



Differences of Sex Development Clinical Pathway Synopsis

Differences of Sex Development Algorithm

Exclusion criteria:

- Children > 1 year of age

If prenatal concern, see [communication strategies](#) and provide [resources](#). (Pediatric Endocrine Society, 2025)

Concerns for Differences of Sex Development (DSD)

- Atypical genital appearance following birth
- Discordance between prenatal testing and postnatal phenotype

Adrenocorticotropic Hormone (ACTH) Stimulation Test

- Infants with adrenal insufficiency often present in adrenal crisis at 7 - 10 days of life
 - If there is a high suspicion for adrenal insufficiency, an ACTH stimulation test should be performed prior to discharge from the nursery
 - If not completed, close follow-up with Primary Care and Endocrinology is warranted
- The ACTH stimulation test at Children's Mercy includes progesterone, 17-OH progesterone, 11-desoxycortisol, cortisol, DHEA, and testosterone at 0 and 60 minutes
- For those with suspected undervirilized male genitalia (46,XY), the addition of 17-OH pregnenolone to this panel may provide additional information about 3-beta-hydroxysteroid dehydrogenase deficiency
- The addition of deoxycorticosterone can provide information about 17-hydroxylase deficiency in those with more typical female genitalia, though 46,XY chromosomal make-up

This testing should be considered in collaboration with a pediatric endocrinologist

Patient presents with a concern for differences of sex development

Physical Exam

Complete physical exam (i.e., full body assessment with detailed genital exam) with particular attention to:

- Midline defects (including cleft lip/palate, omphalocele, heart murmur)
- Gonad location (or noting if not palpable)
- Clitorophallus size (obtain *stretched length*, if possible, and width)
- Urethra location
- Vaginal and urethral openings (separate or not)
- Skeletal anomalies
- Anus patency and location (if concern for anorectal anomaly or cloaca, involve Colorectal Team)

Communication

Discuss concerns with parents/guardian and obtain consent for genetic testing

- Use gender-neutral terms and avoid assigning sex or gender
- Emphasize patient's overall health or address acute medical concerns without solely focusing on atypical genitalia or sex assignment. Balance medical details with affirmations of the child's unique qualities
- Provide accurate terminology for families to use

Link to suggested [communication strategies](#) and [resources](#)

Laboratory Testing

- BMP within 36 hours of life
- Monitor blood glucose (POC)
- Karyotype with FISH for X and Y (including SRY)

Imaging

- Ultrasound of scrotum/labia
 - Ultrasound of pelvis
- Sonographer and radiologist should be familiar with newborn pelvic anatomy. If needed, refer to Children's Mercy Radiology*

Consults or Referrals

If positive newborn screen for congenital adrenal hyperplasia (CAH) or electrolyte derangement, admit to inpatient

- **Inpatient:** Consult Endocrinology, Genetics, and Urology
 - Consider consult to GUIDE psychologist
 - If recommended by Endocrinology or Urology, consult Gynecology
 - Outpatient referrals as recommended (consider [GUIDE Clinic](#) for children with differences of sexual development)
- **Outpatient:** Refer to Endocrinology (within 2 weeks if < 1 month of age; within 4 weeks if ≥ 1 month of age). Endocrinology will coordinate referral to Genetics and Urology and/or Gynecology
 - Consider referral to [GUIDE Clinic](#)
 - Laboratory evaluation may be delayed until the Endocrinology visit, unless there is a concern for adrenal insufficiency or a delay in endocrine care beyond 6 months of life
 - If possible, obtain pelvic and/or scrotal ultrasound prior to the Endocrinology visit

Are male gonads palpated or identified on ultrasound (US) in either inguinal canal or labioscrotal folds?

Yes

No

Complete XY Hormone Evaluation

- Consider 7-dehydrocholesterol level
- Consider **ACTH stimulation test**
- After 1 week and before 6 months of age in an effort to capture minipuberty window: (link to [supporting literature](#))
 - Luteinizing Hormone (ultrasensitive assay)
 - Follicle-Stimulating Hormone (ultrasensitive assay)
 - Testosterone
 - Dihydrotestosterone
 - Anti-Müllerian Hormone

Is a uterus present on US?

Yes

Complete XX Hormone Evaluation

- Evaluate for CAH
 - 17-OH progesterone (Alert: sound alike lab - do NOT order 17-OH pregnenolone)
 - Consider **ACTH stimulation test**

Do labs reveal a diagnosis?

Yes

No

Consider Additional Genetic Testing

- Exome sequencing
- Consider long-read genome sequencing in the presence of additional syndromic features, such as hypotonia

Are labs consistent with CAH?

