in foster families) allows them to continue developing their ideas about future plans.

A story from a mother of a child with AIS

Every once in a while, I find the opportunity to throw another small pebble in my daughter's "pond" of understanding. Pebbling is a way to give information, without causing a huge shocking splash. It allows the body of water, or understanding, to expand

naturally, growing with each small movement. This was evident when we read books, like Katy No Pocket, and discussed how some people were born without a pocket and that it was perfectly okay. It was there when we talked about adoption as a way to have a family and it was there when we discussed how everyone is special. Each time I take these moments with my daughter, I feel like the load of information I am carrying for her lessens and that she is that much closer to developing an understanding of herself with positivity and acceptance. Last night was one of those nights. While washing her hair in the bath, I began. "Do you know that boys and girls are made with different types of juice?" I asked. "They are? What kind of juice do I have?" So I began. It was that simple. The door was open and all I had to do was put it in words she could understand. "Well, that is a neat story," I began. "Do you remember I told you God made you special?" to which she replied "Yes, I know." I started again. "You see, most boys are born with blue juice that makes them a boy, and girls have pink juice… but- there was one special bottle of blue juice left over, so God gave it to you because he knew you liked blue too." "Really?" she asked, "special blue juice?" "Yes. It is what makes you special," I told her. Minutes passed, and I thought maybe she didn't think it was important, or maybe it was too soon to talk about it. Hormones, after all, are a pretty heavy subject for 5-year-olds. I decided not to push it. When it was time to get out, I wrapped her in a warm towel. "Mommy," she said, "I am so glad you told me that. I just love that I have blue instead of pink juice! You just made my day!" There it was again. She had listened. It may not have been true understanding, but it was there to grow on, another pebble in the pond. The next one will be able to build from there, and she will have grown with the information all along.

Tweens (10-12 years)

Children at this age learn about more complex math, grammar, and biology in school. Now would be a good time to explain in a simple way (perhaps with animations or drawings) the function of the hormones and chromosomes in body development. We want your child to understand the basic information because he/she is now participating more and more in his/her health care. Whereas younger children cannot consent but are asked to participate and are being heard (called '"assent"), older children have the privilege to truly participate in decision-making.

A story by a mother of an 11- year- old child with PAIS

When my children were little (ages 3 to 4 years old and onward), I started by always pointing out the ways that we are all different from each other (and pointed out specifics, including how some men are very different from other men and the same for some women being very different from other women), as well as the ways we are similar. Then I started introducing the term DSD and said that part of their body – their genitals or private parts – had developed a bit differently from many other children. I told them that there were lots of other children whose bodies developed differently in this way too. I mostly wanted them to feel that their differences were a natural part of all the differences that make us human and explain to them something about why we went to see special doctors every 6-12 months who sometimes needed to see their private parts. When they were 5-6 years old (and developing more of an understanding of what makes a boy or girl physically different), I talked with the kids about the fact that there are some "juices" (hormones) in their bodies, and that we all – boys and girls, men and women – have some of each kind of juice "green juice" (testosterone) and "purple juice" (estrogen) that helps us grow and develop. I explained that many boys have more green juice, and only some purple juice, but some kids have different mixtures of the juice and they may develop differently because of that. In terms of explaining the gonads and XY chromosomes, I waited until my daughter was 9 or 10 or so…and the conversation came as a natural extension of earlier conversations about the ways her body is different and similar to girls

who don't have a DSD…She understood chromosomes VERY basically as a part of "the map" that gives our body guidance about how to grow. I described to them how everyone's body has a map or plan that it follows when it grows in the uterus and afterwards…The map (chromosomes) can have different roads on it to get to the same place. We talked about how her map ("XY chromosomes") has a path that can lead to someone being a boy, but it also has a path that many girls with DSDs go on that leads to being a girl. The gonads we explained as things that can become ovaries or testicles in a baby…and that in many children with DSDs they don't develop fully into either…so they can be helpful in growing, but at some point they can stop being helpful and we may need to take them out.

For many tweens it is important that they develop physically in the same time frame as their friends and peers. The start of puberty is an important topic to discuss. Tweens wish to be unique individuals but at the same time not too different from their friends. That is why it is also common for them to request operations that would make them look more like their peers. The healthcare team will discuss this with your child and talk about the risks/benefits of irreversible operations- often separately with your tween, as they have come to an age that they want more privacy. These private moments can give your child the chance to ask questions without parents being present (although some teens say they do not mind). Some adolescents also may need to talk about the wide (or not so wide) variety of genitals, and "what genitals are for" with a trusted doctor or counselor to find out more about their anatomy and sexual function. You can help by focusing on the emotional well-being of your child, relationships with friends, and perhaps help mend the first broken hearts. Some adolescents may find out they are not heterosexual and may ask themselves if this is because of the DSD. They need information on sexual orientation in general and your advice and guidance in finding their own interests and pleasures in life.

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Family Name: _____ Date _____
Month/Day/Year

Relationship to Patient:_____

What I Have Learned

Now that you have learned more about DSD, we would like to ask you the same questions we did at the beginning. You may be surprised by which answers change and which stay the same. Please consider bringing this to your next clinic visit.

Please write T for true and F for false on the line. If you are unsure you may leave the space blank.

1. _____ Differences/Disorders of Sex Development (DSD) are conditions in which babies did not develop along the most common sex development pathways.

2. _____ Most DSD have a known genetic cause that can be found with genetic testing.

3. _____ DSD are usually not life-threatening conditions.

4. _____ In most DSD, genital surgery is medically necessary.

5. _____ Genital surgery is only performed on babies or young children.

6. _____ Genital surgery has risks.

7. _____ Most children with DSD will not grow up questioning the feelings they have about themselves as boys or girls.

8. _____ People with DSD are as likely as people without DSD to be not heterosexual.

9. _____ My child's DSD needs to be kept a secret from my child.

10._____ Most people with DSD are not able to have biological children.

11._____ When it is not clear if a baby should be reared as a boy or girl, doctors should decide and then tell the family.

12._____ If surgery is done early enough, there is no need to tell anyone about the DSD.

How certain are you that you can…

Please rate how certain or confident you are that you can do the things that we list below by checking the box next to your choice for each question.

1. Face all the care decisions that might come along the way?

☐ Not at all ☐ A little ☐ Somewhat ☐ Quite a bit ☐ A great deal

2. Get all the information you need (e.g. searching for extra info on your own or with help) to help you make decisions?

☐ Not at all ☐ A little ☐ Somewhat ☐ Quite a bit ☐ A great deal

3. Learn all about the risks and benefits of decisions?

☐ Not at all ☐ A little ☐ Somewhat ☐ Quite a bit ☐ A great deal

4. Identify all the risks and benefits of decisions?

☐ Not at all ☐ A little ☐ Somewhat ☐ Quite a bit ☐ A great deal

5. Figure out how involved you want to be in decisions?

☐ Not at all ☐ A little ☐ Somewhat ☐ Quite a bit ☐ A great deal

6. Work with your partner (your child's other parent) to make decisions that you both agree on?

☐ Not at all ☐ A little ☐ Somewhat ☐ Quite a bit ☐ A great deal

How certain are you that you can...

7. Identify questions that you want to ask doctors?

☐ Not at all ☐ A little ☐ Somewhat ☐ Quite a bit ☐ A great deal

8. Talk to doctors about what matters most to you?

☐ Not at all ☐ A little ☐ Somewhat ☐ Quite a bit ☐ A great deal

9. Ask a doctor for more information if you don't understand what he/she said?

☐ Not at all ☐ A little ☐ Somewhat ☐ Quite a bit ☐ A great deal

10. Figure out what to do when you hear information that does not agree with the things you've already heard?

☐ Not at all ☐ A little ☐ Somewhat ☐ Quite a bit ☐ A great deal

11. Answer questions about your child's DSD if family members ask you about it?

☐ Not at all ☐ A little ☐ Somewhat ☐ Quite a bit ☐ A great deal

12. Talk to your child about the DSD when your child grows up?

☐ Not at all ☐ A little ☐ Somewhat ☐ Quite a bit ☐ A great deal

13. Ask your doctor to put you in touch with families with the same or a similar diagnosis?

☐ Not at all ☐ A little ☐ Somewhat ☐ Quite a bit ☐ A great deal

14. Call, email, or write to a support group or organization to ask for information or support?

☐ Not at all ☐ A little ☐ Somewhat ☐ Quite a bit ☐ A great deal

QUESTIONS TO ASK

Your child's healthcare team is likely to ask you a number of questions. It can help to have answers already prepared before you go to the appointment.