No

Yes

- **Admit** to inpatient, if outpatient
- **Treat** in collaboration with Endocrinology

- **Treat** accordingly, in collaboration with subspecialists as needed
- **Refer** to genetic counseling, if indicated

Ongoing Care

- Decide on sex/gender of rearing, in collaboration with subspecialists and family (this is a dynamic decision and may occur after discharge from the hospital)
- Ensure follow-up with relevant specialties (e.g., [GUIDE Clinic](#), genetic counseling)



QR code for mobile view

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Table of Contents

Differences of Sex Development Algorithm	1
Objective of Clinical Pathway	3
Background	3
Target Users.....	3
Target Population	3
Practice Recommendations.....	3
Additional Questions Posed by the Clinical Pathway Committee	3
Updates from Previous Versions of the Clinical Pathway	3
Measures	4
Value Implications.....	4
Organizational Barriers and Facilitators	4
Bias Awareness.....	4
Clinical Pathway Preparation.....	4
Differences of Sex Development Clinical Pathway Committee Members and Representation.....	4
Clinical Pathway Development Funding	5
Approval Process.....	5
Review Requested	5
Version History	5
Date for Next Review	5
Implementation & Follow-Up	5
Disclaimer	6
References	7

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Objective of Clinical Pathway

To provide care standards for the patient with a concern for differences of sex development. The Differences of Sex Development Clinical Pathway aims to provide guidance for the initial discussion and evaluation of infants with atypical genitalia or another concern for differences of sex development.

Background

Differences of sex development (DSD) are a group of congenital conditions in which the development of chromosomal, gonadal, and/or anatomical sex is atypical (Cools et al., 2018; Davies & Cheetham, 2017; Lee et al., 2016; Ochoa et al., 2024). These conditions may result in variations of external genitalia, internal reproductive organs, or sex chromosome patterns (Allen et al., 2022; Lee et al., 2021; Ochoa et al., 2024). For an infant born with a concern for DSD, an initial evaluation, including a thorough clinical assessment and hormonal laboratory workup, is essential to establish an accurate diagnosis and initiate appropriate management (Ahmed, 2021; Grinspon et al., 2021; León et al., 2019; Weidler et al., 2024).

The Differences of Sex Development Clinical Pathway Committee recognizes that guidance regarding the initial management of infants with suspected DSD is lacking. Therefore, the aim of this clinical pathway is to inform providers within and outside Children's Mercy about the recommended clinical and hormonal workup, necessary consultations or referrals, and best practices for family communication. This pathway does not provide comprehensive guidance on the management of a patient with suspected DSD. Instead, it offers initial guidance to ensure patients can be evaluated and triaged appropriately for multidisciplinary evaluation and care.

The Differences of Sex Development Clinical Pathway is designed for patients less than 1 year of age, as hormonal evaluation during this time is most likely to provide relevant information leading to a diagnosis. While some recommendations may apply to older children with suspected DSD, advanced testing may be required for diagnostic purposes, and conversations may differ about the impact of their underlying condition on their identity due to their already established sex assignment.

Target Users

- Physicians and Advanced Practice Providers (Neonatology, Endocrinology, Urology, Gynecology, Genetics, Hospital Medicine, General Pediatrics, Residents, Fellows)
- Clinical Genetics (genetic counselors, nurses)
- Psychologists
- Social Workers

Target Population

Inclusion Criteria

- Patient with concern for DSD (e.g., atypical genital appearance following birth, discordance between prenatal testing and postnatal phenotype)

Exclusion Criteria

- Children > 1 year of age
- If prenatal concern, see communication strategies (link) and provide [resources](#) (Pediatric Endocrine Society, 2025)

Practice Recommendations

In lieu of a clinical practice guideline fully addressing the management of infants with suspected DSD, guidance from pediatric DSD literature was used in conjunction with the expert consensus of the Differences of Sex Development Clinical Pathway Committee to inform the initial exam, laboratory and imaging workup, consults or referral guidance, and communication in this pathway.

Additional Questions Posed by the Clinical Pathway Committee

No additional clinical questions were posed for this review.

Updates from Previous Versions of the Clinical Pathway

- The Differences of Sex Development Clinical Pathway is a newly developed evidence-based pathway with no previous version for comparison

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Measures

- Access of the Differences of Sex Development Clinical Pathway (website hits)
- Utilization of associated order sets

Value Implications

The following improvements may increase value by reducing healthcare costs and non-monetary costs (e.g., missed school/work, loss of wages, stress) for patients and families, and reducing costs and resource utilization for healthcare facilities.