- ☐ What are your child's symptoms?
- ☐ When did your first begin noticing these symptoms?
- ☐ Do your child's symptoms include feeling fatigued or faint?
- ☐ Do your child's symptoms include feeling nauseated?
- ☐ Is your child experiencing any social problems related to his/her condition?
- ☐ Are you experiencing any problems related to your child's DSD?
- ☐ Is your child satisfied with treatment?
- ☐ Is your child satisfied with the changes to his/her body?
- ☐ Has anyone in your family been diagnosed with a DSD?
- ☐ Are you planning to have more children?

You should have questions ready to ask your child's healthcare team. Here is the list of questions parents have asked. Read over these and check which ones you do not have

answers to yet. Then bring this list with you to clinic so you can be sure to ask the team when you are there.

Answers to these questions may change over time as your child grows and develops. Please review this list from time to time.

General

- ☐ What is likely causing my child's signs and symptoms?
- ☐ What is causing my child to look or act the way he/she does?
- ☐ Are there any other possible causes for these symptoms?
- ☐ Is my child at risk for other medical conditions because of DSD?
- ☐ What kinds of tests does my child need?
- ☐ What treatment approach do you recommend and what is the evidence to support it?
- ☐ Will treatment slow down the rate at which my child is sexually maturing?
- ☐ Will hormone replacement affect my child's health?
- ☐ What are the possible side effects of treatment?
- ☐ What are the treatment alternatives?
- ☐ How will you monitor my child's health over time?
- ☐ What is my child's risk of long-term complications?
- ☐ How do I get a second opinion?

- ☐ Do you recommend that my child receive psychological counseling?
- ☐ Do you recommend that our family meet with a genetic counselor?

Support Groups /Advocacy groups

- ☐ What can parents of children who have the same or a similar diagnosis offer me?
- ☐ What might I learn from talking to adults who have the same or a similar diagnosis?
- ☐ How do I find support groups?
- ☐ What is the purpose of support groups?
- ☐ How are clinicians involved in support groups?
- ☐ What can advocacy groups do for my child or me?
- ☐ Who is involved in advocacy groups?

Privacy

- ☐ What should I do if I am uncomfortable with the way my hospital labels my child's medical condition in their medical records?
- ☐ Will my child's medical information be kept private among the hospital staff?
- ☐ How can I know if the hospital has shared my child's medical information with other people or organizations?
- ☐ If I believe a doctor/hospital has violated my child's privacy rights, what can I do?

Sharing with Others

- ☐ How much information do I want to share with my immediate/extended family, friends, co-workers, daycare providers, etc.?
- ☐ Who do I want to share general information with (For example, that my baby has a medical condition)?
- ☐ Who do I want to share specific information with (For example, that I/we don't know yet if the baby is a girl or a boy or talking about the details of the diagnosis and tests and procedures)?
- ☐ What are some examples of how I could talk to family and friends?
- ☐ What is the right age to tell my child about their condition?
- ☐ What could we tell our other children?

Testing

- ☐ Do I need to decide about this testing right now?
- ☐ What will happen if we wait?
- ☐ Will the results of this test change my child's treatment?
- ☐ What information will testing give me?
- ☐ Will it help me make decisions for the future?

Gender Assignment

- ☐ What is the difference between sex and gender?
- ☐ What is the difference between gender identity and gender role behavior?
- ☐ What is sexual orientation?
- ☐ Should I bring up my child as a boy or girl?
- ☐ What do I call my baby in the meantime?
- ☐ Will my child be able to have children of their own when they are an adult?
- ☐ What will my child's puberty be like as a girl/boy?
- ☐ What could my child's sex life be like as a girl/boy?

- ☐ How could my child's internal anatomy work as a girl/boy?
- ☐ How could my child's external anatomy work as a girl/boy?
- ☐ What does my child's genetics tell me/us about my child's gender?
- ☐ What studies exist to suggest that my child is likely to identify as a boy/girl?
- ☐ Can I see the studies?
- ☐ What if I think my baby was assigned the wrong gender?
- ☐ What if my child later thinks he or she was assigned the wrong gender?