- Decreased risk of inaccurate hormonal laboratory workup
- Decreased risk of missed life-threatening conditions or associated congenital anomalies (i.e., congenital adrenal hyperplasia, Turner syndrome)
- Decreased risk of incorrect or delayed diagnosis
- Decreased risk of an inaccurate sex assignment
- Decreased unwarranted variation in care

Organizational Barriers and Facilitators

Potential Barriers

- Variability in experience among clinicians
- Need for effective communication and coordination among clinicians and specialties
- Challenges with access to healthcare and health literacy faced by some families

Potential Facilitators

- Collaborative engagement across the continuum of clinical care settings and healthcare disciplines during clinical pathway development
- Consistent utilization of the clinical pathway when applicable

Bias Awareness

Bias awareness is our aim to recognize social determinants of health and minimize healthcare disparities, acknowledging that our unconscious biases can contribute to these inequities.

Order Sets

- ICN Ambiguous Genitalia

Associated Policies

- There are no relevant policies associated with this clinical pathway

Educational Materials

- Genetic Testing
 - Found in Cerner depart process
 - Available in English and Spanish

Clinical Pathway Preparation

This pathway was prepared by the EBP Department in collaboration with the Differences of Sex Development Clinical Pathway Committee, composed of content experts at Children's Mercy. If a conflict of interest is identified, the conflict will be disclosed next to the committee member's name.

Differences of Sex Development Clinical Pathway Committee Members and Representation

- Michelle Knoll, MD, MHPE | Endocrinology | Committee Chair
- Shannon Haines, MD, MPH, FAAP | Neonatology | Committee Member
- Kelli Ayars, MSN, RN, NNP-BC | Neonatology | Committee Member
- John Gatti, MD | Urology | Committee Member

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- Joel Koenig, MD | Urology | Committee Member
- Anne-Marie Priebe, DO | Gynecology | Committee Member
- Jeanette Higgins, RN, MSN, CPNP | Gynecology | Committee Member
- Anna Egan, PhD, ABPP | Developmental and Behavioral Health | Committee Member
- Gail Robertson, PhD, ABPP | Developmental and Behavioral Health/Endocrinology | Committee Member
- Cassandra Barrett, PhD, MS, CGC | Clinical Genetics | Committee Member
- Holly Welsh | Clinical Genetics | Committee Member
- Sarah Dierking, MSN, RN, CPHQ | Clinical Practice and Quality | Committee Member

Patient/Family Committee Member

- Brianna Schmitz | Committee Member

EBP Committee Members

- Kathleen Berg, MD, FAAP | Evidence Based Practice
- Kelli Ott, OTD, OTR/L | Evidence Based Practice

Clinical Pathway Development Funding

The development of this clinical pathway was underwritten by the following departments/divisions: Endocrinology, Neonatology, Urology, Gynecology, Developmental and Behavioral Health, Clinical Genetics, Clinical Practice and Quality, and Evidence Based Practice.

Conflict of Interest

The contributors to the Differences of Sex Development Clinical Pathway have no conflicts of interest to disclose related to the subject matter or materials discussed.

Approval Process

- This pathway was reviewed and approved by the EBP Department and the Differences of Sex Development Committee after committee members garnered feedback from their respective divisions/departments. It was then approved by the Medical Executive Committee.

Review Requested

Department/Unit	Date Obtained
Endocrinology	January 2026
Neonatology	January 2026
Urology	January 2026
Gynecology	January 2026
Developmental and Behavioral Health	January 2026
Clinical Genetics	January 2026
Clinical Practice and Quality	January 2026
Patient and Family Engagement	January 2026
Evidence Based Practice	December 2025

Version History

Date	Comments
January 2026	Version one – (developed algorithm and the associated synopsis, and revised educational materials)

Date for Next Review

- January 2029

Implementation & Follow-Up

- Once approved, the pathway was implemented and presented to the appropriate care teams:
 - Announcements made to relevant departments
 - Additional institution-wide announcements were made via the hospital website and relevant huddles
 - Community clinics affiliated with Children's Mercy received announcements via "Progress Notes"

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- Order sets consistent with recommendations were reviewed for the Neonatal Intensive Care Unit
- Care measurements may be assessed and shared with appropriate care teams to determine if changes need to occur.
- Pathways are reviewed every 3 years (or sooner) and updated as necessary within the EBP Department at Children's Mercy. Pathway committees are involved with every review and update.

Disclaimer

When evidence is lacking or inconclusive, options in care are provided in the supporting documents and the power plan(s) that accompany the clinical pathway.

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Weidler, E. M., Ochoa, B., & van Leeuwen, K. (2024). Prenatal and postnatal evaluation of differences of sex development: A user's guide for clinicians and families. *Current Opinion in Pediatrics*, 36(5), 547-553.
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