Genetics

- ☐ Should I be tested?
- ☐ Should my partner be tested?
- ☐ Should my other children be tested?
- ☐ Should I talk with other family members about getting testing for themselves?
- ☐ What if genetic tests find other things that are not directly related to my child's DSD?

Physical or Genital Exams / Photography

- ☐ How many people will be in the room for a physical exam?
- ☐ How often does my child need to have this kind of exam?
- ☐ How long should we wait between exams?
- ☐ Can this exam be postponed?
- ☐ Will the results of this genital exam change my child's treatment?
- ☐ How do I prepare my child?
- ☐ Should I consent to medical photography of my child's genitalia?
- ☐ If pictures are taken for treatment purposes, where are these stored and who will have access to them?
- ☐ Will my child's genital photographs be used in case conferences or educational presentations?

Hormone replacement therapy (HRT)

- ☐ Why is HRT necessary?
- ☐ What changes will the recommended HRT cause?
- ☐ What alternatives are there?

- ☐ Which of these changes will be permanent?
- ☐ Can we put off this decision until my child is older?
- ☐ Does my child understand the implications of HRT?
- ☐ How do I know my child will be comfortable with these changes?

Surgery and Other Procedures

- ☐ Why is the surgery performed?
- ☐ How is the surgery performed?
- ☐ What will recovery be like?
- ☐ What are the short-and long-term risks involved?
- ☐ What are the benefits?
- ☐ Will my child need multiple surgeries?
- ☐ How will the surgery affect my child's genital function or sensation?
- ☐ How will the surgery affect my child's genital appearance?
- ☐ How will the surgery affect my child's quality of life?
- ☐ Will my child remember the surgery if done in childhood?

- ☐ How much time do I have to make a decision?
- ☐ Could this procedure be done later?
- ☐ Is this a decision my child could make for him or herself later?
- ☐ Can you please define what you mean by "successful outcome"?
- ☐ What are alternatives to surgery?
- ☐ Do you have research that supports your opinion?
- ☐ What do people who have had this surgery in the past say about it?
- ☐ If our decision about gender assignment turns out to be wrong, what will this surgery mean for our child?
- ☐ Is it likely that there will be improvements in surgical technique before my child is an adult?
- ☐ What is life like for people like my child if they don't have early genital surgery?
- ☐ Are there other surgeons who would recommend a different technique and what are their reasons?
- ☐ Is this procedure "reversible"? Has anyone ever reported a successful reversal?

- ☐ How many of these procedures has my surgeon done?
- ☐ What are the complication rates?
- ☐ Can I see pictures of the results?
- ☐ Can I talk to some satisfied patients?
- ☐ What will my child's sexual function and sensation be like without surgery?
- ☐ What will their genitals look like in 20 years if they have this surgery?
- ☐ Do you have photos of grown patients who had this procedure in childhood?

Research

- ☐ Should I give permission for my child to participate in research?
- ☐ Should I and/or my family members participate in research?
- ☐ What are the pros and cons of participating in research?
- ☐ Is there any cost associated with participating in research?
- ☐ Which of these procedures or exams are going to be helpful to my child, and which are for research purposes only?
- ☐ Can my child refuse to participate in research?

☐ Can I change my mind about participation?

☐ If I refuse to participate in research, will it change the medical care my child receives?

Other questions I have…

1. _____

2. _____

3. _____

4. _____

5. _____

6. _____

7. _____

8. _____

9. _____

10. _____

GLOSSARY

#

17ß hydroxysteroid dehydrogenase deficiency (17ß HSD) and 5α reductase deficiency (5α RD): A genetic condition that results in the inability of the body to make a certain type of androgens (Dihydrotestosterone or in short DHT) in children with 46, XY chromosomes. As a result, the genitals may not have grown much. Usually, children have more female or ambiguous looking private parts at birth, but may become more masculine looking at puberty, when the testes are left in place. Because of the Y chromosome, there is no uterus and no menstruation.

A

Ambiguous: Of doubtful or uncertain nature; difficult to comprehend, distinguish, or classify.

Androgens: Any substance that promotes male characteristics.

Androgen insensitivity syndrome (AIS): A genetic condition that results in the decreased ability of the body to respond to androgens, so that the androgens cannot function properly in children with 46, XY chromosomes. This problem can be partial (PAIS) or complete (CAIS). In children with CAIS, the external genitals are feminine. However, because of the Y chromosome, there is no womb and no menstruation. In children with PAIS, there is a wide range of variation possible in how the genitals look on the outside, depending on how much the body can respond to the androgens. There is also no womb in these children, because of the Y chromosome.

B

Biochemical: Relating to the chemical processes and substances which occur within living organisms.

C

Cervix: The lower part of the uterus that leads to the vagina.

Chromosome: A threadlike structure of nucleic acids and protein found in the nucleus of most living cells, carrying genetic information in the form of genes.

Cloaca: The cavity at the end of the digestive tract into which the intestinal, genital, and urinary tracts open.

Cloacal and bladder exstrophy: Exstrophy literally means “turned inside out.” In cloacal and bladder exstrophy, a portion of the large intestine and bladder lies outside of the body. In girls, the clitoris is split and there may be one or two vaginal openings. In boys, the penis is usually flat and short with the exposed inner surface of the urine tube on top. The penis is sometimes split into a right and left half.

Congenital: Relating to a condition present at birth, whether inherited or caused by the environment, especially the uterine environment.

Congenital adrenal hyperplasia (CAH): A family of genetic conditions caused by defects in the production of certain steroids by the adrenal glands (*cortisol, the stress hormone and/or aldosterone, the salt balance hormone*). This may lead to an overproduction of androgens,

which can cause more masculine looking genitals at birth (such as enlarged clitoris) in girls.

Cryptorchidism: One or both testes do not move into the scrotum.

D

Disorder/Difference of Sex Development (DSD): An inborn condition in which development of chromosomes, gonads (ovaries or testes) and internal reproductive and external genitalia are not in line with each other. All DSD are present at birth, but they sometimes go unnoticed for months or years. That is because some DSD only affect how the reproductive organs look on the inside, while others might also affect how the genitals look on the outside, making them more noticeable at birth or soon after birth.

Duct: Any tube, canal, pipe, or conduit by which a fluid, air, or other substance is conducted or conveyed.

Dysgenesis: Defective development especially of the gonads.

Dysphoria: A state of feeling unwell or unhappy.

E

Epididymis: The cordlike structure along the border of the testes. It provides for storage, movement and maturation of the sperm cells.

Estrogen: Any of a group of steroid hormones that promote the development and maintenance of female characteristics of the body.

F

Feminization: To cause feminine characteristics (as by implantation of ovaries or administration of estrogenic substances).

G

Gender identity: The sense of oneself as a boy or girl.

Gender role behavior (sex-typical behavior): Behaviors that are culturally associated with boys or girls.

Gender dysphoria: Unhappiness with one's gender and gender role, with the desire for the body and role of the other gender.

Gene: The basic physical unit of heredity; a linear sequence of nucleotides along a segment of DNA that provides the coded instructions for synthesis of RNA, which, when translated into protein, leads to the expression of hereditary character.

Genotype: The entire genetic constitution of an individual.

Gonad: An ovary, testis or ovotestis (combined ovary and testis).

Gonadal dysgenesis: The gonads did not fully differentiate on the pathway to becoming testes (also called "streak gonads") and as a consequence, do not produce (enough) hormones, such as testosterone.

Gonadectomy: Surgical removal of one or both gonads.

Gynecomastia: Breast growth in boys/men.

H

Hormones: A regulatory substance produced in an organism and transported in tissue fluids such as blood to stimulate specific cells or tissues into action.

Hormone replacement therapy: Involves replacing hormones that the body is not making in "normal" amounts. Some children need hormones that are necessary for the body to survive – such as the stress hormone cortisol. Other children need sex hormone replacement – replacing the hormones estrogen and testosterone, which are hormones responsible for breast development, pubic hair and development of the genitals in puberty, but also bone growth and general health.

Hypogonadism: A condition resulting from decreased function of the gonads (ovaries, testes), with delayed growth and sexual development.

Hypospadias: The urethral opening is not on the tip of the penis, but somewhere below.

I

Intersex: One having both male and female sexual characteristics and organs. Now called Disorder/Difference of Sex Development (DSD).

K

Karyotype: Chromosome pattern. Each person usually has 46 chromosomes, including two sex chromosomes, XX or XY. We usually get one X from our biological mother, and an X or Y from our biological father. But there are various combinations of sex chromosomes possible. Sometimes, there is an atypical number of chromosomes, for instance 45 chromosomes (only one X) or 47 chromosome (XXY). Other people have combinations of sex chromosomes that differ from cell to cell (called "mosaicism"), with some cells having XX and others XY. Other differences in number or structure of the chromosomes are also possible.

Klinefelter syndrome: Babies with Klinefelter syndrome have an extra X chromosome (47, XXY), but have a male external and internal sex anatomy. However, they have very small testes. When puberty starts and boys' bodies begin to make sex hormones, boys with Klinefelter syndrome usually do not produce as much testosterone, which can affect their penis and testicle growth.

L

Libido: Sexual desire, drive, or interest.

M

Masculinization: Cause to appear or seem masculine.

Menstruation: The periodic discharge of blood and mucosal tissue from the uterus, occurring approximately monthly from puberty to menopause in non-pregnant women

Micropenis: A penis significantly smaller than the average male.

Mayer-Rokitansky-Küster-Hauser syndrome: In girls with MRKH, the female internal sex organs have not fully developed. Some girls might have ovaries that function, but there is usually no womb or cervix, and no upper vaginal canal, but only a very small vaginal opening (also called "dimple"). MRKH can also lead to other symptoms. In some women with MRKH, the kidneys are abnormally formed or positioned in different places, and other women have only one kidney that can be positioned in various places

throughout the abdomen/belly. Other symptoms include skeletal abnormalities, hearing loss and/or ringing in the ears (tinnitus) and heart defects.

Müllerian ducts: Either of the pair of ducts that are present in the human embryo (alongside the pair of Wolffian ducts). The Müllerian ducts develop into the fallopian tubes and the uterus in typical female development and disappear in typical male development.

O

Ovary: A female reproductive organ in which ova or eggs are produced, present in humans and other vertebrates as a pair.

Ovotesticular DSD: Both ovarian and testicular tissue are present.

P

Pelvis: Large bony structure near the base of the spine to which the hind limbs or legs are attached in humans and many other vertebrates.

Perineum: The pelvic floor and the associated structures occupying the pelvic outlet.

Phenotype: What an individual looks like as a result of the interaction of its genotype and the environment - the entire physical, biochemical and physiological make-up of an individual.

Physiology: The way in which a living organism or bodily part functions.

Primary Sex Characteristics: The physical characteristics directly involved in reproduction.

Puberty: The period during which adolescents reach sexual maturity and become capable of reproduction.

R

Rough-and-tumble play: Play behavior characterized by overall body contact or playful aggression.

S

Scrotum: The pouch that contains the testes in boys.

Secondary sex characteristics: Any physical characteristic developing at puberty which distinguishes between the sexes but is not directly involved in reproduction.

Sex: Biological or physical features such as genitals, hormones, reproductive organs and chromosomes.

Sex differentiation: The process of development of the differences between males and females from an undifferentiated zygote.

Sexual dimorphism: Technically meaning “two forms,” mostly interchangeable with sex difference: any psychological or behavioral characteristic that differs on average for males and females.

Sexual orientation: Erotic attraction to/ interest in sexual partners of the same versus the other sex.

Sperm: A male reproductive cell.

Surgical reassignment: Surgery to change the sex of a person.

T

Tomboy: (slang) A girl who likes toys, clothes and activities associated with or usually preferred by boys and who likes to play with boys.

Transgenderism: A person whose gender identity is opposite the sex the person had or was identified as having at birth.

Turner syndrome: Girls with Turner syndrome are born with only one X chromosome (45X) or they are missing part of one X chromosome. The effects vary widely among girls with Turner syndrome, although they are usually short in height. In addition to growth problems, Turner syndrome prevents the ovaries from developing properly, which affects a girl's sexual development and the ability to have children. Because the ovaries are responsible for making the hormones that control breast growth and menstruation, most girls with Turner syndrome will not go through all of the changes associated with puberty until they get estrogen treatment for the condition. Nearly all women with Turner syndrome will need medical assistance to become pregnant.

U

Urethra: The canal conveying urine from the bladder to the exterior of the body.

Urogenital sinus: The vagina and urethra open into a common channel, rather than separately.

Uterus: The Reproductive organ in women that is responsible for fetus development.

V

Vanishing testes syndrome: A condition in boys characterized by the absence of the testes at birth. When both testes are absent, the individual will not undergo puberty without testosterone supplements. The testes are thought to have been present in the embryo, but to have "vanished" before completion of male sexual differentiation in the womb (also called "embryonic testicular regression syndrome").

Virilization: Masculinization; the development of male physical characteristics in a female or precociously in a boy, typically as a result of excess androgen production.

W

Wolffian ducts: A pair of ducts that are present in the human embryo (alongside the pair of Müllerian ducts). They develop into the male internal reproductive tract if testes are present.

ADDITIONAL RESOURCES

Condition Specific Support and Resource Organizations

Accord Alliance

The Accord Alliance is a US based organization that brings together patients and families, healthcare administrators, clinicians, support groups, and researchers to facilitate open communication and collaboration among all persons working together to improve care of those affected by DSD. Their website contains a link to an excellent book written by experts including families and adults living with DSD (Handbook for Parents), other educational materials, information from DSD specialists, and updates on recent research.

DSD Families

An extensive information and support resource created by parents, for parents of children, teens and young adults with DSD. It contains information about medical care and decision-making as well as peer support. A very useful brochure for parents is the Early Days Brochure, when your child is born with a genital difference.

The AIS –DSD Support Group for Women and Families

This group (formerly AISSG USA) provides access to a teen email group, as well as to the excellent AIS-DSD parent email group.

Cares Foundation: CAH

The CARES Foundation reaches out to families and individuals with Congenital Adrenal Hyperplasia (CAH) via one-on-one support and local support groups across the USA.

Informed Medical Decisions Foundation

An organization that advocates for public policy to help people to set and reach health behavior goals and to improve the care they receive. Includes videos on shared medical decision making and videos on shared decision making in practice.

HEA: Hypospadias and Epispadias Association (USA)

HEA provides support and education of people born with hypospadias or epispadias and their families, loved ones, and medical care givers.

Turner syndrome

The official website of the Turner Syndrome Society of the United States provides a family guide and clinical practice guidelines, as well as extra information and support from other with TS who have dealt with similar issues.

MRKH syndrome

An informative website, providing up-to-date medical information, a link to a MRKH Support and Awareness Facebook site, sister-to-sister mentoring program and various types of support for all who are affected by MRKH.

Klinefelter syndrome

Website providing more information and support for individuals with one or more X or extra Y chromosomes and their families.

Sex Development in Kids

Hospital for Sick Children: About Kids Health- Sex Development Animations

Created by healthcare providers at Toronto's Hospital for Sick Children. It has interactive animations that contain detailed pictures and text about sex development and its variations.

It also has information about puberty, genetics and some specific conditions like Congenital Adrenal Hyperplasia (CAH), Androgen Insensitivity syndrome (AIS), 5-Alpha-Reductase Deficiency syndrome (5-ARD) and hypospadias.

Your Child

Created by healthcare providers at the University of Michigan Health System. It provides information about typical development as well as the development of children with a variety of medical conditions, including DSD.

Disorders of Sex Development: A Guide for Parents and Physicians

A book created by experts including families and adults living with DSD and providers at the University of Oklahoma Health Sciences Center.

Online Medical Information Resources

HealthFinder

This site is supported by the US Department of Health and Human Services and serves as a gateway to selected consumer health and human services by providing basic information on health topics. You can find health information, a health library, a medical dictionary and encyclopedia, and information on how to locate physicians, support, and self-help groups. Information is available in English and Spanish.

National Human Genome Project

A website that gives you tips on how to find reliable health information online and directs you to some good websites.

Medline Plus

This site is supported by the US National Library of Medicine and the National Institutes of Health (NIH) and provides up-to-date information on a number of different health topics, a medical encyclopedia and a dictionary, drug and medication information, current health news, and links to other related resources. Information is available in English and Spanish.